

Spinal epidural abscess penetrating into retroperitoneal space in patient with diabetes mellitus type 2: early diagnosis and treatment requirement

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Abstract: Spinal epidural abscess (SEA) is a rare condition with very serious prognosis. Predisposing factors for SEA include bacterial infections, immunocompromised states such as diabetes mellitus, intravenous drug abuse, alcoholism, AIDS, as well as spinal surgery and modern techniques of epidural anesthesia. The most common causative agent for SEA is *Staphylococcus aureus*. The typical clinical signs of SEA are back pain, fever and neurologic deficit. Magnetic resonance of the spine and vertebral column is the best imaging diagnostic method in suspected cases. Emergency surgical decompression combined with intravenous antibiotics is the therapeutic method of choice. Conservative treatment may be appropriate in selected patients. Unless the typical presentation of SEA correct diagnosis of this illness is often overlooked and not considered initially. It delays suitable management and leads to poor outcome. We report a classic case of SEA in a woman with a history of diabetes mellitus.

Key words: diabetes mellitus, diagnosis, spinal epidural abscess, treatment

INTRODUCTION

Spinal epidural abscess (SEA) is a rare disease with high risk of disability and death. Its estimated incidence is 1/20,000 hospital admissions [1]. Despite extensive progress in diagnostic and therapeutic procedures, an early diagnosis and treatment of SEA remain a great challenge for the physician. There is a number of predisposing factors for SEA (Tab.). However, in nearly 20% of cases no risk factor can be identified [2,3]. The most common etiologic factor is *Staphylococcus aureus*, with increasing role of other microorganisms, due to progress made in neurosurgical techniques [1,4]. The most common localization of SEA is the thoracic and lumbar spine [5].

Clinical symptoms of SEA may depend on the triad of clinical symptoms such as localized spine pain, progressive sensorimotor deficits and radicular pain [1,4,5]. The case of the "classic" SEA of the lumbar spine in a 77-year-old patient with long-term history of diabetes presented here, confirms diagnostic difficulties and poor prognosis in such patients.

CASE REPORT

A 77-year-old female with a 12-year history of type 2 diabetes was admitted to the Internal Department with severe lumbar pain radiating to the right lower limb, muscular weakness of lower limbs (particularly the right one), fever and excessive thirst. The symptoms appeared about two months earlier. Since then she was hospitalized twice due to fever, lumbar and lower limb pain and symptoms of urinary tract infection in the Internal and Rheumatology Departments. The diagnosis of urinary tract infection had been confirmed by *Staphylococcus aureus* and *Enterococcus faecalis* isolation from the urine. In the Rheumatology Department the diagnosis of lupus-like syndrome was made with a characteristic clinical feature, the presence of anti-nuclear antibodies (ANA), proteinuria (2.9 g/24h) that persisted despite antibiotic therapy, together with high sedimentation rate and C-reactive protein (CRP) levels. An X-ray of hand and foot joints showed degenerative and proliferative lesions with geodes that led to the diagnosis of connective tissue pathology with even higher probability. Cancer considered as a potential cause of symptoms presented was excluded by means of computed tomography (CT) scan of the spine (revealing degeneration and L3-L4 and L4-L5 discopathy with L5 root compression), abdominal ultrasound, chest radiogram and specialist counseling. Treatment with high doses of nonsteroidal anti-inflammatory drugs and antibiotics administered according to antibiotics sensitivity profile (amoxi-

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Table. Spinal epidural abscess predisposing factors [2]

Predisposing factors	Incidence (%)
Infection	44
Abscess of skin and soft tissue	
Vertebral bone inflammation and myelitis/discitis	
Pulmonary tissue infection/mediastinitis	
Sepsis	
Immune deficiency	34
Diabetes	
Drug addiction/alcoholism	
Chronic renal failure	
Neoplastic disease	
AIDS	
Surgery of the vertebral spine/anesthetic procedures	22
Injury	10
No predisposing factors	20

collin + clavulanic acid with ciprofloxacin) were ineffective, thus corticosteroids were introduced (methylprednisolone *i.v.* 1000 mg daily for 5 days, subsequently prednisone 60 mg *p.o.* daily). The treatment of diabetes was modified, therapy with glimepiride was discontinued and human insulin twice daily (Mixtard 30 HM 42 U/24h) was initiated. That strategy resulted in clinical improvement and pain relief. The patient was released from hospital with the treatment recommended as follows: prednisone 20 mg/24h, diclofenac 100 mg/24h, omeprazole 20 mg/24h, insulin Mixtard 30 HM – 32 U/24h in two doses, lerivon 10 mg/24h. However, mild fever and lower limb (mainly the right one) muscle weakness that precluded to walk persisted. In about two weeks after the discharge of the patient from the hospital was again admitted to hospital because of general condition deterioration with severe lumbar pain, fever and uncontrolled diabetes evidenced by polydipsia.

