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Clinical Cases in Internal Medicine: Learning Through Practice
(7th McMaster International Review Course in Internal Medicine,
September 29–October 1, 2022, Kraków, Poland, hybrid course)

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ABSTRACT PROCEEDINGS OF THE BEST CASE REPORT CONTEST 2022

Clinical Cases in Internal Medicine: Learning Through Practice
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AWARD-WINNING CASES

1ST PLACE: SARAH GALBRAITH

Lemierre's syndrome: should neck imaging be performed in all young patients with cavitating pneumonia?

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INTRODUCTION Lemierre's syndrome was originally characterized as an oropharyngeal infection with anaerobic bacteremia, typically caused by *Fusobacterium necrophorum*, and thrombophlebitis of the internal jugular vein (IJV). Here, we review 3 previously healthy patients with Lemierre's syndrome, who presented to the same health board over a period of 6 months. Their presenting symptoms, results, and suspected sources of infection were not in keeping with the classic triad, and each posed their own diagnostic challenge. They were all critically unwell and took an average of 13 days to diagnose. We aim to raise awareness of atypical presentations of this rare, life-threatening disease, and advocate early imaging of the neck to aid diagnosis.

CASE REPORT An 18-year-old woman was admitted with swollen glands, sore throat, and dry cough. She was hypotensive, and examination revealed tender cervical lymphadenopathy and right basal crackles. She had a raised C-reactive protein level, acute kidney injury, and thrombocytopenia. She had bilateral, cavitating, pulmonary lesions with associated respiratory failure. The diagnosis of Lemierre's syndrome was raised on the fourth day of her admission, and a neck computed tomography (CT) confirmed a right IJV thrombus. Metronidazole was added to her antibiotic regime and she improved. Microbiology was negative throughout.

Another 19-year-old man was admitted with shortness of breath, productive cough, and fever that began following dust inhalation. Examination revealed tachypnoea, tachycardia, and hypoxia that required intubation. He had raised inflammatory markers, renal impairment, thrombocytopenia, and hyperbilirubinemia. Imaging revealed bilateral, cavitating pulmonary lesions, hepatosplenomegaly, and right clavicular osteomyelitis. He improved with antibiotics, however, pyrexia persisted for 3 weeks into his admission. Neck ultrasound confirmed a left IJV thrombus and the diagnosis of Lemierre's syndrome was reached. He underwent surgical debridement of his osteomyelitis with local implantation of antibiotics and improved rapidly. *F. necrophorum* was detected by 16S bacterial polymerase chain reaction screening of the bone biopsy but was not grown on culture.

Finally, a 29-year-old man presented with shortness of breath, cough productive of black sputum, and fever. He later complained of right-side hearing loss with associated discharge. He had raised inflammatory markers and hyperbilirubinemia. Imaging revealed bilateral, cavitating, pulmonary lesions with a normal neck ultrasound. Head and neck CT was performed 1 week into admission confirming the presence of a right IJV thrombus clinching the diagnosis of Lemierre's syndrome. There was also evidence of a right cholesteatoma. Metronidazole was added to his antibiotic regime and he improved. Microbiology was negative throughout.

CONCLUSIONS These cases demonstrate the diagnostic challenge that Lemierre's syndrome poses and the role neck imaging has to play in the diagnosis. We suggest that clinicians have a low threshold for arranging imaging of the neck when young, typically well patients present with cavitating pneumonia. These cases also remind us that Lemierre's syndrome does not solely relate to infections of the oropharynx, and other sources, such as the inner ear, need to be considered.

Key words

Fusobacterium necrophorum, internal jugular vein thrombus, septic emboli

2ND PLACE: SUYASH ANSHUMALI

Rare neurological manifestation of uncontrolled diabetes

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INTRODUCTION Type 2 diabetes (T2D) has become a ubiquitous metabolic disease and not having a clear picture of its myriad forms of presentation, even those rare ones, seems disconcerting. Diabetic striatopathy, also known as diabetic hemichorea hemiballismus (diabetic HCHB), nonketotic hyperglycemic hemichorea (NHH), or chorea hyperglycemia basal ganglia (CHBG) syndrome, belongs to rare neurological manifestations of T2D. It is seen mostly in elderly T2D women with hyperglycemia predominantly without ketosis. It is characterized by choreiform movements of the body due to dysfunction of the basal ganglia. Its rarity makes it a poorly understood condition in terms of pathophysiology, and well-established guidelines regarding treatment strategies are lacking. It is also imperative to educate young clinicians on this condition, as they may initially not take it into consideration during diagnosis. Finally, rational and safe workup, diagnosis, and treatment should be planned.

CASE REPORT A 65-year-old chronically diabetic woman with a history of inconsistent use of insulin presented with choreiform movement of her left arm and left leg for the last month. It initially affected the hand but moved gradually proximally to involve larger muscle groups. Involvement of the left leg occurred just 3 days prior to the presentation. The trunk was spared.

On examination in the emergency department her vitals were stable, the tongue was dry, and bedside capillary blood glucose was high, indicating the level of at least above 625 mg%. Glasgow Coma Scale was 15/15 with no deficit in higher mental functions.

Cranial nerves were intact and motor and sensory functions were within normal limits. Deep tendon reflexes were normal in all 4 limbs and plantars showed bilateral flexor response.

Blood sugar was brought under control on day 1 after admission and dehydration was corrected using regular insulin infusion and crystalloids, respectively. However, the choreiform movements did not disappear or alleviate with glucose control.

Brain computed tomography was performed and it revealed age-related cortical atrophy only. On day 3, clonazepam (0.5 mg) at bed time was added to control chorea, insulin infusion was stopped, and biphasic insulin was started at 20 units and 16 units in the morning and night, respectively. Brain magnetic resonance imaging (MRI) was advised.

MRI showed T1-weighted hyperintensity in the right lentiform nucleus, which is the most consistent with diabetic striatopathy. The patient was discharged on day 6 on her request, as she intended to report to a specialist center for treatment of chorea.

CONCLUSIONS Diabetic striatopathy is considered a reversible condition. However, remission may take days to months, and specific antichorea medications may need to be added to control the condition. Achieving consistent euglycemia is the key to reverse the disease process, and it may take many days to months for symptoms to subside. Hypoglycemia may exacerbate the condition and inhibit its reversion, and thus it must be prevented.

Key words

basal ganglia syndrome, hemichorea, hyperglycemia, hypoglycemia, striatopathy

3RD PLACE: EMILIA BLOMERUS

A rare cause of galactorrhea in autosomal dominant polycystic kidney disease: pituitary stalk compression by an intracranial aneurysm

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INTRODUCTION Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited genetic disorder worldwide and it is characterized by bilateral cyst growth and accumulation in the kidney. It presents heterogeneously with involvement of several organ systems including development of intracranial aneurysms (ICAs). This important extra-renal manifestation occurs in 5%–10% of adult patients with ADPKD, and its prevalence is 3–5 times higher than in the general population.

CASE REPORT A 25-year-old man of Black African ethnicity living with ADPKD on continuous ambulatory peritoneal dialysis since 2018, presented with swollen and tender breasts in March 2021. Clinical examination revealed bilateral gynecomastia with galactorrhea. Neurological examination was normal. Biochemistry confirmed elevated prolactin level of 26.7 mcg/l (normal range, 3.0–11.6 mcg/l). Adrenocorticotropic hormone dropped to 0.9 pmol/l (normal range, 1.6–13.9 pmol/l), and cortisol was at a normal level of 306 nmol/l (normal range, 133–537 nmol/l). Other pituitary lines were unaffected. Magnetic resonance angiography (MRA) of the brain was then undertaken, and it revealed 2 ICAs. A fusiform right distal internal carotid artery aneurysm was 6.5 mm long with 9.9 mm maximal diameter, and a saccular left middle cerebral artery aneurysm measured 1.7 mm at the neck and 4.5 mm × 5.2 mm at the dome. Local mass effect around the internal carotid artery aneurysm with compression of the pituitary stalk was noted. This finding accounted for hyperprolactinemia and the resultant galactorrhea.

DISCUSSION Most intracranial aneurysms in ADPKD are located in the anterior circle of Willis. Risk factors for aneurysm formation include smoking, hypertension, family history and more advanced stage of kidney failure. Increased size, posterior location, family history of ICA and previous known subarachnoid hemorrhage are important risk factors for rupture. The most common presentation of ICA in ADPKD is a rupture with subarachnoid hemorrhage. Presentations of unruptured ICA may include focal signs or transient ischemic attacks. Given the absence of these risk factors in our patient, a conservative approach was adopted by our center's neurosurgical team. Serial MRA imaging at 6-month intervals will be performed to assess if endovascular coil embolization may be indicated in the future. Medical therapy for galactorrhea was offered in the interim. Pituitary stalk compression by multiple ICAs in the setting of ADPKD is an unusual cause for galactorrhea. Our patient presented at a younger age than the average of 40 years, at which most aneurysms manifest clinically.

CONCLUSIONS Early detection of ICAs is essential to prevent significant morbidity and mortality associated with ICA rupture. Current guidelines recommend screening for ICAs in patients with ADPKD with a known family history of ICAs, if neurological symptoms develop, and the patients perform high-risk professions. Clinicians should maintain a high index of suspicion and be wary of the potential for unusual presentations including that of galactorrhea as a rare endocrinological manifestation. This in turn should prompt a low threshold for ICA detection, as early diagnosis may ameliorate life-threatening complications associated with aneurysmal rupture.

Key words
galactorrhea, intracranial aneurysm, kidney failure

ORAL PRESENATIONS

ASLIHAN E. APAYDIN ROLLAS

A rare cause of fever of unknown origin in a renal transplant patient: disseminated *Nocardia* infection

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INTRODUCTION We report a rare case of a patient who presented with fever of unknown origin (FUO) 9 months after renal transplantation, and a difficult diagnosis of disseminated *Nocardia* infection with pulmonary and central nervous system (CNS) involvement.

CASE REPORT A 68-year-old woman with living-donor kidney transplantation diagnosed with familial Mediterranean fever, hypertension, type 2 diabetes, and nephrolithiasis was admitted to the nephrology department with complaints including 2 weeks of fever, cough, and shortness of breath 5 months after the transplantation. A thorax computed tomography (CT) revealed a 44 × 43 mm diameter consolidation area in the left lung inferior lingular segment. Levofloxacin was given for 5 days with a preliminary diagnosis of pneumonia. Valganciclovir was given until the negative viral load was reached, as on admission the patient had a high cytomegalovirus (CMV) load. The patient was discharged after the treatment when her symptoms and fever resolved. However, she reported again 2 weeks later because the fever (38.0 °C and above) continued intermittently every 3–4 days. Repeated thorax CT revealed an increase in the size of the consolidated area to 44 mm × 55 mm. Transthoracic fine-needle aspiration biopsy was performed to rule out malignancy due to the increased size of the consolidated area, which revealed focal suppurative inflammation and mixed inflammatory cells. However, aerobic, fungal, and *Mycobacterium tuberculosis* cultures were negative. Another culture was taken from the pus that developed at the needle entry site 1 week after the biopsy, and it was positive for *Nocardia* species. Although the patient's neurological examination was completely normal, cranial magnetic resonance imaging (MRI) was performed to exclude central nervous system involvement. On cranial MRI, lesions suggesting bilateral cerebral and cerebellar focal infectious abscesses were revealed. Antibiotic therapy was changed to trimethoprim-sulfamethoxazole (TMP/SMX – 5 mg/kg TMP every 8 hours) and imipenem (500 mg every 6 hours). After 6 weeks of treatment, control thorax CT revealed a significant resolution of the consolidation. Moreover, the fever and respiratory system symptoms relieved from the first week of the treatment. The patient was discharged with continued antimicrobial therapy (TMP/SMX) for 9 or 12 months, depending on her response to treatment.

DISCUSSION The most often causes of immunodeficiency-associated FUO, especially in organ transplant recipients, are due to viruses, donor-derived infections, opportunistic fungal infections, rejection, and, in rare cases, graft-versus-host disease, graft intolerance syndrome, old nonfunctioning arteriovenous grafts, hemophagocytic lymphohistiocytosis, ureaplasma-related hyperammonemia syndrome, and *Strongyloides stercoralis* hyperinfection. *Nocardia* is a species of saprophytic, gram-positive aerobic bacteria that is an uncommon cause of opportunistic infections. Although one-third of cases occur in the immunocompetent population, *Nocardia* is particularly an opportunistic infection agent in immunocompromised recipients. *Nocardia* species are uncommon but hazardous pathogens, particularly in solid organ transplantation (SOT) recipients, as they impair T-lymphocyte cell-mediated immunity provided by immunosuppression therapy. However, even though the incidence is rare, nocardiosis must be kept in mind in the case of patients who present with FUO, particularly SOT recipients, and patients with a history of using high-dose corticosteroids, high median serum calcineurin inhibitor levels, and CMV infection. Antimicrobial therapy as monotherapy (TMP/SMX) for 9 or 12 months, depending on the patient's response, is the recommended treatment.

Key words
fever of unknown origin, *Nocardia*, renal transplantation

DAGMARA BRASLAVSKÁ

Massive hemoptysis in a young patient

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INTRODUCTION Goodpasture syndrome is a rare autoimmune disease of small vessels, with the highest incidence in the third decade and in the sixth to seventh decades, especially in smoking men. It is characterized by circulating antibodies directed against the antigen of the glomerular basement membrane (GBM) and alveolar basement membrane, resulting in rapidly progressive glomerulonephritis and/or alveolar hemorrhage. Most patients (approximately 90%) with anti-GBM disease present with clinical features of rapidly progressive glomerulonephritis. Between 25% and 60% present with concomitant alveolar hemorrhage, and only a small proportion of patients present with an isolated pulmonary disorder. Diffuse alveolar hemorrhage can lead to rapid development of respiratory insufficiency and anemia. The diagnosis of anti-GBM disease requires detection of anti-GBM antibodies. Flexible bronchoscopy with sequential bronchoalveolar lavage is the gold standard for the diagnosis of diffuse alveolar hemorrhage. Early diagnosis is critical for achieving the best response to therapy. The standard therapy of Goodpasture syndrome includes immunosuppressive agents (glucocorticoids and cyclophosphamide) in conjunction with plasmapheresis.

CASE REPORT We present a case of a 21-year-old patient, a smoker, without comorbidities, repeatedly hospitalized for dyspnea and hemoptysis. Upon the first admission, bilateral pulmonary opacities were seen on the X-ray, with rapid regression after an empirical antibiotic and antiviral therapy combined with glucocorticoids. No renal involvement was detected. At the time of the first presentation, the patient underwent diagnostic evaluation including the laboratory testing for autoantibodies (antinuclear and antineutrophil cytoplasmic antibodies*)*. Within 1 month, the patient returned with the same complaints and findings, that is, dyspnea and hemoptysis, anemia and bilateral pulmonary opacities on the chest X-ray. All symptoms rapidly regressed when the corticosteroid therapy was restarted. The patient was discharged with prednisone therapy. On the next day (within 24 hours after almost normal high-resolution computed tomography lung scan) massive hemoptysis led to readmission with the need for prolonged noninvasive pulmonary ventilation, high dose of methylprednisolone, and repeated erythrocyte transfusions. Highly positive anti-GBM antibodies were detected in serum and the patient continues to be treated on an outpatient basis with high doses of prednisone.