On physical examination the patient had excruciating pains, was in grave general condition, immobilized, body mass index 24.5 kg/m², blood pressure 180/90 mmHg, body temperature 39°C, regular pulse, heart rate 100/min, heart sounds loud and hollow; single crackles at lung base, liver and spleen of normal size; painful, warm, oval skin lesion of the left olecranon process region, lumbosacral pain on palpation; peripheral lymph nodes not enlarged.

On neurological examination, the following findings were made: absence of meningeal signs, right lower limb muscle atrophy, particularly thigh muscles: quadriceps femoris muscle, adductor muscle and gluteus maximus muscle. Moreover, deep pain and sensory deficit on the right thigh below L1 with concomitant lack of deep reflexes in the left lower limb and left upper limb and proximal paresis of lower limbs was discovered. Extensor plantar response was ambilaterally negative.

Signs of root compression were impossible to assess because of severe pain. Stool and urine passing was normal. The left elbow synovitis was diagnosed by a consultant surgeon who recommended incision of the lesion that was performed the next day with synovial fluid aspiration for microbiology testing. Laboratory tests on admission showed leukocytosis ($18 \times 10^9/l$), elevated CRP (244 mg/l), elevated sedimentation rate (116 mm/h), hyperglycemia (248 mg/dl), elevated alanine aminotransferase (102 U/l), decreased total protein (4.9 g/dl), abnormal HbA_{1c} – 9.2%. Lipid profile was as follows: total cholesterol 189 mg/dl, triglycerides 267 mg/dl, high-density lipoprotein cholesterol 34 mg/dl, low-density lipoprotein cholesterol 101.6 mg/dl. Urinalysis revealed proteinuria (280 mg/dl). Microbiologic examination of synovial fluid aspirated from the left elbow joint showed in culture the growth of *Staphylococcus aureus*. Urine and blood cultures were performed three times and were negative for aerobic and anaerobic bacteria.

Magnetic resonance (MR) scan of thoracic and lumbosacral spine showed epidural abscess with destruction of the vertebral body L4-L5 with concomitant infiltrative (inflammatory) lesions in the nerve roots L4-L5, extensor muscles, multipartite back muscles and psoas major muscles.

The ECG at rest showed sinus tachycardia and left axis deviation.

Transthoracic echocardiography did not show any symptoms of infective endocarditis or any other serious cardiac pathology.

Treatment with intravenously administered antibiotics (cefuroxime 1.5 g every 8 hours, gentamycin 80 mg every 12 hours), opiates (morphine, fentanyl transdermal therapeutic system TTS) and intensive insulin therapy (human insulin Actrapid HM before meals in accordance with plasma glucose level, Insulatard HM 12 U before sleep with a total daily dose of 30–40 U) were administered. Considering venous thrombotic risk factors (age, immobilization, lower limb paresis, severe infection) prophylaxis with low-molecular-weight heparin was performed (enoxaparin 40 mg/24h). In view of clinical features and results of laboratory tests the diagnosis of epidural spinal abscesses penetrating into retroperitoneal space was established and, since the left elbow synovitis was suspected to be a trigger of the abscess, clindamycin was added according to the antibiogram results (clindamycin *i.v.* 600 mg every 12 h). Clinical improvement had not been reached despite a broad spectrum antibiotic therapy therefore the patient was consequently consulted by a neurosurgeon and neurosurgical procedure was performed (drainage of spinal abscesses with decompressive laminectomy of L4-L5 vertebral body, drainage and evacuation of retroperitoneal abscesses on the consecutive day). Bacteriological culture of drainage fluid was negative (including tuberculosis). After the surgery procedure the patient clinical condition was significantly improved, with alleviation of lumbar pain, normal body temperature, and normalization of the biochemical and clinical diabetes parameters (receding of polydipsia, normalization of glycemia with a decrease of in-

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sulin requirement to 24 U/24h). Neurological deficit in the lower limbs remained as anticipated. During the postoperative course a broad spectrum antibiotic (piperacillin *i.v.* 1 g every 8 hours) was used and antithrombotic prophylaxis with subcutaneous injections of enoxaparin 40 mg/24h was continued.