DISCUSSION Our case report documents the necessity of broad differential diagnostics in the patients presenting with hemoptysis. In the presence of bilateral pulmonary infiltrates and anemia, diffuse alveolar hemorrhage due to autoimmune disease should always be considered. One of the causes of this condition may be Goodpasture syndrome, rare even without the presence of kidney involvement. The patients with diffuse alveolar hemorrhage suspected to be due to autoimmune disease treatment should be promptly put on

systemic glucocorticoids (pulses of methylprednisolone). Early initiated immunosuppressive therapy can be lifesaving in these cases.

Key words
diffuse alveolar hemorrhage, hemoptysis, Goodpasture syndrome, glucocorticoids

RIHARDS BUSS

Aggressive form of inflammatory myopathy complicated by ventilatory insufficiency and acute renal failure

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INTRODUCTION Idiopathic inflammatory myopathies (IIM) are a group of rare, heterogeneous, multisystem autoimmune conditions that predominantly cause muscle inflammation, but several extramuscular manifestations have been established. Typically, the disease presents insidiously with gradual progression, but on rare occasions, symptoms can develop acutely with rapid progression leading to complications with high morbidity and mortality rates.

CASE REPORT This case report presents a 67-year-old man who attended the emergency department with anuria for the past 48 hours and a history of dermatomyositis type of skin rash for several weeks. Biochemistry test results revealed C-reactive protein (CRP) elevated at 214 mg/l, creatine kinase 149 430 U/l, serum creatinine 1098 μmol/l, and urea 29.5 mmol/l with the last 2 indicating acute kidney injury stage 3. On day 2 of admission, the patient experienced respiratory arrest requiring transfer to an intensive care unit (ICU) for intubation and invasive ventilation and emergency hemofiltration. After skin and muscle biopsies were obtained, the patient was commenced on intravenous methylprednisolone (1 g for 3 days) and intravenous immunoglobulins (2 g/kg over 2 days) followed by a weaning dose of parenteral glucocorticoids.

After initial therapy was given, rapid normalization in creatine kinase and CRP levels was observed followed by complete resolution of the skin rash in the following weeks. However, severe global muscle weakness persisted. The patient failed a trial of extubation, had a tracheostomy inserted, and remained on mechanical ventilation by tracheostomy throughout his stay in the ICU. There was no evidence of interstitial lung disease on serial imagining throughout his admission. Given no improvement in the muscle strength, the patient received rituximab therapy (2 doses of 1 g 2 weeks apart).

Changes seen on skin biopsy favored dermatomyositis but muscle biopsy findings were more suggestive of an immune-mediated necrotizing myopathy. Assays for 3-hydroxy-3-methylglutaryl-CoA reductase and anti-signal recognition particle antibodies were negative. Antinuclear antibody screen was positive with elevated Ro-60 antibodies at 4.1 kIU/l and La antibodies at 5.4 kIU/l. Associated malignancy was not seen on computed tomography scan of the chest, abdomen, and pelvis.

The admission was complicated with 3 episodes of hospital-acquired pneumonia and perforated duodenal ulcer with peritonitis. The patient remained hemodialysis-dependent with minimal recovery of renal function and on continuous mechanical ventilation support with no evidence of progress in his overall clinical condition. On day 55 of ICU admission his condition started to deteriorate again, and after discussion with the family active treatment and respiratory support were withdrawn in the patient's best interest. The patient died after 2 days.

CONCLUSIONS Ventilatory insufficiency due to respiratory muscle weakness and acute renal failure secondary to rhabdomyolysis are rare manifestations of IIM. Early recognition of the condition and prompt induction of immunosuppressive treatment are important for better clinical outcomes due to high associated mortality.

Key words
dermatomyositis, idiopathic inflammatory myopathy, immune-medicated necrotizing myopathy

UDDALAK CHAKRABORTY

Eye of the storm: a neurovascular diagnostic dilemma

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INTRODUCTION Primary angiitis of the central nervous system (PACNS) is a single-organ vasculitis without any systemic manifestations and protean clinical manifestations with a challenging road to diagnosis. PACNS involving small vessels (SV-PACNS) is characterized by a usual presentation of cognitive impairment, encephalopathy, and seizures, whereas large vessel involvement (LV-PACNS) tends to present with focal neurological deficits. The spectrum of brain imaging may include bihemispheric infarcts involving variable vascular territories of varying size at different stages of healing, and meningeal enhancement and intracerebral bleeds are commonly detected. The conventional angiography may reveal multiple areas of short segment stenosis and dilatation or multilocular occlusions with or without development of fusiform arterial dilatations, collaterals, and delayed contrast enhancement; however, angiography may be normal in a considerable number of patients with SV-PACNS. Extensive workup is warranted to rule out other etiologies that encompass the causes of secondary vasculitis (infective and noninfective), although reversible cerebral vasoconstriction syndrome and invasive CNS lymphoma are close differentials.

CASE REPORT A 23-year-old man, a migraineur, presented with sequential neurological deficits with a new-onset left hemicranial headache of severe intensity. Neurological examination revealed a right-sided pupil sparing oculomotor nerve palsy and a right-sided lower motor neuron type facial palsy, without any evidence of long tract signs and meningism. Brain imaging revealed the presence of bihemispheric T2 hyperintensities and bleeds, which prompted us to consider the possibility of vasculitis. A cerebrospinal fluid (CSF) assay revealed marked lymphocytic pleocytosis with low glucose and elevated protein levels, which tended to deviate from the conventional CSF analysis of a noninfective vasculitis. Hence, an extensive evaluation to rule out an infectious cause as well as lymphoma was carried out before making a provisional diagnosis of probable PACNS in the absence of histopathological confirmation due to unavailability of consent. A high-resolution magnetic resonance imaging of the vessel wall revealed eccentric thickening with enhancement of bilateral petrous internal carotid artery, which confirmed the diagnosis. The patient was initiated on pulse intravenous methylprednisolone, followed by oral prednisolone taper along with monthly cycles of cyclophosphamide awaiting a maintenance therapy. He had a remarkable response to immunosuppressive therapy with marked resolution of the neurological deficits as well as radiological resolution at 1-month follow-up.

CONCLUSIONS The road to the diagnosis of PACNS may be challenging at times due to a variety of presentations, atypical CSF findings, and normal conventional angiography results. A histopathological confirmation mandates a definitive diagnosis of PACNS.

Key words
central nervous system, primary angiitis of the central nervous system, vasculitis

BRONA DINNEEN

VEXAS, a newly reported hemato-immune disease presenting with striking ocular and systemic inflammatory features

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INTRODUCTION VEXAS syndrome is a novel hemato-immune condition first reported in 2020. It is the result of an acquired somatic mutation affecting methionine-41 of the X-linked gene *UBA1*, responsible for ubiquitylation. It is characterized by vacuoles in myeloid and erythroid precursors, autoinflammatory features, almost exclusive male predominance, and a median age of onset of 64 years. Treatment options are limited, requiring high-dose steroids, with early evidence suggesting benefits of interleukin-6 and Janus kinase (JAK) inhibition. Severe cases require autologous hematopoietic stem cell transplantation. Mortality is as high as 25%.

The objective of this case report is to highlight this recently documented condition and its unusual constellation of symptoms in order to avoid an incorrect diagnosis.

CASE REPORT We herein report a rare case of VEXAS in a 69-year-old man presenting with orbital apex syndrome, chondritis, macrocytic anemia, venous thrombosis, pyrexia of unknown origin, and inflammatory rash, with a fluctuating 2-year history of unexplained autoinflammatory symptoms.

The patient presented to the eye emergency department with a 3-day history of vertical diplopia, left eye pain, left eye proptosis, and jaw pain. He also had a 1-week history of right calf swelling and right ear pain and swelling in addition to a diffuse maculopapular rash. The patient was noted to have left hypertropia and proptosis accompanied by pain on extraocular movement and facial pain. Investigations revealed a raised erythrocyte sedimentation rate, C-reactive protein, ferritin, and D-dimer. Full blood count revealed a macrocytic anemia, neutropenia, lymphopenia, and decreased monocytes. Ultrasound Doppler of the right lower limb revealed superficial thrombophlebitis. Brain magnetic resonance imaging confirmed inflammation of the left orbital apex and chondritis of the right ear. Punch biopsy of the diffuse papular rash showed fibrin thrombi consistent with a vasculopathic reaction. Bone marrow biopsy confirmed the presence of vacuoles, and genetic testing confirmed the presence of a mutation in *UBA1*.

CLINICAL RESOLUTION The patient was treated with pulsed intravenous methylprednisolone (500 mg) for 3 days, followed by oral prednisolone (40 mg) daily. Following steroid treatment, the patient showed rapid and almost complete resolution of ocular symptoms, chondritis, and rash within 2 weeks. He was discharged on oral prednisolone, and despite initial improvement, suffered a relapse of symptoms within 2 months. The patient has since been commenced on tofacitinib, a JAK inhibitor and remains in remission with ongoing steroid taper.

DISCUSSION This is a newly described condition with a prevalence estimated between 1:20 000 and 1:30 000. VEXAS should now be considered as a differential diagnosis in elderly men with macrocytic anemia and systemic inflammation, including ocular presentations.

Key words
macrocytic anemia, ocular symptoms, systemic inflammation, *UBA1* mutation, VEXAS syndrome

SOUMAYA ELBACHIRI

TNF blockers in IRIS-tuberculosis: a case report illustrating the role of infliximab

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INTRODUCTION Tuberculosis-immune reconstitution inflammatory syndrome (TB-IRIS) is a deterioration of the clinical state, with an increase in lesions or an appearance of new tuberculous lesions following the introduction of an effective antibacillary treatment in patients with immune deficiency (eg, HIV or on immunosuppressive therapy). This reaction was described in patients infected with HIV, but recently a few papers reported the same reaction in patients under biotherapy.

CASE REPORT We report a case of a 28-year-old man followed for ankylosing spondylitis, on tumor necrosis factor (TNF) blocker therapy (certolizumab every 2 weeks). The patient had negative results of interferon-gamma release assay (Qantiferon) before the initiation of the biotherapy.

Six years after the initiation, he presented with miliary tuberculosis with pulmonary and meningeal localizations. Certolizumab therapy was interrupted and a quadritherapy against tuberculosis was started with 6 pills of rifampicin/isonisazid/pyrazinamide 300 mg/50 mg/120 mg and 2 pills of ethambutol 500 mg, combined first with corticotherapy at 40 mg/d, and then at 100 mg/d of prednisone in the presence of persistent, badly tolerated fever of 39 °C.

After initial apyrexia on day 15 of the antituberculosis treatment, we observed the recurrence of fever spikes up to 40 °C, associated with an increased inflammatory syndrome with C-reactive protein (CRP) at 122 mg/l, and an increase in the size of the mediastinal and hilar adenopathy on computed tomography. After verification of the patient's compliance and the absence of microbiological failure, the diagnosis of TB-IRIS was retained. We decided to treat the patient with a TNF-α blocker, infliximab, 5 mg/kg every 2 weeks on 3 occasions, while continuing the corticosteroid therapy. The evolution was favorable after the first course of infliximab, with apyrexia on the second day of the injection, and a decrease in the inflammatory syndrome (CRP $<$10 mg/l).

DISCUSSION In the case of corticosteroid therapy resistance, the use of TNF-α blockers such as infliximab is promising with a remarkable response without major adverse effects. Infliximab was found effective in the treatment of TB-IRIS associated with HIV infection. The same result was achieved in immunocompetent patients. In addition, the efficacy of adalimumab was described in a steroid-refractory neuromeningeal form of TB-IRIS. Overall, the prognosis remains good, except for neurological forms where the risk of sequelae is very high.

LESSONS TO BE LEARNED

- Interruption of the immunosuppressive therapy (eg, TNF-α blockers) may be a risk factor of TB-IRIS.
- Infliximab may be the treatment of TB-IRIS in the case of corticosteroid resistance.

Key words
infliximab, IRIS-tuberculosis, paradoxical reaction, TNF blockers

GIULIANA L. GUIDARELLI

Rapidly progressive renal failure due to oxalate tubulointerstitial nephritis associated with chronic pancreatitis

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INTRODUCTION The intratubular deposition of oxalate crystals is a well-known cause of kidney damage, in cases of primary or secondary hyperoxaluria. Rapidly progressive renal failure due to enteric hyperoxaluria caused by chronic pancreatitis is an uncommon form of presentation.

CASE REPORT We present a case of a 69-year-old man with a history of type 2 diabetes mellitus, essential hypertension, and dyslipidemia with diffuse carotid atheromatosis. In April 2018, he was consulted for chronic steatorrhea-type diarrhea associated with abdominal distension, without nausea, vomiting, or fever, and 12% weight loss in 2 months. Complementary tests showed a creatinine level of 1.30 mg/dl (normal values, 0.7–1.3 mg/dl), Modification of Diet in Renal Disease (MDRD) estimated filtration glomerular rate (eFGR) of 58 ml/min/1.73 m^2, decreased fecal elastase, normal amylase, normal IgG4, and contrast-enhanced helical tomography of the abdomen showed pancreas decreased in size with multiple scattered calcifications compatible with chronic pancreatitis. One month after the tomography, the patient developed a rapidly progressive renal failure, doubling creatinine in 3 weeks from 2.0 to 3.38 mg/dl, with MDRD eFGR drop to 15 ml/min/1.73 m^2. The ultrasound showed normal kidneys, without evidence of kidney stones. Antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA) were negative. Renal biopsy revealed an intratubular birefringent "seashell" crystal deposit with tubulointerstitial inflammatory infiltrate compatible with interstitial nephritis due to oxalate crystal deposits. Oxaluria was 84.1 mg/24 h (normal values, 7–44 mg/24 h). A low-oxalate diet and pancreatin supplementation were indicated, leading to an improvement in renal function that has remained stable for 4 years after the diagnosis (creatinine, 1.71 mg/dl; MDRD eFGR, 47.7 ml/min/1.73 m^2; oxaluria, 29 mg/24 h) without dialysis requirement.

CONCLUSIONS We highlight the importance of incorporating oxalate tubulointerstitial nephritis into clinical evaluation of the causes of rapidly progressive renal failure in patients with predisposing conditions for hyperoxaluria, such as chronic pancreatitis, even though there can be other vascular, metabolic, or toxin-related reasons that could explain it. Establishment of simple therapeutic measures can prevent its irreversible progression.

Key words
acute kidney injury, chronic pancreatitis, hyperoxaluria

MASOOMA HASHMAT *(PRESENTED BY NABEEL AKBAR CHAUDHRY)*

Clinical presentation of cutaneous polyarteritis nodosa as pyoderma gangrenosum-like skin lesion: a rare case report

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CASE REPORT Polyarteritis nodosa (PAN) is a medium vessel vasculitis with multiple organ involvement. Cutaneous polyarteritis nodosa is a rare variant of classic PAN limited to the skin. We report a rare presentation of PAN that posed a diagnostic challenge with isolated cutaneous involvement in a young woman. She presented with recurrent multiple ulcerated skin lesions that have been clinically mimicking pyoderma gangrenosum for 4 years.

Key words
polyarteritis nodosa, pyoderma gangrenosum, vasculitis

SALMAN KHAN

Gunther's disease

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INTRODUCTION Gunther's disease, also known as congenital erythropoietic porphyria (CEP), is an extremely rare autosomal recessive photosensitive porphyria. It is due to a markedly deficient activity of uroporphyrinogen 3, resulting in the accumulation of nonphysiological porphyrin isomers, uroporphyrin 1 and coproporphyrin 1, culminating in the clinical expression of CEP. So far, only 200 cases have been reported worldwide.

CASE REPORT A 60-year-old woman from a remote mountainous region of northern Pakistan was admitted as a case of leprosy with deformities of the nasal septum and both upper limb digits. Initially, leprosy diagnosis was suspected but it was never confirmed due to a very unusual presentation. The patient was admitted for a workup of anemia, persistent hematuria, acute kidney injury, shortness of breath, and abdominal distention. On general physical examination, the patient was thin, pale, and ill-looking, with red dry eyes, increased facial hair along with prominent and elongated canine teeth, nasal septum deformity, bilateral autoamputation of digits, gross ascites, bilateral pitting pedal oedema, reddish urine, and low blood pressure with anemia. Systemic examination showed splenomegaly with ascites and bilaterally decreased air entry at the bases of the lungs. Echocardiography showed cor pulmonale with right ventricular systolic pressure of 54, and abdominal ultrasound showed splenomegaly. Creatinine was 3.4 mg/dl, hemoglobin 8.9 g/dl, alanine transaminase 212 U/l, and total bilirubin 3.2 mg/dl.

The presence of splenomegaly, jaundice, ascites, and hematuria that was never picked up in urine analysis and a shock due to low blood pressure made us reconsider the diagnosis as clinical presentation of leprosy was not matching. The reddish coloration of urine persisted and urine was negative for red blood cells. A consultant dermatologist suggested to consider a very rare case of CEP, as all the symptoms matched this condition. The diagnosis of CEP was confirmed based on clinical signs and raised uroporphyrin 1 and coproporphyrin 1 levels. Unfortunately, we lost the patient due to septic shock despite good antibiotic and inotropic support, as she suffered from persistent hypotension with worsening acute kidney injury.

DISCUSSION The unique presentation of CEP in the form of splenomegaly, ascites, anemia, nasal septum and digits amputation, along with a positive childhood history of blisters and presumptive diagnosis of leprosy made it a challenging case. It also highlighted the importance of out-of-the-box thinking in diagnosis as well as the value of interdepartmental consultation that could well save the resources and improve patient care at tertiary level. The lesson learned in this case is to increase awareness of negative consequences of consanguinity, which is frequently practiced in our community, in order to avoid congenital diseases.

Key words
congenital erythropoietic porphyria, coproporphyrin 1, leprosy, uroporphyrin 1

JI-YEON KIM

Mass lesions that almost fill the ascending aorta: when to operate?

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INTRODUCTION Although a thrombus in the ascending aorta is rare because of high-flow velocity, early diagnosis and treatment are important to prevent life-threatening distal arterial embolisms. Aortic sarcomas have 2 varieties: mural and intimal. The intimal form often develops into intraluminal polyps or extensive longitudinal forms. Thus, intimal varieties can lead to distal embolization or aortic obstruction. The mural types originate from the media or adventitia and usually grow outward to invade the periaortic tissue.
CASE REPORT A 73-year-old man with a history of early gastric cancer, hypertension, and diabetes mellitus presented to the outpatient clinic with left knee pain for a week. Before excisional biopsy of the left proximal tibia, a mass lesion almost filling the ascending aorta was revealed on preoperative echocardiography. Transesophageal echocardiography revealed a 33 mm × 15 mm, highly mobile mass lesion with irregular surfaces attached to the ascending aortic wall. Contrast-enhanced computed tomography demonstrated a huge mass lesion in the ascending aorta and aortic arch without contrast enhancement. The patient underwent the excisional biopsy for the left proximal tibia and was diagnosed with sarcoma. We initiated an anticoagulant therapy to evaluate the possibility of a thrombus associated with an increased thrombogenicity. However, the mass lesion did not respond to the therapy for 7 days. Thus, the possibility of a thrombus was excluded, and the patient was treated with a mass excision and replacement of the ascending aorta and the aortic arch. The excised ascending aorta and aortic arch were filled with tumors, and undifferentiated pleomorphic sarcoma was confirmed.
CONCLUSIONS Since the surgical removal of an ascending aortic mass is very difficult, it is hard to decide on an immediate surgical removal when an aortic mass is found. If this kind of tumor is suspected, it is important to consider differential diagnoses including a thrombus of the tumor, and surgical removal is the recommended treatment when anticoagulation fails to resolve it. A combination of surgical removal and chemotherapy offers the greatest survival benefits in patients with aortic sarcomas, with a median survival rate of 12 months.

Key words
anticoagulation, ascending aorta, sarcoma

ELIANE A. LUCASSEN

Fitz-Hugh-Curtis syndrome identified by gallbladder gonococcal polymerase chain reaction

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INTRODUCTION Fitz-Hugh-Curtis syndrome (FHCS) is a perihepatitis linked to pelvic inflammatory disease that is often confused with acalculous cholecystitis. It is crucial to distinguish between these conditions, because a cholecystectomy is only indicated in cholecystitis. Even after a cholecystectomy is performed, it is important to differentiate between these conditions if diagnostic uncertainty persists, because additional treatment is warranted in FHCS. In this case report, we describe that a local gallbladder gonococcal polymerase chain reaction (PCR) can aid in the distinction of FHCS and acalculous cholecystitis.
CASE REPORT We describe the case of a 42-year-old woman who presented to the emergency department with severe abdominal pain in the right lower quadrant, a fever (38.5 ºC), elevated inflammatory markers (C-reactive protein, 42 mg/l; leukocyte count, 12.9 × 10^9 cells/l), and normal pancreatic and liver enzymes. Urinary analysis, vaginal ultrasound, and abdominal computed tomography scan were normal. The vaginal swab for *Neisseria gonorrhoeae* (PCR) was positive. An abdominal ultrasound made 2 days after the admission because of ongoing severe abdominal pain showed mild intrahepatic biliary dilatation without gallstones. Under the suspicion of acalculous cholecystitis a cholecystectomy was performed. To better differentiate between acalculous cholecystitis and FHCS, we performed a PCR test of the gallbladder tissue, which was positive for *N. gonorrhoeae*. This proved a local infection of the perihepatic region with *N. gonorrhoeae*, consistent with FHCS. Ceftriaxone was given for 3 days in total.
DISCUSSION In our patient, we were in doubt whether FHCS or acalculous cholecystitis caused her symptoms. The positive vaginal swab for *N. gonorrhoeae* raised our suspicion of perihepatitis. However, a positive vaginal swab does not prove infection in the higher pelvic region. To the best of our knowledge, a PCR assay of the gallbladder tissue specimen to check for the presence of *N. gonorrhoeae* has not been performed previously. The confirmation of the presence of *N. gonorrhoeae* in this tissue was fundamental to the final diagnosis of FHCS in our patient.

It is important to distinguish FHCS from cholecystitis even after a laparoscopic cholecystectomy is performed, because FHCS requires screening for other sexually transmitted infections, partner treatment, and requires a different antibiotic treatment depending on the microorganism involved. For a gonococcal infection confined to the cervix, rectum or urethra, a single dose of ceftriaxone suffices, but a longer treatment is recommended for disseminated infection to prevent scarring and adhesion formation, which can result in chronic pelvic pain, infertility, and ectopic pregnancy. This is important to address, especially in women who want to have children.
CONSLUSIONS In the present manuscript, we showed that a PCR assay of the gallbladder tissue specimen was fundamental to distinguishing FHCS from acalculous cholecystitis, which warranted additional treatment.

Key words
cholecystitis, Fitz-Hugh-Curtis, gonorrhea, pelvic inflammatory disease, perihepatitis

GIOVANNA MACELLO

Immunotherapy-induced inflammatory arthritis: a new diagnostic and therapeutic challenge

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INTRODUCTION Immunotherapy is an innovative type of antineoplastic therapy that uses immune-modulating molecules to treat cancer. Its aim is to enhance or restore the antitumor capacity of the immune system and to overcome the tumor escape mechanisms. Due to its ability to block immune checkpoints (ICs), immunotherapy has become the standard treatment for several types of tumors.

Inhibition of ICs targeting cytotoxic T-lymphocyte protein 4 (CTLA-4: ipilimumab and tremelimumab), and programmed cell death protein 1 (PD-1: nivolumab and pembrolizumab) and its ligand (PD-L1: atezolizumab and durvalumab), has significantly improved survival in non–small cell lung cancers, metastatic melanomas, Hodgkin lymphomas, and renal and urothelial carcinomas.

Immunotherapy is responsible for immune-related adverse effects (IRAEs) in which rheumatic diseases seem to play an important role. The pathophysiological mechanism is related to the loss of self-tolerance of T lymphocytes, autoantibody production, and induction of proinflammatory cytokines (interleukin 17).
CASE REPORT We present a patient diagnosed with Hodgkin lymphoma refractory to multiple therapeutic strategies, who started immunotherapy with pembrolizumab. After 6 weeks, he was consulted for oligoarthritis. First, in suspicion of septic arthritis, he received antibiotics; however, following a cytological study with inflamma-

tory fluid and negative cultures, he started treatment with steroids under strong suspicion of IRAEs.

DISCUSSION IRAEs usually appear within the first 3–6 months of the administration and in some cases are predictors of good response to treatment. The most common are inflammatory arthritis and polymyalgia rheumatic. Sicca and connective tissue diseases, such as inflammatory myopathies, giant cell arteritis-type vasculitis, systemic lupus erythematosus, or sarcoidosis have also been described.

Treatment should be staggered, taking into account that depending on the degree of severity of IRAEs, treatment differs, even recommending the use of biologic therapy and the suspension of immunotherapy.

Currently, there is no definition or tool for reporting IRAEs in clinical trials and there is concern that they may be underdiagnosed.

Key words
arthritis, immune-related adverse events, pembrolizumab

MICHELLE MADDEN

Aseptic meningoencephalitis and myelitis temporally associated with SARS-CoV-2 vaccination

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INTRODUCTION Mass vaccination programs have been pivotal in reducing mortality and morbidity from SARS-CoV-2 infection. Worldwide, there has been rapid distribution of vaccines to populations over a short time frame. Some adverse events have been reported. We describe a case of meningoencephalomyelitis occurring in close temporal association with SARS-CoV-2 vaccination.

CASE REPORT A 35-year-old South African man presented to a hospital in Ireland with systemic symptoms, confusion, and headache. He returned from South Africa 35 days earlier, having spent 4 weeks there in an urban center. He did not take malaria prophylaxis and denied insect bites and contact with sick people. He was well during his stay and remained so for 16 days after his return. Fourteen days prior to the presentation he received a booster dose of the Pfizer-BioNTech SARS-CoV-2 vaccine. He had previously received Pfizer-BioNTech for the first 2 doses and on both occasions he developed fever and prominent headache lasting for several days. There was no history of primary SARS-CoV-2 infection. He was in a monogamous heterosexual relationship and denied intravenous drug use.

Headaches, fevers, and myalgia persisted for 2 weeks following vaccination and new-onset confusion prompted presentation. He was febrile on examination, disorientated to person and place with nuchal rigidity. Within 48 hours he developed a rapid ascending flaccid paralysis with bulbar involvement and features of autonomic instability. He was transferred to an intensive care unit requiring intubation.

Initial cerebrospinal fluid (CSF) showed 134 white blood cells per mm^3 with a lymphocytic predominance (90%), CSF protein was 2.55 g/l and glucose was 1.9 mmol/l (serum glucose, 5.2 mmol/l). Magnetic resonance imaging of the brain and spine showed diffuse abnormal signal within the sulci, leptomeningeal enhancement, and long segment hyperintense signal with associated edema in the cord, suggestive of meningomyelitis.

The patient was put on empiric antimicrobial cover for bacterial, viral, rickettsial and mycobacterium tuberculosis infections pending results. Blood cultures on day 1 of admission were positive for *Fusobacterium* and 4 subsequent blood cultures were negative. Computed tomography angiogram of the neck vessels was normal. Extended autoantibody testing was unremarkable.

With a negative workup for infectious etiology and concern about an immune-mediated condition, high-dose methylprednisolone and intravenous immunoglobulin treatment was commenced. Complete recovery of cognition followed but flaccid paralysis persisted. Plasmapheresis was tried with marked improvement of power in the distal upper limbs. After 7 weeks in the hospital, the patient returned to South Africa for rehabilitation.

DISCUSSION Guillain-Barre syndrome has been reported post-vaccination, including SARS-CoV-2 vaccination. There are several case reports in the literature describing encephalitis post SARS-CoV-2 vaccination; all responded well to glucocorticoids, intravenous immunoglobulin, and plasmapheresis. In this case, the temporal association with vaccination and absence of an alternative diagnosis suggests an immune-mediated meningoencephalomyelitis triggered by SARS-CoV-2 vaccination. To our knowledge, this is the first such report in Ireland and the condition is rarely reported following a booster dose.

CONCLUSIONS Serious vaccine-related adverse effects are rare, but should be reported to detect patterns of adverse events. This allows vaccine safety monitoring systems to conduct follow-up studies. The genetic make-up of individuals who develop presumed immune-mediated post-vaccine phenomena deserves further research.

Key words
COVID-19, encephalitis, myelitis, SARS-CoV-2, vaccination

NABEEHAH MOOLLAN

A tale of two pregnancies

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INTRODUCTION Systemic lupus erythematous (SLE) primarily affects women of childbearing age. Although SLE does not adversely impact fertility, it is associated with higher rates of preterm birth, pre-eclampsia, intrauterine growth restriction, fetal loss, and neonatal lupus. Predictors of adverse pregnancy outcomes include active disease, prior nephritis, hypocomplementemia, anti–double-stranded DNA (dsDNA) antibodies, antiphospholipid antibodies, thrombocytopenia, and the use of antihypertensives. We present a case of a patient diagnosed with SLE during pregnancy, which resulted in lupus nephritis, antiphospholipid syndrome (APS), stroke, hypertension, and seizures leading to early fetal demise, who after achieving disease remission proceeded to have a successful pregnancy.

CASE REPORT A 35-year-old woman of 20 weeks' gestation presented following a generalized tonic-clonic seizure. She was found to be hypertensive, with proteinuria, and as such was treated as for pre-eclampsia. Her background included an in vitro fertilization (IVF) pregnancy, miscarriage at 10 weeks' gestation, primary infertility, and previous immune thrombocytopenia. Medications included aspirin and prophylactic low-molecular-weight heparin (LMWH). On admission she had thrombocytopenia, elevated creatinine levels, low C3 and C4, and high anti-dsDNA antibody levels, and was triple antiphospholipid antibody–positive. Brain magnetic resonance imaging showed old infarcts. Renal biopsy confirmed active lupus nephritis. For nephritis she was commenced on azathioprine, hydroxychloroquine, and prednisolone, for APS on therapeutic LMWH and aspirin, for hypertension on labetalol, and for seizures on levetiracetam. However, despite this treatment, her baby died in utero at 25 weeks' gestation. Despite the pregnancy complicated by lupus nephritis, APS, stroke, hypertension, seizures, and early fetal demise, our patient had a strong wish for a further pregnancy. Azathioprine was switched to mycophenolate mofetil, labetalol to ramipril, and LMWH to warfarin. At review 1 year later, she had a normal blood pressure, renal function and platelet count, with improvement in dsDNA antibodies and C3 and C4 counts. She was switched back to azathioprine, continued prednisolone and hydroxychloroquine, ramipril was stopped, she was switched to therapeutic LMWH and continued on aspirin, she was also given 2 cycles of rituximab, and

continued on levetiracetam. The IVF cycle was successful and she remained normotensive, nonproteinuric and seizure-free throughout the pregnancy. She delivered a healthy baby at 37 weeks' gestation.

DISCUSSION Our case highlights the importance of preconception planning and achieving disease remission in patients with SLE in order to optimize pregnancy outcomes.

Key words
lupus nephritis, maternal medicine, systemic lupus erythematous

HAPPY NKAMBULE

COVID 19–associated nephropathy (COVAN) in a kidney allograft

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INTRODUCTION COVID-19 is a multisystemic heterogenous disease. Renal manifestations include proteinuria, hematuria, acute tubular injury, thrombotic microangiopathy, and as recently described, podocytopathy. COVID-19–associated nephropathy (COVAN), a collapsing glomerulopathy, has mainly been described in native kidneys with few reports in allografts. We describe the first reported case of COVAN in Africa in a kidney allograft, in a setting of a low-risk apolipoprotein A-1 variant.

CASE REPORT A 55-year-old African man with end-stage kidney disease secondary to hypertensive nephropathy received a nonrelated living donor kidney transplant in 2010 from his wife. In February 2021, he contracted COVID-19 whilst unvaccinated and received home-based care, including oxygen. In May 2021, after recovery, he received the Pfizer vaccine. His estimated glomerular filtration rate (eGFR) at COVID-19 diagnosis was 27 ml/min/1.73 m^2 and 36 ml/min/1.73 m^2 in September 2020. This decline continued, and in February 2022 he presented with hypertension, eGFR of 8 ml/min/1.73 m^2, and fluid overload requiring hemodialysis initiation. Oral immunosuppression was stopped, intravenous hydrocortisone was initiated, and a renal allograft biopsy was performed. The renal biopsy revealed a collapsing form of focal segmental glomerular sclerosis with moderate interstitial fibrosis and tubular atrophy. There was no evidence of cellular or antibody-mediated rejection, or acute or chronic calcineurin effect. BK virus staining was negative. Human immunodeficiency virus, parvovirus B19, and antinuclear antibody serology were negative. BK and cytomegalovirus loads were negative. He had no prior exposure to bisphosphonates, interferon, or heroin. Apolipoprotein A1 (*APOL-1*) genotyping revealed a low-risk genotype (homozygous G0/G0) for both the donor and the recipient.

CONCLUSIONS Renal manifestations of COVID-19 are varied and include COVAN, which should be considered as a cause of allograft dysfunction in a setting of previous or recent COVID-19 infection, irrespective of the severity of respiratory symptoms. This is the first reported case of COVAN in a renal allograft in Africa in a patient with low-risk *APOL-1*, and it highlights the need for renal allograft biopsies in transplant recipients with worsening renal function in the era of COVID-19. Furthermore, this case highlights that the pathogenesis of COVAN is likely multifactorial.

Key words
allograft dysfunction, collapsing glomerulopathy, COVAN, podocytopathy

ROLAND ORAVSKÝ

A rare case of an unawakenable patient

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INTRODUCTION Acute disorders of consciousness require immediate and effective examination to prevent progression and irreversibility of the clinical condition.

CASE REPORT The author presents a case of a patient with acute disorder of consciousness of the nature of sopor, with unremarkable medical history. The immediate computed tomography angiography (CTA) of the head and neck showed no signs of acute stroke. Extensive laboratory tests were negative and neurological examination revealed no clear neurological deficits. Additional magnetic resonance imaging angiography of the brain demonstrated occlusion of the artery of Percheron, which is a variant of the posterior cerebral circulation in which a single arterial trunk arises from the posterior cerebral artery and supplies both sides of the thalamus and mesencephalon. It is a very rare cause of acute stroke, which cannot be usually diagnosed with CTA. It represents an estimated 0.1%–2% of all strokes.

DISCUSSION As this case proves, negative CTA does not exclude the possibility of an acute stroke and an internist could be the physician of the first contact. Therefore, broad knowledge on differential diagnosis of disorders of consciousness, even outside the professional field, is necessary for an internist in the emergency department.

Key words
artery of Percheron, AOP infarction, stroke, thalamic infarction

HYUNHO SEOL

Hyperammonemic encephalopathy after high-dose dexamethasone suppression test for Cushing's disease

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INTRODUCTION Ornithine transcarbamylase deficiency (OTCD) is a rare X-linked urea cycle disorder. Gene mutation analysis can confirm the diagnosis of OTCD. Affected men show lethargy, anorexia, vomiting, and altered mental status immediately after birth and usually die of cerebral edema. On the contrary, women being OTCD carriers do not show symptoms until ornithine transcarbamylase is overwhelmed by its substrate. Encephalopathy can be triggered by specific circumstances such as starvation, infection, and steroid use, in which a large amount of body protein is degraded.

CASE REPORT We report the case of a 46-year-old woman with altered mentality who was recently diagnosed with Cushing's syndrome and underwent high-dose dexamethasone suppression test 3 days before hospitalization. Her Glasgow Coma Scale score at the time of arrival was 10. Initial laboratory results showed normal liver and renal function but significant hyperammonemia (170 μmol/l). Initial electroencephalography (EEG) showed triphasic morphology, indicating the possibility of metabolic encephalopathy with no pathologies at the brain imaging workup. After detailed history taking, we found that she is an OTCD carrier. She learned about her mutation 15 years ago because of the perinatal death of her brother and her son; however, she had no problems to date. As glucocorticoids increase the levels of protein catabolism byproducts including ammonia, we assessed her for hyperammonemic encephalopathy

triggered by steroid-induced protein catabolism, because she was the OTCD carrier. We administered ammonia-lowering agents and continuous renal replacement therapy (CRRT). After 3 days of CRRT, her serum ammonia level decreased (46 μmol/l), cognitive impairment resolved, and EEG findings improved. She was discharged without any sequelae and asked to maintain a low-protein diet. After the high-dose dexamethasone suppression test, the diagnosis of adrenocorticotropic hormone-independent Cushing's syndrome was confirmed because of the presence of a right adrenal mass. Although unilateral adrenalectomy is a standard therapy, we decided to follow-up as postoperative steroid replacement is necessary, likely to cause hyperammonemic encephalopathy again.

DISCUSSION Steroids are used for various purposes in the medical field and are generally safe. However, they can trigger ammonia toxicity in patients with urea cycle disorders. OTCD should be considered in patients with adult-onset hyperammonemic encephalopathy because asymptomatic carriers can develop OTCD when triggered by factors that increase protein catabolism, such as steroids. To treat hyperammonemic encephalopathy, early hemodialysis is very important for correcting hyperammonemia with the use of benzoate and phenylacetate, which help to excrete excess nitrogen.

Key words
Cushing's syndrome, encephalopathy, high-dose dexamethasone suppression test, hyperammonemic, ornithine transcarbamylase deficiency

OTHER PRESENTATIONS

M. SEREN AKSUN

A rare case of multiple myeloma presenting with seropositivity of anti-double stranded DNA autoantibody

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CASE REPORT Malignancies have a variety of presentations, whereas seropositivity of anti-double stranded DNA (anti-dsDNA) antibodies is uncommon and this makes it difficult to diagnose. Our case report refers to a 67-year-old Caucasian man who was admitted to a hospital with abdominal pain and bloating. Portal vein thrombosis was detected, and subsequently hematological and rheumatological diseases were investigated for differential diagnosis. With these examinations, the anti-dsDNA antibody level was found to be very high but the patient did not fulfill diagnostic criteria of systemic lupus erythematosus (SLE). A *Crithidia luciliae* indirect immunofluorescence test for anti-dsDNA was negative. Consequently, the patient was diagnosed with multiple myeloma based on bone marrow aspiration biopsy and renal biopsy results. As the detection of certain autoantibodies in some malignancies without underlying rheumatological process has increased, the interpretation of clinical manifestations is crucial. Appropriate interpretation of the techniques used in anti-dsDNA antibody determination is important in the diagnosis of SLE.

Key words
autoantibody, cancer, multiple myeloma, serology, systemic lupus erythematosus

ANNA BRASZAK-CYMERMAN

From Cushing's syndrome to lipodystrophy: a case report of an ultra-rare *MFN-2*–associated lipomatosis

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INTRODUCTION Lipodystrophies are rare diseases characterized by a total or partial loss of adipose tissue. Lack of subcutaneous depots and ectopic fat tissue accumulations in the liver, muscle, pancreas, and blood vessels leads to metabolic disorders, such as insulin resistance, diabetes mellitus, nonalcoholic fatty liver disease, and hypertriglyceridemia. The clinical picture is usually accompanied by a low concentration of leptin.

CASE REPORT A 33-year-old woman was admitted to a hospital due to abdominal pain and severe hypertriglyceridemia. The patient was also diagnosed with type 2 diabetes, hypertension, high insulin resistance, and polycystic ovary syndrome. The patient was hospitalized twice due to a cushingoid appearance, but based on laboratory and imaging studies, Cushing's syndrome was excluded. Laboratory tests revealed mild hypertransaminasemia, severe hypertriglyceridemia, high ferritin levels, increased level of lactic acid, and very low leptin level. Hemochromatosis, Wilson's disease, and autoimmune hepatitis were excluded. Computed tomography confirmed fatty liver and hepatomegaly. Magnetic resonance imaging showed a particular accumulation of subcutaneous fat in the neck and back, and almost complete disappearance of subcutaneous fat in the arms, hips, and legs. At the age of 34, the patient began to report paresthesia in the feet and increasing pain in the extremities of the nature of neuropathy. Genetic testing did not confirm a mutation in the *LMNA* gene. Mutations in this gene are responsible for the majority of lipodystrophies with a partial familial lipodystrophy phenotype. Whole exome sequencing was then performed. The pathogenic c.2119C>T p.Arg707Trp variant and the c.1496-2A>G p.? variant were found, each in a single copy of the *MFN-2* gene. A review of the available literature made it possible to diagnose a patient at the age of 35 with *MFN-2*–associated lipomatosis, classified as lipodystrophy, caused by biallelic mutations of the *MFN-2* gene, one of which is the p.Arg707Trp mutation.

DISCUSSION In recent years, there have been reports describing patients with homozygous mutations at p.Arg707Trp in the *MFN-2* gene presenting multiple symmetric lipomatosis with neuropathy. Then it was revealed that also biallelic *MFN-2* mutations and at least one p.Arg707Trp allele induce mitochondrial dysfunction leading to upper body adipose hyperplasia and suppression of leptin expression. To the best of our knowledge, our case is only the third such published case with described biallelic mutation.

The *MFN-2* gene encodes mitofusin 2, which is involved in mediating mitochondrial fusion, plays a role in mitochondrial autophagy, mitochondrial motility, lipid transfer, and serves as a bond for other organelles. So far, it has been shown that impairment of these functions caused by a mutation in the *MFN-2* gene was responsible for the development of the peripheral neuropathy, that is, Charcot–Marie–Tooth disease. A deeper understanding of the pathophysiological basis of mitochondrial diseases may in the future lead to a better understanding of these diseases and introduction of targeted treatment.

LESSONS TO BE LEARNED Lipodystrophies are a heterogeneous group of diseases that still require a better understanding. Rare occurrence of the disease, a clinical picture similar to the metabolic and Cushing's syndrome, and difficulties in pinpointing the diagnosis based on genetic testing may result in underdiagnosis. Increasing the awareness of the disease may contribute to more frequent diagnosis of lipodystrophy, interdisciplinary efforts to improve treatment, and the availability of already existing treatment with leptin analogs.

Key words
adipose tissue, leptin, lipodystrophy, mitofusin, neuropathy

KATEŘINA BLÁHOVÁ

RECOGNIZED FOR BEST POSTER

Torsade de pointes as an unexpected result of common medication changes

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CASE REPORT Our patient, an older woman, was hospitalized after several collapses with serious ion imbalance, which was discovered to be iatrogenic, specifically due to indapamide and desmopressin recently combined in her medication. She was admitted to the intensive care unit with hyponatremia and hypochloremia (Na, 118 mEq/l; Cl, 80 mEq/l), hypokalemia (3.12 mEq/l), and hypomagnesemia (0.58 mEq/l), and her electrocardiogram showed a prolonged QT interval. During her hospital stay, she developed several episodes of symptomatic "torsade de pointes" terminated by acute cardioversion. In the patient's family history, we discovered the Romano–Ward syndrome, a variant of long QT syndrome caused by a defective *KNCH2* gene, in her sister, nephew, and niece, who had already received an implantable cardioverter-defibrillator (ICD) to prevent the episodes of ventricular arrhythmia. Our patient was also scheduled for an ICD implantation, which went through successfully.

The patient was taking 2 different drugs with hyponatremic effects prescribed by doctors of 2 different specializations. Her urologist prescribed desmopressin to treat nycturia and urinary

incontinence. At the time, she used angiotensin-converting enzyme inhibitors and calcium channel blockers for her hypertension, but the latter had been exchanged for a diuretic by her general practitioner. Desmopressin's effect of lowering plasma sodium level due to water retention was therefore increased by the concurrent treatment with diuretic causing hyponatremia by increased natriuresis. In our patient's case, the hereditary tendency to long QT intervals aggravated the influence of iatrogenic ion imbalance (hyponatremia and hypochloremia, hypokalemia, hypomagnesemia) on QT interval. Iatrogenic causes of hyponatremia, despite being the most preventable, seem to be among the most prevalent in patients hospitalized in internal medicine wards. And despite polypragmasia being much discussed, especially in recent years, we are still not sufficiently aware of its various dangerous consequences on an everyday basis, as this case shows.

Key words
hyponatremia, QT interval, Romano–Ward syndrome, torsade de pointes

DENIZ CENGIZ

SGLT-2 inhibitor-related euglycemic diabetic ketoacidosis in a COVID-19 pneumonia patient: a case report

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INTRODUCTION Sodium-glucose cotransporter 2 (SGLT-2) inhibitors are one of the most commonly used oral antidiabetic agents, but despite their established benefits might, on rare occasions, cause life-threatening complications in selected patients.

CASE REPORT A 74-year-old woman with known type 2 diabetes mellitus and COVID-19 pneumonia was transferred to our facility due to metabolic acidosis. Laboratory tests revealed pH of 7.08, HCO_3 concentration of 8 mmol/l, and glucose concentration of 189 mg/dl. The patient was cachectic and her oral intake of food was reduced. She was treated for COVID-19 pneumonia established based on thoracic computed tomography (CT) and polymerase chain reaction results. Her condition further deteriorated even though she had mild COVID-19–related symptoms. When transferred to our unit, the patient was on dapagliflozin and had ketonemia. She recovered after administration of ketoacidosis protocol. During her admission and treatment, the patient was not intubated or hypoxic and did not require continuous oxygen therapy. She did not have any significant COVID-19–related respiratory symptoms or fever. Her blood glucose levels were between 152 mg/dl and 307 mg/dl. She was treated according to the thoracic CT results, and the underlying diabetic complication due to SGLT-2 inhibitor dapagliflozin was overlooked because of her cachectic state and lack of aberrant hyperglycemia. A lack of sufficient intravenous hydration, insulin treatment, and caution caused the patient's deterioration.

DISCUSSION During the COVID-19 pandemic, several case reports and reviews suggested the importance of not overlooking the obvious culprits because of the fear and unknown created by the pandemic. Many of the severe COVID-19 pneumonia cases were diagnosed in the geriatric population, and diabetes mellitus was one of the most common comorbidities. Increased use of SGLT-2 inhibitors among diabetic patients should direct our attention to early detection of euglycemic diabetic ketoacidosis, which requires a high level of awareness due to its atypical presentation.

Key words
COVID-19, euglycemic ketoacidosis, SGLT-2 inhibitors

MERVE GÜZEL DIRIM

Atypical presentation of cytomegalovirus-associated cryoglobulinemic vasculitis following SARS-CoV-2 infection

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INTRODUCTION Cryoglobulinemia is a rare disease that frequently presents with small vessel vasculitis. The skin, joints, peripheral nervous system, and kidneys are the most commonly involved organs. Etiology includes autoimmune diseases, infections, or malignancy. The preferred therapeutic approach is to treat the underlying cause.

CASE REPORT A 46-year-old Caucasian woman presented to the internal medicine department with complaints of shortness of breath and edema in the legs, which started approximately 1.5 month ago. She had a history of hospitalization due to severe COVID-19 2 months before and steroid use for 1 month.

On physical examination she had exertional dyspnea. She also had hepatomegaly, dullness over Traube's space, and diminished bibasilar lung sounds. There were more than 3 pitting edemas and an annular, nonblanching, purpuric rash on the lower extremities. Blood tests revealed normocytic anemia (hemoglobin, 9.7 g/dl; mean corpuscular volume, 85 fl), hypoproteinemia of 5 g/dl (reference range, 6–8 g/dl), and elevated levels of N-terminal pro–B-type natriuretic peptide of 5100 pg/ml (reference range, 0–125 pg/ml). Thoracic and abdominal computed tomography angiography showed bilateral pleural effusion and free fluid up in the pelvis. Pericardial fluid (12 mm) was present along the left ventricular posterior wall on transthoracic echocardiogram. The sample of pleural fluid was consistent with transudative effusion. Hypogammaglobulinemia (immunoglobulin G, 464 mg/dl) was present in serum electrophoresis. The level of C3 was in the normal range (96 mg/dl). A low level of C4 (2.3 mg/dl) and an elevated level of rheumatoid factor (RF) (234 IU/ml) were consistent with cryoglobulinemia. Also, the cryoglobulin test was positive. A few damaged small-diameter vessel walls and intense neutrophil infiltration were noted in the biopsy of the purpuric lesion. It was compatible with leukocytoclastic vasculitis, and the diagnosis of cryoglobulinemic vasculitis was made.

The patient was evaluated for underlying etiology. The Schirmer test was normal (25/27 mm). QuantiFERON, viral serology, and HCV-RNA levels were negative. Tumor markers were within the normal range. Positron emission tomography-computed tomography showed no abnormal findings. There was no evidence of lymphoproliferative disease in the bone marrow biopsy. Serum cytomegalovirus (CMV) DNA level was 67 500 copies/ml. CMV viremia was considered a consequence of immunosuppression after COVID-19. Pericardial effusion might be related to CMV-associated pericarditis. Cryoglobulinemia-related pericarditis and serositis due to post-COVID-19 syndrome are the other usual suspects. Finally, methylprednisolone 20 mg/day was started in addition to ganciclovir 5 mg/kg/day. Pericardial effusion, purpuric lesions, and hepatosplenomegaly resolved 1 month after CMV treatment. Antiviral and steroid treatments were completed after 2 months, and serum CMV DNA was negative at the last 2 outpatient visits.

DISCUSSION In this case, we thought that the patient's COVID-19 and the immunosuppressive treatment at hospitalization were predisposing factors to CMV viremia. Also, we considered that the CMV infection triggered cryoglobulinemia, after the exclusion of other causes. Severe pericardial effusion could be related to CMV pericarditis, post-COVID-19 serositis, or cryoglobulinemia with cardiac involvement.

LESSONS TO BE LEARNED Cryoglobulinemia should be kept in mind in the differential diagnosis of patients with isolated low C4 and RF positivity. Cardiac involvement could be a rare presentation of cryoglobulinemic vasculitis.

Key words
cytomegalovirus infection, cryoglobulinemia, pericarditis

HEBA FAHMY

An acute hot swollen joint: it is not always crystal clear

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INTRODUCTION An acute hot joint is a presentation frequently encountered by clinicians. Despite this, studies demonstrate a widespread lack of confidence in dealing with this common presentation and resultant suboptimal management.

Septic arthritis (SA) is a medical emergency that confers over 10% mortality with a single joint involvement, and rising above 50% in polyarticular disease. Crystal arthropathies, chiefly gout and calcium pyrophosphate deposition, represent the major alternative diagnoses. Prompt differentiation of these pathologies by diagnostic joint aspiration is crucial to commence appropriate targeted therapies. We present a case which elucidates the paramount importance of joint aspiration in determining the underlying diagnosis

CASE REPORT An 80-year-old woman presented to our hospital in October 2020 with confusion, fever, and arthralgia. She was well known to the local rheumatology department with a background history of rheumatoid arthritis (RA) diagnosed in 1988, managed with methotrexate monotherapy since 1995. Other notable past medical history included bronchiectasis, osteoarthritis, and previous biliary sepsis. Upon admission to the hospital, intravenous antibiotic therapy was commenced for presumed urinary or chest infection. Relevant bacteriological cultures were negative, including for COVID-19. Left elbow pain and swelling became evident on review, thus empirical treatment for SA was commenced. A radiograph was obtained, showing changes consistent with known RA. Elbow joint subsequently aspirated by the rheumatology team demonstrated calcium pyrophosphate dihydrate (CPPD) crystals, with Gram stain and culture negative. Antibiotics were discontinued and targeted management for acute crystal arthritis led to marked clinical improvement sufficient for discharge from the hospital. The patient represented 2 weeks later with recurrence of delirium, fever, and widespread arthralgia. Despite scattered small joint synovitis, the left elbow remained disproportionately swollen and tender. Further aspiration of the elbow demonstrated CPPD crystals; however, bacteriology confirmed bloodborne Gram-negative bacilli. The patient was commenced on intravenous antibiotics for Gram-negative SA with resultant clinical improvement.

DISCUSSION Here we present a patient with RA, CPPD, and SA coexisting, with several risk factors for Gram-negative SA. Predominant causative organisms include *Staphylococcus aureus* and *Streptococcus* species, though Gram-negative organisms pose a risk in patients with immunosenescence or other forms of immunosuppression. As many as 1%–5% of patients with acute crystal arthritis have concomitant SA. Patients with rheumatic and musculoskeletal diseases may present atypically without classic features of SA, conferring poorer prognosis due to diagnostic delays. Although SA is usually monoarticular, as in our patient, polyarticular presentations can occur (15% cases) and are associated with higher mortality rates (>50%). Fundamentally, though the differential diagnosis is wide, all patients presenting with an acute hot joint should be assumed to have SA until proven otherwise and undergo diagnostic joint aspiration.

Key words
acute monoarthritis, crystal arthritis, septic arthritis

ANDREI-CRISTIAN-DAN GHEORGHE

An unusual cause of cholestasis and sepsis in an oncological patient

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INTRODUCTION Small bowel cancers are rare but aggressive tumors, and 15% of them are malignant connective tissue tumors. As many as 85% small bowel malignant connective tissue tumors are derived from interstitial cells of Cajal (gastrointestinal stromal tumors [GISTs]). The mainstay of treatment is a surgical resection followed by adjuvant therapy with protein kinase inhibitor imatinib, but the rate of recurrence is 40% and there is a high prevalence of liver metastases, which have an early manifestation as clinically and laboratory-proven cholestasis. However, not all cholestatic syndromes in such patients are metastatic. We present a case of a late surgical complication after GIST resection responsible for cholestasis and sepsis.

CASE REPORT We present a case of a 77-year-old man with duodenal GISTs who underwent pancreaticoduodenectomy, cholecystectomy, metallic biliary stent implantation, and gastrointestinal and biliointestinal anastomosis (Whipple procedure) 5 years ago. Since the surgery, he has received imatinib mesylate.

He presented to the hospital with chills, abdominal pain, and emesis with bile. Laboratory tests showed cholestasis, inflammation, blood culture positive for *E. coli*, and abdominal ultrasound raised a suspicion of the left hepatic biliary duct dilation, hepatic metastasis, and thrombus in the right hepatic vein. The first diagnostic hypothesis was cancer relapse and hepatic metastasis but it was not confirmed by magnetic resonance imaging and liver computed tomography. The imaging showed hepatic microabscesses, dilatation of the left biliary tract, and raised a suspicion of a proximal migrated metallic stent.

The patient improved after an antibiotic therapy for *E. coli*–related cholangitis and liver microabscesses. Right suprahepatic vein thrombosis also disappeared, suggesting that it was an infectious event. The patient then went into surgery during which numerous calculi were evacuated from the dilated left biliary tract. The postoperative course was uneventful.

DISCUSSION Biliary strictures and cholangitis occur in 8% of patients 3 to 4 years after the Whipple procedure but the real burden of these late complications is difficult to estimate because the 5-year survival rate is only 25%. Stent dislocation and proximal or distal migration after endoscopic placement of a biliary endoprosthesis are uncommon, with an overall incidence of up to 6%. In our patient, this rare complication together with changes in the upper gastrointestinal anatomy due to the Whipple procedure were the causes of the cholestasis, intrahepatic lithiasis, and cholangitis, even though liver metastasis would be more probable to occur and to explain the clinical and laboratory picture.

LESSONS TO BE LEARNED This case illustrates the need to investigate in depth even seemingly clear oncological cases with a usually bad prognosis to find potentially reversible causes of their symptoms that could be cured.

Key words
biliary stent migration, biliary tract dilatation, cholestasis, duodenal cancer, intrahepatic lithiasis

MARYAM HAROON

Dancing movements due to endocrine deficiency: a case report

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INTRODUCTION Choreiform-ballistic movements have often been associated with lesions in basal ganglia and subthalamic nucleus. For a patient with dancing movements, hyperglycemia might be an initial presentation. We hereby present a case of a 19-year-old woman already on insulin who presented with subacute onset of abnormal movements. Laboratory investigations revealed raised blood sugar level, decreased arterial pH, positive urinary ketones, reduced serum calcium level, increased serum phosphate level, increased serum intact parathyroid hormone, hyper intensities at the level of basal ganglia on computed tomography (CT) brain plain. The purpose of this case report was to elaborate on the possibility of choreiform movements as a rare presentation of an endocrine deficiency, such as type 1 diabetes, in association with pseudohypoparathyroidism as well as the role of insulin, calcium, and vitamin D analogs in reducing the frequency and severity of these movements. Literature review showed a similar presentation with HONK/HHS secondary to type 2 diabetes in middle-aged and elderly patients but so far not in young individuals with type 1 diabetes and other underlying endocrine abnormalities.

CASE REPORT We report a rare case of a 19-year-old woman of Asian origin who had type 1 diabetes and developed choreiform-ballistic type movements. She had ketoacidosis secondary to uncontrolled hyperglycemia along with hypocalcemia secondary to either pseudohypoparathyroidism or an ongoing autoimmune process indirectly influencing the calcium metabolism by acting on the parathyroid gland. On CT brain plain basal ganglia were heavily calcified. We optimized her diabetes management along with calcium and vitamin D analogs (calcitriol or alfacalcidol) and her symptoms improved dramatically without using any specific antidopaminergic therapy or nerve stabilizers.

CONCLUSIONS Adults with mixed endocrine deficiencies can present with unique symptoms, such as choreiform-ballistic type movements that can be improved with exogenous administration/replacement of deficient hormone analogs, as in our case with insulin as well as calcium and vitamin D analog supplementation.

Key words

ballistic movements, basal ganglia, intact parathormone level, pseudohypoparathyroidism, type 1 diabetes

SHARLENE HO

Silicosis, dermatomyositis, and tuberculosis: uncovering the hidden links

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INTRODUCTION Silicosis has been associated with autoimmune diseases, such as rheumatoid arthritis (Caplan syndrome) and systemic sclerosis (Erasmus syndrome). However, its association with dermatomyositis is rare, with fewer than 20 cases reported in the literature. Silicosis also increases the risk of tuberculosis (TB) by 2- to 3-fold. We report a case of a missed diagnosis of silicosis, which linked 2 seemingly unrelated conditions of dermatomyositis and TB in the same patient.

CASE REPORT A 65-year-old construction worker presented with a 2-week history of dyspnea, fever, weight loss, and rash. On examination, he had erythematous plaques over his upper chest and back, extending to his upper arms. Neurological examination revealed proximal myopathy affecting both his lower limbs. Respiratory examination revealed decreased breath sounds with dullness to percussion over the right lower chest.

Given the characteristic skin rash (shawl sign) and symmetrical proximal myopathy, a diagnosis of dermatomyositis was made when further investigations revealed elevated muscle enzymes and irritable myopathy on electromyography.

Chest imaging showed a 3.5-cm hypodense mass with consolidations in the right lower lobe, loculated right pleural effusion, and enlarged right hilar and mediastinal lymph nodes. Diagnostic thoracocentesis showed lymphocytic exudate with raised adenosine deaminase. The pleural fluid acid fast bacilli (AFB) smear was negative and cytology was unrevealing.

He underwent thoracotomy, decortication, and wedge biopsy of the right lower lobe mass. Histology of the visceral pleura showed the presence of AFB with necrotising granulomatous inflammation, and the wedge biopsy of the lung mass showed hyalinizing granuloma. He was treated with anti-TB medications for 6 months, and immunosuppressive therapy (corticosteroids and intravenous immunoglobulin) for dermatomyositis.

His dyspnea gradually worsened over the next 3 years. Follow-up imaging showed persistence of the right lower lobe mass, which prompted repeat biopsies to rule out malignancy, given its strong association with dermatomyositis. There was also worsening of centrilobular nodules with eggshell calcification of the mediastinal lymph nodes. These radiological features were reminiscent of silicosis. Re-examination of his previous lung mass histology showed palisading granulomas and necrosis with many polarisable particles that were later identified as silicon dioxide. Further occupational history revealed unprotected exposure to silica for 40 years. His diagnosis was revised to progressive massive fibrosis (PMF), complicated by TB, with concurrent dermatomyositis.

DISCUSSION Critical examination of clinical information is essential in challenging cases like our patient in order to uncover the diagnosis of silicosis, which linked 2 seemingly unrelated conditions of TB and dermatomyositis. Silicosis is a form of pneumoconiosis characterized by inflammation and scarring of the lungs, with the formation of nodular lesions that can coalesce to form PMF. TB is a long-recognized complication of silicosis. Less known is the rare association between silicosis and dermatomyositis. The exact pathogenic mechanism is unknown; however, it is thought to be linked to immune dysregulation and alteration in the B- and T-cell function. Patients with dermatomyositis also have an increased risk of TB, especially those on chronic immunosuppressive therapy.

CONCLUSIONS A history of silica exposure should be actively sought in patients with dermatomyositis and/or TB.

Key words

autoimmunity, dermatomyositis, silica exposure, silicosis, tuberculosis

BERKAN KARABUĞA

Bilateral renal metastatic diffuse large B-cell lymphoma presenting with acute pancreatitis as a paraneoplastic syndrome: a case report

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INTRODUCTION Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) in the

world. The disease can involve many different parts of the body and is usually diagnosed with large masses in the abdomen. While the most common causes of acute pancreatitis are gallstones and alcohol, malignancies involving the pancreas are also included in the etiology. We present a rare case of a DLBCL patient with bilateral multiple renal metastases concomitant with paraneoplastic acute pancreatitis without pancreatic involvement.

CASE REPORT A 24-year-old woman with no known history of any disease was admitted with abdominal pain radiating to the back. The patient, who had significant amylase elevation in the tests, was hospitalized with a preliminary diagnosis of acute pancreatitis. While no pathologic finding in the pancreas and biliary tract was detected in imaging studies, a single mass in the left lung and bilateral multiple masses in the kidneys were found. The patient was diagnosed with DLBCL after further evaluation.

DISCUSSION In acute pancreatitis cases, the most frequently identified causes are gallstones and alcohol. Anatomical malformations, various drugs, and malignancies are also considered in the etiology. In our patient, no etiologic cause was found in the detailed history and imaging studies, and DLBCL was diagnosed with no pancreatic involvement, and it was thought that acute pancreatitis emerged as a paraneoplastic syndrome due to an existing malignancy. In addition, bilateral renal metastatic lesions are extremely rare in DLBCL clinical presentation.

CONCLUSIONS Our case report is remarkable in that it described the clinical presentation of paraneoplastic acute pancreatitis due to DLBCL without pancreatic involvement and bilateral multiple renal involvement, which is extremely rare in DLBCL.

Key words
acute pancreatitis, diffuse large B-cell lymphoma, metastasis, paraneoplastic syndrome

DONG JUN KIM

BAP1 mutation presenting with double primary renal cell carcinoma and mesothelioma misdiagnosed as metastatic renal cell carcinoma

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INTRODUCTION *BAP1* tumor predisposition syndrome is a rare hereditary cancer syndrome inherited in an autosomal dominant pattern, characterized by an increased risk of a variety of tumors, most commonly certain types of tumors in the kidneys, mesothelium, eyes, and skin. Here, we report a case of *BAP1* tumor predisposition syndrome presenting with double primary cancers, localized renal cell carcinoma (RCC), and metastatic peritoneal malignant mesothelioma, which could be misdiagnosed as metastatic RCC.

CASE REPORT A 51-year-old man came to our hospital complaining of left side pain in November 2020. The chest-abdomen-pelvis computed tomography showed a cystic mass in the lower pole of the kidney, omental cake with probable malignant ascites, and multiple lymph node enlargements at cardiophrenic, internal mammary, and mediastinal prevascular stations that were considered metastases from RCC by a urologist. He underwent radical nephrectomy and the pathologic diagnosis was pT1 clear cell carcinoma with Fuhrman nuclear grade 3/4. He was referred to an oncology department in December 2020 for systemic treatment for RCC. However, as the pattern of spread (omental cake and cardiophrenic and internal mammary lymph nodes) was atypical for RCC, the possibility of a double primary cancer was considered. He had a family history of multiple cancers: his second elder brother was diagnosed with peritoneal carcinoma, fourth elder brother was diagnosed with renal cancer, and his mother also died of gastric cancer. Therefore, laparoscopic biopsy of the omental mass was conducted, and the pathologic report confirmed diffuse epithelioid malignant mesothelioma. In the germline genetic test, a *BAP1* mutation (c.799C>T) was detected, which was considered a pathogenic variant. As RCC was a localized disease but mesothelioma was metastatic, he has received systemic treatment for metastatic peritoneal mesothelioma since January 2021.

DISCUSSION *BAP1* tumor predisposition syndrome is rare, and the double primary kidney and peritoneal cancer in this syndrome is even rarer. Our case demonstrates that the pattern recognition and clinical suspicion are important in detecting rare hereditary cancer syndromes and providing precise treatment.

Key words
BAP1 mutation, *BAP1* tumor predisposition syndrome, hereditary cancer syndrome

MAHLATSE MANKGELE

RECOGNIZED FOR BEST POSTER

Index presentation of atypical cystic fibrosis/cystic fibrosis transmembrane conductance regulator-related disorder/dysfunction presenting with severe COVID-19 pneumonia

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CASE REPORT The novel SARS-CoV-2 that causes COVID-19 has had a significant impact on all global functions. Although much is still being unveiled about the virus, it affects multiple organ systems and has a predilection for patients with certain risk factors including older age, high body mass index, chronic kidney disease, cardiovascular disease, chronic respiratory disease, and diabetes mellitus. In this case report, we shall explore a case of a young, previously healthy Afro-African woman hospitalized for COVID-19 during the first wave of the pandemic in South Africa. It was subsequently revealed that she had underlying atypical cystic fibrosis, the symptoms of which were unmasked by COVID-19.

Key words
atypical cystic fibrosis, bronchiectasis, COVID-19, cystic fibrosis

BEATRIZ MARTIN RAMOS

A wave as a trigger to a genetic disorder

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INTRODUCTION McArdle disease is a condition characterized by intense generalized tiredness with exercise intolerance and fatigue. The infrequency with which it is encountered makes it a formidable diagnostic challenge.

CASE REPORT A 45-year-old woman consulted with the emergency services due to intense muscle pain and a feeling of extreme contraction. She reported intense stiffness and tiredness. Later on she started with dark and foul-smelling urine. Clinical diagnosis of rhabdomyolysis was made. The blood test revealed high levels of creatine kinase (CK) and kidney failure, and urinalysis showed myoglobinuria. Other diagnostic tests including ultrasonography and chest X-ray were normal. The patient was discharged in good

clinical condition but at consecutive medical appointments she still complained of tiredness and had high levels of blood CK, so a genetic study was done that revealed a mutation in the *PYGM* gene. The patient has remained with fewer symptoms since she started on a carbohydrate-free diet and decreased the intensity of exercise.

This case illustrates the potential importance of following up on our patients once they are discharged with the purpose of reevaluation that, together with a clinical suspicion, can lead to a final diagnosis.

Key words
glycogen disease, rhabdomyolysis, trigger

MIQUEL MARTIN SOLIS

Diabetes insipidus secondary to bone metastasis in the clivus due to prostatic adenocarcinoma

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CASE REPORT Diabetes insipidus (DI) is a rare condition caused by hypothalamic alterations in the production of antidiuretic hormone (ADH), neurohypophysis dysfunction regarding its storage, or resistance of the renal cells to ADH. It involves dysregulation of water metabolism, resulting from a total or relative deficit of ADH. Typical clinical manifestations are polydipsia and polyuria, and analytical parameters of dehydration such as hypernatremia and elevated plasma osmolarity and inability to concentrate urine, that is, decreased urinary osmolarity. The main differential diagnosis is primary polydipsia. We present a case of a 66-year-old man who was admitted to the internal medicine ward for a workup of a possible prostatic syndrome and was finally diagnosed with stage IV prostatic adenocarcinoma with multiple bone M1 and clivus lesions that caused a pituitary infiltration leading to clinical symptoms of polydipsia, polyuria, hypernatremia, and high urinary osmolarity. After performing the Miller's test, the diagnosis of complete central DI was confirmed.

Key words
ADH, central diabetes insipidus, hypernatremia, polyuria, prostate adenocarcinoma

CLAYTON MICALLEF

Apixaban-induced vasculitis

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INTRODUCTION Apixaban is a rare cause of leukocystoclastic vasculitis. We present a case of a man who developed a vasculitic rash 4 days after starting apixaban following a cardioembolic stroke from a left ventricular thrombus.

CASE REPORT A 57-year-old man presented with a cardioembolic stroke from a left ventricular thrombus following a delayed presentation of a myocardial infarction. Apixaban was started 9 days later once a safe oral route was possible.

After 4 days he developed a vasculitic rash but remained systemically well. Blood tests including renal function and a vasculitis screen were within normal limits. A nephrology and dermatology review confirmed that the rash was likely a vasculitic reaction caused by apixaban. The drug was stopped and subcutaneous low-molecular-weight heparin was prescribed instead. Betnovate ointment twice daily and 50:50 ointment were also prescribed.

There was clinical improvement in the rash following cessation of apixaban and a biopsy was therefore felt unnecessary. Although a plan to start rivaroxaban had been made, the patient self-discharged and was lost to a follow-up.

DISCUSSION Apixaban is recognized as a rare cause of leukocytoclastic vasculitis. This reaction is secondary to immune complexes generated by the drug. Although the complication is rare, apixaban-like drugs are being increasingly often used in stroke medicine. The management of these cases is to stop the offending drug and consider immunosuppressive treatment. It is regarded safe to start an alternative anticoagulant due to different molecular structures of the drugs.

LESSONS TO BE LEARNED Direct oral anticoagulant (DOAC)-induced vasculitis is a rare complication but these drugs are increasingly often used in stroke medicine. In these cases, the offending drug should be stopped and an alternative DOAC should be started. Oral steroids should be considered if there is secondary organ or severe skin involvement.

Key words
apixaban, stroke, vasculitis

OVIDIU I. NEACSU

Unusual etiology of pulmonary hypertension

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INTRODUCTION Intravenous injection of crushed oral tablets may lead to pulmonary angiogranulomatosis as a result of excipient particles lodging into the pulmonary arterial bed. The condition termed excipient lung disease (ELD), described first in the 1950s but still underrecognized, is potentially fatal and requires a high index of suspicion and familiarity with the imaging findings, as patients may not admit to drug abuse. The most common excipient is talc, an inert insoluble particle that causes occlusion of the pulmonary arterioles due to foreign body granulomas leading to pulmonary hypertension.

CASE REPORT We report a case of a 43-year-old man presenting with a history of 6-month progressive exertional dyspnea and bilateral painful lower limb edema. He had a history of heroin abuse, being enrolled in a methadone rehabilitation program for the last 3 years. On clinical examination the following were observed: dyspnea at rest, 85% blood oxygen saturation in room air, arterial hypotension, tachycardia, normal body temperature, jugular vein distention, bilateral edema, bibasal crackles upon pulmonary auscultation.

Echocardiography tracing showed classic signs of right heart strain, confirmed by the echocardiogram that revealed a marked septal bounce and high probability of pulmonary hypertension, with otherwise normal left ventricular systolic and diastolic function. Chronic thromboembolic pulmonary hypertension was suspected and a computed tomography scan was performed but failed to confirm the diagnosis, showing diffuse bilateral centrilobular nodules. A suspicion of tuberculosis was raised, but both microscopy and sputum cultures were negative. The major diagnostic challenge was identifying the pulmonary granulomatosis that resulted in chronic cor pulmonale. Given the history of intravenous drug abuse, we considered ELD, and proceeded with the help of the patient's mother. She provided information on how the patient had started crushing, dissolving and injecting methadone into his legs, in a period which coincided with the onset of his symptoms. While adherence to the gold standard of diagnosis (which is pulmonary biopsy analysis) was impossible due to high bleeding risks, the constellation of imaging findings, the patient history, and analysis of the bronchoalveolar lavage fluid made the diagnosis of ELD a reasonable assumption.

Although the systemic congestion regressed following administration of diuretics, the pulmonary function aggravated in the next weeks and the patient died.

DISCUSSION The diagnostic challenge in this case was differentiating from tuberculosis, the radiological findings of centrilobular micronodules being more commonly caused by a bronchiolar than an arteriolar disease. The diagnosis of ELD, besides a high index of suspicion, requires familiarity with the imaging findings. From the therapeutic point of view, the options are limited. Although stopping the exposure is the most important measure, ELD is a progressive condition, leading to respiratory failure even years after the injection has ended.

LESSONS TO BE LEARNED This case report highlights the importance of integrating the clinical and paraclinical findings into the patient's context as the key step for diagnosis of ELD, which is currently a rare condition, but with increasing prevalence as the number of susceptible patients rises.

Key words
cor pulmonale, excipient lung disease, pulmonary hypertension, talcosis

ELIF B. ÖZBEN

Rare association detected along a long road to diagnosis: primary hypertrophic osteoarthropathy and myelofibrosis

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INTRODUCTION Primary hypertrophic osteoarthropathy (PHO; pachydermoperiostosis) is a rare autosomal recessive disease that develops as a result of prostaglandin-degrading enzyme 15-hydroxyprostaglandin dehydrogenase (HPGD) deficiency or mutations in the prostaglandin transporter *SLCO2A1* gene, impairing prostaglandin metabolism and causing multisystemic involvement. The disease is mainly characterized by hypertrophic skin changes, clubbing, and gradually developing periostosis of the distal bones of the leg and forearm. It has been reported that myelofibrosis can be seen in the form that develops due to mutations in the *SLCO2A1* gene.

CASE REPORT A 28-year-old man reported with complaints of swelling in the knees, wrists, and ankles, excessive sweating and thickening of the skin, droopy eyelids, weakness, and abdominal pain, which started to be noticed by the age of 22 and progressed over the years. The patient had been under investigation for intermittent anemia and spleen enlargement for about 10 years, and vitamin B_{12} and folate deficiency were detected, but the etiology could not be determined.

On physical examination, the patient was pale, his facial skin was very thick and with acne, his facial features were coarse, and he had bilateral blepharoptosis with deep lines on the forehead, thickening and curving of the scalp (cutis verticis gyrate). His knees, wrists, and ankles were enlarged, and clubbing was present in his fingers. Signs of arthritis were not detected. On abdominal examination, the liver was palpable 4 cm below the rib and the spleen extended into the left inguinal region.

Peripheral smear revealed pancytopenia (white blood cells, 3.79 x 10^9/l; neutrophils, 2960 x 10^9/l; hemoglobin, 7 g/dl; hematocrit, 22.4%; mean corpuscular volume, 87 fl; platelets, 64 x 10^9/l) in hemogram, and leukoerythroblastosis and diffuse tear cells in erythrocytes were observed. Bone marrow aspiration was dry-tap, increased imprint and dysplastic megakaryocytes were seen. Bone marrow biopsy was hypocellular and consistent with myelofibrosis. The *JAK2* V617F and *JAK2* exon 12 gene mutations were not detected.

Cortical thickening in the long bones was seen on bone radiography. Diffuse increased activity uptake was observed on the whole body bone scintigraphy and the findings were found to be compatible with hypertrophic osteoarthropathy.

Secondary causes were primarily investigated for hypertrophic osteoarthropathy, but no pathology was found. No pathology was detected in the tests for storage diseases. The *SLCO2A1* homozygous mutation was detected in the molecular genetic whole-exon sequencing analysis of the patient, and secondary causes were excluded. The patient was diagnosed with primary hypertrophic osteoarthropathy and myelofibrosis associated with this disease.

DISCUSSION PHO with multisystem involvement stabilizes and even resolves approximately 10 years after the first onset of symptoms. However, patients may develop significant comorbidities, such as bone marrow fibrosis and compressive neuropathy. Primary hypertrophic osteoarthropathy is usually treated symptomatically with nonsteroidal anti-inflammatory drugs (NSAIDs) and plastic surgery. NSAIDs do not cause regression of skeletal findings. Treatment is difficult in patients who develop myelofibrosis and there is no effective treatment method. It has been shown on a case-by-case basis that corticosteroids can reduce transfusion dependence in this patient group in which classic JAK/STAT inhibitors do not work.

Key words
blepharoptosis, clubbing, myelofibrosis, primary hypertrophic osteoarthropathy, *SLCO2A1* gene

ARIANNA PANNUNZIO

Differential diagnosis of syncope and anemia in a newly discovered systemic transthyretin amyloidosis

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INTRODUCTION This is a case of transthyretin wild type amyloidosis (ATTRwt), a rare condition associated with extracellular deposits of a misfolded protein. An 87-year-old man reported to the emergency department for rectorrhagia resulting in anemia whose extent did not correlate with the laboratory parameters and seemed of multifactorial origin. Treating all its components, we focused on syncopal episodes and, together with echocardiography and other diagnostic studies, made a diagnosis of amyloidosis. Then we looked for its cause and checked for extracardiac involvement.

CASE DESCRIPTION The patient reported to the hospital for rectorrhagia. He was recently discharged after an episode of syncope treated with transfusion for anemia. His medical history included ischemic heart disease with a recent stenting in the course of double antiplatelet therapy, chronic kidney disease, arterial hypertension, hyperthyroidism, aortic stenosis and insufficiency, and multiple syncopal episodes. He was on ramipril, ticagrelor, salicylic acid, allopurinol, calcitriol, furosemide, atorvastatin, and tapazole.

He was alert, oriented, eupneic, and apyretic. His blood pressure was 130/70 mm Hg, heart rate 60 bpm. Systolic aortic murmur 3/6, known in anamnesis. A rectal examination revealed bright red blood. Chemistry tests demonstrated anemia and increased creatinine, with the remaining parameters unaffected.

Colonoscopy evidenced internal hemorrhoidal congestion. Laboratory tests confirmed normochromic normocytic anemia with reduced transferrin saturation, and decreased folic acid and erythropoietin. Serum and urine immunofixation, β-2 microglobulin, and Bence-Jones proteinuria were within the limits of normal.

The rectorrhagia was a minor bleeding due to constipation from easily bleeding hemorrhoids when on double antiplatelet therapy. Cardioaspirin and ticagrelor were interrupted and replaced by clopidogrel. Furthermore, all deficient factors were restored.

With regard to syncope, the clino-orthostatic test was positive. The tilt test confirmed orthostatic hypotension with reduced sinus

vagal modulation. Considering the patient's myocardial ischemic disease, his syncope was highly suspected to be of cardiogenic origin. However, 24-hour echocardiographic monitoring did not evidence any significant arrhythmia. The echocardiogram showed features indicating cardiac amyloidosis: granular sparkling, increased valve thickness, and reduced longitudinal strain with apical sparing.

To confirm this hypothesis, the myocardial scintigraphy was performed and confirmed a grade 2 of the Perugini score. The saliva test with amyloidotic *TTR* gene research was negative. In accordance with the diagnosis of cardiac ATTRwt amyloidosis and taking into account the bilateral tunnel carpal syndrome, the patient showed a severe axonal sensory-motor neuropathy.

Under the new recommendation of the 2021 European Society of Cardiology guidelines on chronic heart failure, the patient started treatment with tafamidis to reduce symptom severity as well as the risk of hospitalization and mortality.

DISCUSSION We reported a case of minor bleeding in a multifactorial anemia in a patient with syncopal episodes due to orthostatic hypotension and polyneuropathy. A new diagnosis of systemic amyloidosis was made and tafamidis treatment was started.

LESSONS TO BE LEARNED It is correct to start with an analysis of symptoms and signs on admission but it is mandatory to consider the patient's medical history as well as the results of the physical examination and routine tests. Internists play a key role in raising the clinical suspicion of amyloidosis in a multidisciplinary team. Making a diagnosis of ATTR, even at an advanced stage of the disease, brings about new therapeutic implications.

Key words
anemia, longitudinal strain, polyneuropathy, syncope, transthyretin amyloidosis

ARNAB PURKAYASTHA

A woman with short stature and amenorrhea

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CASE REPORT Pituitary stalk interruption syndrome (PSIS) is a rare condition with a prevalence of 0.5 per 1 000 000 births. PSIS is defined by the presence of a thin or missing pituitary stalk, a hypoplastic or aplastic anterior pituitary, and an ectopic posterior pituitary on magnetic resonance imaging (MRI). A 38-year-old woman with short stature presented with amenorrhea along with headache and vomiting on and off for the last week. The patient also complained of weight gain and lethargy for the past couple of months. On examination, she was afebrile, alert, conscious, and oriented to time, place, and person. Her height was 114 cm, weight was 32 kg, arm span was 116 cm, upper segment was 50 cm, lower segment was 64 cm, and the upper/lower segment ratio was 0.78. Laboratory investigations revealed a hemoglobin level of 7.9 g/dl (reference range [RR], 12–15 g/dl), total counts of 9940/mm^3 (RR, 4000–11 000/mm^3), and a random blood glucose level of 99 mg/dl (RR, 70–139 mg/dl). Red blood cells were hypochromic, renal function tests and liver function tests were within normal limits, growth hormone level was below 0.05 ng/ml (RR ≤8 ng/ml), thyroid stimulating hormone was 21.7 mIU/l (RR, 0.465–4.680 mIU/l), free thyroxine was 0.13 ng/dl (RR, 0.93–1.70 ng/dl), adrenocorticotropic hormone was 22 pg/ml (RR ≤46 pg/ml), cortisol at 8 am was 8.75 µg/dl (RR, 4.82–19.5 µg/dl), prolactin was 7.50 ng/ml (RR, 4.79–23.3 ng/ml), follicle-stimulating hormone (basal) was 1.16 mIU/ml (RR, 3.5–12.5 mIU/ml), and luteinizing hormone (basal) was 0.40 mIU/ml (RR, 2.4–12.6 mIU/ml). Brain MRI showed hypoplastic anterior pituitary with thin infundibulum. The posterior pituitary was ectopic and located along the median eminence in the floor of the third ventricle with absent posterior pituitary bright spot on T1 sequence, suggestive of pituitary stalk interruption syndrome. In a large Chinese study of 55 individuals with PSIS, 85.5% of patients had short stature, with a mean (SD) bone age delay of 7.26 (5.37) years. The prevalence of different hormonal deficits was 100% for growth hormone, 95.8% for gonadotropins, 81.8% for corticotrophin, and 76.3% for thyrotropin. As many as 36.4% of the patients tested positive for hyperprolactinemia. In 92.7% of the patients, there were more than 2 anterior pituitary hormone deficits. When posterior pituitary is present in the median eminence or the hypothalamic area, there is a larger frequency of anterior pituitary hormone deficiencies.

Key words
amenorrhea, pituitary stalk interruption syndrome, short stature

ANUM QAYUM

Recurrent sinonasal NUT midline carcinoma: the first ever case of a negative *p63* mutation

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INTRODUCTION NUT midline carcinoma (NMC) is an unusual malignancy arising due to differentiation of squamous cells, and it can grow in any place in the body but usually involves the head, neck, and lungs. The objective of this case report is to highlight the prognostic gravity of a negative *p63* mutation in NUT midline carcinoma.

CASE REPORT A 62-year-old woman presented with a 3-year history of recurrent frontal headaches, intermittent nasal bleeding, difficulty in breathing, and perception of a mass in her left nasal cavity. She demonstrated typical signs of malignancy of the head and neck. Based on incisional biopsy, it was confirmed to be a poorly differentiated NMC in the left maxillary sinus. Functional endoscopic sinus surgery was carried out with a complete removal of the mass, followed by chemoradiotherapy for 6 months. The patient showed recurrence after 8 months along with level II cervical lymphadenopathy. For this reason, medial maxillectomy and lateral rhinotomy were performed, during which the tumor was resected entirely and the normal structures were preserved. Two months later, the patient presented again with signs and symptoms of recurrence, and a computed tomography scan revealed a 4.0 cm × 3.4 cm × 2.5 cm, heterogeneously-enhanced, eroding mass. Subsequently, the patient underwent total maxillectomy—the entirety of the maxilla was resected, together with healthy structures along the lateral nasal wall, inferior turbinates, and hard palate. She was declared cancer-free after the surgery, with no residual disease.

CONCLUSIONS Our case is the only one reported in the literature where the NMC was negative for p63. This allowed us to hypothesize why the overall prognosis and survival for NMC are so good in our patient as compared with other cases reported in the literature.

Key words
midline carcinoma, *p63*, *NUT*, squamous

HÜSEYIN SEMIZ

A case of primary Sjögren's syndrome detected by refractory hypokalemia due to type 1 renal tubular acidosis

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CASE REPORT A 56-year-old woman with no chronic illness and drug use history reported to our emergency room with general weakness and muscular aches for about 10 days. On physical examination her muscle strength of the upper extremity was 4/5–4/5 and of the lower extremity 4/5–4/5. Laboratory results were as follows: sodium, 141 mEq/l (reference range [RR], 136–145 mEq/l), potassium, 1.9 mEq/l (RR, 3.5–5 mEq/l), chloride, 110 mEq/l (RR, 96–110 mEq/l), urine pH 8.0, and arterial blood gas analysis showed hypochloremic hypokalemic metabolic acidosis. The patient had refractory hypokalemia despite intravenous and oral potency. It was diagnosed as type 1 distal renal tubular acidosis (RTA) with the present findings. When the patient was examined in terms of systemic diseases accompanying RTA, there was no complaint of joint pain but she mentioned dryness in her mouth and eyes. Antinuclear antibody (ANA) level was found to be 1/2560 in granule, anti–Sjögren's syndrome type B and anti–Sjögren's syndrome–related antigen A antibodies were positive in ANA profile, and rheumatoid factor was 15.7 IU/ml (RR <14 IU/ml). The Schirmer test results were 3 mm/5 min (without anesthesia), breakup time was 4 seconds, minor salivary gland biopsy lymphocyte score was 2. Finally, the patient was diagnosed with primary Sjögren's syndrome. Symptomatic treatment for the ophthalmic dryness and methotrexate tablets were prescribed at a dose of 7.5 mg/week. The patient is now clinically stable and the treatment and follow-up are continued.

Key words
refractory hypokalemia, renal tubular acidosis, Sjögren's syndrome

ALI SHAKEEL

A rare association of Kartagener's syndrome with disseminated discoid lupus erythematosus

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INTRODUCTION Kartagener's syndrome (KS) is a rare form of primary ciliary dyskinesia inherited in an autosomal recessive pattern and characterized by a triad of situs inversus totalis, bronchiectasis, and chronic sinusitis. The main pathophysiological problem is impaired ciliary motility due to abnormal ciliary function or structure. Discoid lupus erythematosus is the most common form of chronic cutaneous lupus erythematosus and it can present either as localized form (80%) or disseminated discoid lupus erythematosus (DDLE) (20%). The DDLE is associated with an increased risk of progression to systemic lupus erythematosus. This case represents an unusual association between DDLE and KS.

CASE REPORT A 36-year-old woman, mother of 3 children, presented with recurrent episodes of nasal congestion and productive cough for 3 years. She also complained of multiple skin lesions on her abdomen, back, and forehead for 2 years. She has been treated multiple times with different courses of antibiotics, ointments, and other symptomatic remedies. Also, she had taken 1 full course of antituberculosis drugs without clinical improvement, rather worsening of the skin lesions.

On examination she was thin, lean, conscious, and oriented. There was no evidence of pallor, jaundice, or cyanosis but grade 2 clubbing was observed. Jugular venous pressure was not elevated and there was no pedal edema. On auscultation there were diffuse bilateral rhonchi throughout the chest along with scattered coarse crepitations in the infrascapular regions. Her heart sounds were not audible over the left apical region and were rather appreciable on the right side. There were multiple discoid, well-marginated, hyperpigmented plaques scattered over the front and back of the trunk and the forehead. The rest of the systemic examination was unremarkable.

Complete blood count showed neutrophilic leukocytosis with mildly raised erythrocyte sedimentation rate. Sputum and Gene Xpert were negative for acid fast bacilli. Tuberculosis gold QuantiFERON was negative. Echocardiography (ECG) was suggestive of dextrocardia. Radiography of the paranasal sinuses demonstrated haziness in the maxillary sinuses. Chest radiography showed right-sided cardiac apex with bronchiectatic changes. ECG confirmed dextrocardia. Further high-resolution computed tomography (HRCT) of the chest confirmed the presence of bronchiectasis. The ultrasound and CT scan of the abdomen showed the reverse alignment of abdominal viscera. All these features were suggestive of situs inversus totalis, and a final diagnosis of KS was made. Skin biopsy exhibited interface dermatitis with perivascular and periadnexal lymphocytic inflammation suggestive of DDLE. The antinuclear antibodies and anti-double stranded DNA antibodies were also positive. The patient was treated with intravenous and oral antibiotics, bronchodilators, nasal decongestants, mucolytics, and chest physiotherapy. Also, short courses of systemic steroids, topical steroids, hydroxychloroquine and sunblocks were advised for DDLE with significant improvement.

DISCUSSION KS should be considered in a patient presenting with recurrent sinopulmonary infections especially in the populations from countries with low socioeconomic status where the facilities for investigations are not readily available and the patient may be mistreated as having pulmonary tuberculosis. The association of KS and DDLE is extremely rare and is of clinical importance as the management of DDLE requires immunosuppression and steroids that can exacerbate infection in bronchiectasis.

Key words
disseminated discoid lupus erythematous, Kartagener's syndrome, primary ciliary dyskinesia, situs inversus totalis

DEBANJAN SINHA

A rare presentation of Wilson disease in a child under 2 years of age: hepatic encephalopathy in the presence of elevated aminotransferases without hyperbilirubinemia

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INTRODUCTION Wilson disease (WD) is an autosomal recessive disorder of copper metabolism, resulting in chronic liver disease and degenerative changes in the brain and other organs. The disease is usually observed to be detected after the age of 5 years, and the diagnosis before the age of 2 is challenging due to the atypical presentation at that age. Clinically, WD may present as acute liver disease, and the spectrum may vary from asymptomatic increase in the level of serum transaminases to fulminant hepatic failure. Hepatic manifestations of WD are rare in patients younger than 2 years, while neurological manifestations are extremely rare below the age of 5 years. In this background, we report a rare case of WD presenting with acute liver failure at 1.5 years. Another interesting finding was the absence of jaundice in spite of acute liver failure.

CASE REPORT A girl aged 1 year and 6 months presented initially with features of acute encephalopathy. A complete blood count, malarial parasites and antigens, as well as serology related to dengue, scrub typhus, and Japanese encephalitis were performed considering the possibility of tropical etiology of encephalopathy in the south-east Asian region. The cause remained undetected. The ultrasound examination at this stage showed mild ascites. The patient developed bleeding from the upper gastrointestinal tract. Liver function test showed elevated levels of alanine transaminase (3620 IU/l), aspartate aminotransferase (1790 IU/l), prolonged prothrombin time (29.8 s) with an international normalized ratio of

2.98, and activated partial thromboplastin time of 37.1 s. Serum level of bilirubin was 0.7 mg/dl. Sepsis screening was negative. Lumbar puncture ruled out meningitis, and magnetic resonance imaging of the brain excluded any structural abnormality in the central nervous system, including acute demyelinating encephalomyelitis. Clinically, jaundice was not present. Altered sensorium persisted and convulsion occurred. Transaminase levels remained elevated on serial reporting. Serum ceruloplasmin level was 16.7 mg/dl and 24-hour urinary copper was estimated to be 383.82 μg/day. As per the recent ESPHAGAN & NASPHAGAN guidelines, a diagnosis of WD was confirmed as the FERENCI score was 6. The child dramatically improved after 2 weeks of D-penicillamine and oral zinc therapy.

After a careful search of the literature, this appears to be the first case reporting such a rare presentation of WD manifesting as anicteric hepatic encephalopathy. Only 1 case of WD at 9 months of age was reported from South Korea, where the disease was confirmed genetically. In our case, genetic testing was not performed as the FERENCI score was 6, which is confirmatory as per the recent guidelines.

CONCLUSIONS Numerous infections may give rise to such an acute encephalopathy in the tropical region of south-east Asia. Thus, the diagnosis of WD is not straightforward. A high degree of suspicion is required in such clinical scenarios. However, emphasis should always be put on the diagnosis of WD as it is treatable. Therefore, a screening test for WD is to be considered in all cases of hepatic failure, whether acute or chronic, with encephalopathy and neuropsychiatric disorders.

Key words
acute encephalopathy, acute liver failure, FERENCI scoring, Wilson

PIOTR SKONIECZNY

Atypical hemolytic-uremic syndrome due to a scleroderma renal crisis treated with eculizumab

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INTRODUCTION The most serious manifestation of kidney involvement in systemic sclerosis (SSc) is scleroderma renal crisis (SRC), which is characterized by acute kidney injury and a sudden increase of blood pressure, sometimes accompanied by microangiopathic hemolysis. There are suggestions that activation of the complement system may be involved, which leads to the indication that eculizumab can be a successful treatment of this condition.

CASE REPORT A 46-year-old patient was hospitalized due to atypical chest pain. Heart magnetic resonance imaging revealed acute myocarditis of a viral etiology. On high-resolution computed tomography (HRCT) of the chest suspicious eosinophilic granulomatosis with polyangiitis (EGPA) or postinflammatory fibrosis were noticed. Additional tests were performed due to increased eosinophilia, and therapy with oral steroids was started because of deteriorated well-being. Due to the suspicion of progressive anemia and thrombocytopenia in the course of thrombotic microangiopathy (TMA), a therapy with freshly frozen plasma (FFP) and pulses of methylprednisolone was applied. As an increase in renal parameters and features of TMA were noted, plasmapheresis on FFP was performed and after the second exchange the patient's general condition deteriorated, showing overhydration, further worsening of the laboratory results, and an increase of blood pressure.

After capillaroscopy, a rheumatological consultation, and the result of ADAMTS-13 assay, the overall clinical image allowed a diagnosis of limited SSc, and a suspicion of an atypical hemolytic uremic syndrome (aHUS) in the course of SRC, which led to qualification for an aHUS treatment program with eculizumab. During the 3-month treatment with eculizumab, a significant improvement in hemoglobin and the number of platelets was observed, as well as a reduction in the level of lactate dehydrogenase. No side effects of the treatment were observed. The patient remains dependent on dialysis. In the genetic tests, variants of *CFH* and *ADAMTS13* were found, which may correspond to an increased risk of aHUS and a severe course of the disease.

DISCUSSION The role of complement in SSc and SRC remains unclear. Corticosteroids were used in our patient causing a deterioration of the general condition. However, the signs of TMA started before the administration of steroids. Nevertheless, the diagnosis of SSc was very difficult due to a nonobvious course. The patient never noticed Raynaud syndrome, and musculoskeletal symptoms were considered to be related to his past as a sportsman. Also, in the interview, eosinophilia and HRCT suggested the recognition of EGPA. The usual treatment of TMA was unsuccessful, and the treatment with eculizumab led to immediate improvement. Side effects of eculizumab were not observed. Studies on the use of eculizumab in SRC have several limitations, such as the small number of patients, lack of a control group, and coexisting effects of other drugs which are also used due to the life-threatening condition of the patients. Our patient is actually still dialysis-dependent, and he will be put on the transplantation waiting list.

CONCLUSIONS SSc is a systemic disease which can have a very tricky course and serious complications, including TMA. In severe cases of SRC complicated with TMA, eculizumab treatment can be life-saving, however, further studies are needed.

Key words
atypical hemolytic uremic syndrome, eculizumab, scleroderma renal crisis, systemic sclerosis, thrombotic microangiopathy

MEGAN SMITH-UFFEN

Presumptive diagnosis of MRSA bacteremia delays closure of symptomatic patent foramen ovale and leads to complications of antimicrobial therapy

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INTRODUCTION Presumptive diagnoses are common in the diagnostic process. The exact etiology of a patient's complaint may not be clear at initial presentation, and a working diagnosis may be needed to start empiric therapy, particularly if initial workup indicates a potentially lethal diagnosis. Initial diagnoses may lead to unintended consequences, including a delayed access to alternative treatment.

CASE REPORT A 70-year-old man presented to a hospital with altered level of consciousness (LOC). One of 2 peripheral blood cultures showed polymicrobial growth including methicillin-resistant *Staphylococcus aureus* (MRSA); complete workup was otherwise unrevealing. Given the positive blood culture and no other clear causes for his altered LOC, he was diagnosed with presumed uncomplicated MRSA-bacteremia and treated with intravenous antibiotics. Mentation normalized during his hospital course. Recurrent episodes of altered LOC resulted in multiple readmissions, with subsequent workup revealing new subacute bilateral intracranial infarcts, and echocardiographic evidence of a patent foramen ovale (PFO), right-to-left shunt, and Chiari network. Surgical closure of his PFO was carefully considered, however deferred due to his diagnosis of MRSA bacteremia. A prolonged course of antibiotics was pursued. His admission was complicated by antimicrobial-related cytopenias and line-related fungemia. He underwent PFO closure as an outpatient and has not had altered LOC episodes since.

DISCUSSION While it was prudent to treat the MRSA bacteremia, as it is associated with high morbidity and mortality, the underlying process for the patient's recurrent cerebrovascular events may well have been thromboembolic. The patient had several risk factors for thrombotic complications and a demonstrated anatomical mechanism (Chiari network and PFO). His diagnosis of MRSA bacteremia was equivocal, informed by a single positive culture with polymicrobial growth, and no risk factors or clear source of infection. Empiric treatment for a presumptive bacteremia delayed surgical intervention for an alternate presumptive process underlying his cerebrovascular events.

Percutaneous PFO closure reduces the risk of recurrent stroke when compared with medical therapy. However, active endocarditis/bacteremia is a contraindication. Risks of untreated MRSA bacteremia may also be balanced against adverse effects associated with antimicrobial therapy. Our patient developed thrombocytopenia attributed to vancomycin, and neutropenia attributed to ceftaroline. While neutropenic, he developed line-associated candidemia requiring antifungal treatment.

This case provides a valuable opportunity to reflect on challenges in dealing with coexisting presumptive diagnoses where treatment may not be pursued concurrently and may instead be precluded or delayed by the alternate diagnosis.

LESSONS TO BE LEARNED Clinicians may consider empiric treatment where a presumptive diagnosis, if left untreated, may lead to significant morbidity. Where coexisting presumptive diagnoses exist, clinicians may not be able to pursue treatments concurrently, and treatment for one diagnosis may preclude or delay treatment for another. Empiric therapy may be associated with unintended harms, including adverse effects directly associated with therapy, and delayed or missed treatment for competing possible diagnoses. New diagnostic data warrant frequent re-evaluation regarding relative likelihoods of possible diagnoses, associated benefits and harms of pursuing treatment for each, urgency of potential intervention, and the balance between overtreatment and undertreatment.

Key words
MRSA bacteremia, overdiagnosis, overtreatment, presumptive diagnosis, PFO closure

FATIMA SULEMAN

Episcleritis followed by COVID-19 pneumonia after COVID-19 vaccination

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CASE REPORT A 56-year-old man presented to the emergency department with bilateral eye pain, itching and watery discharge for 10 days, fever for 7 days, and cough for 1 day. He had been vaccinated against COVID-19, and had developed ocular symptoms 2 days after receiving the second dose of the Sinopharm vaccine. Investigations revealed that the nasal polymerase chain reaction was positive for COVID-19. We managed the patient on the lines of episcleritis but he developed critical COVID-19 pneumonia and was treated accordingly. The patient later deteriorated, and was intubated. He died on the 6th day of hospitalization as a result of a protracted disease course and ST-segment elevation myocardial infarction. Episcleritis was transient, and resolved after 12 days. We report the development of episcleritis and critical COVID-19 infection after COVID-19 vaccination to emphasize the consideration of antibody-dependent enhancement after vaccination.

Key words
COVID-19 vaccines, scleritis, SARS-CoV-2

LUCILA TORASSO

Longitudinal extensive transverse myelitis and mixed connective tissue disease: an unusual association of a rare disease

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INTRODUCTION Transverse myelitis is an acute or subacute inflammatory manifestation of the spinal cord with sensitive, motor, and autonomic compromise, which leads to great disability. It has a prevalence of 1 to 4 new cases per 1 million inhabitants, affecting individuals of all ages. It is usually associated with systemic autoimmune pathologies, mainly systemic lupus erythematosus (1%–2%) and Sjogren's syndrome (1%), with few reported cases associated with mixed connective tissue disease.

CASE REPORT A 53-year-old woman with a history of Raynaud's disease, dysphagia lasting for 4 months, and a low-grade squamous intraepithelial lesion due to HPV reported with 20-day-long lower limb paresthesia originating distally, with bilateral and symmetric ascending progression up to the thigh ligament, associated with gait disorder. Physical examination showed preservation of strength and deep sensitivity in both lower limbs with loss of thermalgesia, presence of hypoesthesia and paresthesia at the T4–T5 level, intact reflexes, bilateral positive Babinski reflex, and no sphincter control. Other symptoms included reduced mouth opening, peribuccal wrinkles and telangiectasias, skin thickening in the extremities, and widened fingers.

The laboratory tests were unrevealing. Lumbar puncture showed rock crystal liquid, glucose level of 65 mg/dl, protein level of 1 g/dl, and lactate dehydrogenase level of 3 UI/l, acellular. Anti–aquaporin-4 antibody and anti–myelin oligodendrocyte glycoprotein antibody tests were negative. Magnetic resonance imaging (MRI) showed isolated hyperintense focal images in T2 and fluid-attenuated inversion recovery at the level of the subcortical white matter of both cerebral hemispheres, with gliotic and nonspecific brain damage. Spinal MRI showed disc-osteophyte protrusion on the right side in segments C5–C6 with foraminal repercussion and, in segments T3–T6 and T8–T9, the spinal cord signal was altered in a spinal center disposition, bright in T2 and short-T1 inversion recovery, with no intravenous contrast backup.

Rheumatologic laboratory workup showed positive FAN (thick and big nuclear granular and nuclear homogeneous), positive anti-double stranded DNA, and positive anti-U1RNP antibodies. Due to the patient's history of dysphagia, serial esophagogastroduodenal X-ray was performed, showing a dilated aperistaltic esophagus in the middle and lower third, with evacuating retardation.

The patient was diagnosed with longitudinal extensive transverse myelitis with mixed connective tissue disease. Pulse methylprednisolone therapy was administered for 3 days; the patient responded well and cyclophosphamide treatment finally resolved the case.

DISCUSSION Mixed connective tissue disease presents a clinical picture and laboratory results suggestive of systemic lupus erythematosus or scleroderma-polymyositis, either simultaneous or chronological, with Raynaud's syndrome as an initial finding, and presence of anti-U1RNP antibodies. The neurological manifestations are relatively frequent, developing in 10% of patients, and transverse myelitis represents a rare complication (only 10 cases have been published in the literature). The pathogenesis is not completely understood, but it may include spinal cord artery vasculitis and the presence of circulating antibodies.

CONCLUSIONS Despite limited global experience, the prognosis of this association of pathologies is usually favorable, with good

response to high doses of steroids and immunosuppressive therapy, evolving with mild sequels and, in some cases, full recovery.

Key words
longitudinal extensive transverse myelitis, mixed connective tissue disease

FAISAL ZAHEER

The first reported case in medical literature: Lane-Hamilton syndrome and congestive cardiac failure

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CASE REPORT Lane-Hamilton syndrome (LHS) is a rare association of idiopathic pulmonary hemosiderosis (IPH) and celiac disease (CD). The definitive pathophysiological link is unknown, but the syndrome has been described as co-occurring with other diseases. Few children with CD had respiratory symptoms including hemoptysis that were compatible with IPH and were later labeled as LHS (IPH associated with CD). So far, in the medical literature only around 30 pediatric patients with LHS have been described with only 1 case with both LHS and congestive cardiac failure (CCF). We describe the first reported case of adult Lane-Hamilton syndrome and CCF. Lane-Hamilton syndrome associated with CCF may prove fatal if undiagnosed. As in CD, a gluten-free diet may prove beneficial in ameliorating the signs and symptoms of LHS as well as associated CCF. It is suggested that LHS associated with CCF may be renamed as LH Plus syndrome.

Key words
celiac disease, congestive cardiac failure, idiopathic pulmonary hemosiderosis, Lane-Hamilton syndrome

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When gastroenterology meets hematology: clinical picture suggesting Crohn disease as the manifestation of acute myeloid leukemia

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CASE REPORT Acute myeloid leukemia (AML) is the most common acute leukemia affecting adults, with at least 20% blasts in the bone marrow. Gastrointestinal lesions are found in approximately 25% of patients with leukemia and are usually detected in individuals with relapsed disease. On colonoscopy, infiltrates of the underlying disease or hemorrhagic lesions are usually found. Thickening of the intestinal wall is observed on ultrasound imaging and computed tomography. Crohn disease (CD) is a chronic inflammatory bowel disease the etiology of which is not fully known, however, it is documented that both genetic and environmental factors are involved. Here, a case of a 51-year-old woman with clinical picture suggesting CD as the manifestation of AML is reported.

Key words
abdominal pain, acute myeloid leukemia, Crohn disease, diarrhea, obstruction