On the 4 day after surgery the patient condition suddenly deteriorated. The patient suffered from dyspnea at rest, weakness with atypical chest pain, cough and anxiety. On physical examination, tachypnea 30/min, blood pressure 90/60 mmHg, fast, irregular pulse rate 130/min, single crackles at the lung base were detected. On ECG there were left axis deviation, atrial fibrillation with ventricular rhythm about 130/min, incomplete right bundle branch block. Laboratory tests showed elevated D-dimers 6.4 ug/ml, normal troponin T (below 0.01 µg/l), low blood oxygen in blood gasanalysis (pO_2 64.1 mmHg). On echocardiographic examination enlargement of right ventricle with tricuspid valve regurgitation with elevated right ventricle pressure (50 mmHg) was shown. The time to peak flow in pulmonary artery (acceleration time – AcT) was reduced to 70–80 ms and regional myocardial contraction dysfunction of the left ventricle (hyperkinesis of the back wall middle segment and the apex) was diagnosed. These dysfunctions were not present during a baseline examination. Considering clinical features and laboratory tests, the diagnosis of pulmonary embolism was established. Enoxaparin dose was increased to 80 mg every 12 hours with dopamine intravenous infusion (10 µg/kg/min) and oxygen therapy (5 l/min). Because of early postoperative course with retroperitoneal drainage, no thrombolytic therapy was introduced. Despite optimal treatment provided, sudden asystolic cardiac arrest developed. Immediate cardiopulmonary resuscitation was ineffective and the patient died.

DISCUSSION

Spinal epidural abscess (SEA) is a rare disease with a double incidence increase in the last 20 years due to population ageing, neurosurgery techniques development, and immunologic deficiencies occurring in several diseases [1].

A majority of patients with SEA have one or more predisposing factors with more frequent immunologic deficiency due to diabetes and concomitant focal infection in skin, soft tissue and other organs (Tab.). In that case infection is spread with blood, localizes in epidural space and then may spread to adjoining tissues, mainly bones and muscle of the spine. The infection may spread further with blood to distant organs, particularly the endocardium [1]. Similar natural disease history was observed in the case described of diabetic patient with infection assumed to have arisen from the left elbow synovitis infection point and lead to SEA formation with infiltration and degeneration of adjoining vertebra and penetration to the retroperitoneal space. Prolonged treatment with high doses of steroids before the diagnosis was made is assumed to be an additional predisposing factor of such an extensive spread of in-

fection. Available data showed that about 75% of cases of SEA is associated with *Staphylococcus aureus*, a typical skin and soft tissue pathogen, which was also isolated from synovial fluid aspiration. Remarkably, other microorganisms may also cause SEA. These are mainly methicillin-resistant *Staphylococcus aureus* (MRSA) which may cause nearly 40% of SEA in some centers (mainly neurosurgery) [1]. Other significantly less common pathogens are *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, anaerobic *Actinomyces* and mycobacteriae, fungi and parasites [2,6]. The SEA is localized in the epidural space, normally filled with fatty tissue and vein plexus. It is limited by the spinal dura and bone wall of the spinal canal. Spinal epidural abscess is usually localized in the thoracic or lumbar spine (50% and 34%, respectively), where the epidural space is relatively broad, mainly in the posterior part, where abscess may be localized. Infrequently, SEA may be seen in the cervical spine [3,5,6]. The disease usually involves three or four adjoining vertebra but rare cases of the whole vertebra involvement was also described [7]. The abscess in the retroperitoneal space causes the damage of spinal cord by direct compression and indirectly as a result of epidural vein thrombosis [1,4]. This results in typical clinical appearance which may change with disease progression. Darouiche [1] described SEA by four clinical stages: phase 1 – localized spinal ache in the involved region; phase 2 – root pain associated with the involved spinal region; phase 3 – muscular weakness, sensory deficit and sphincter muscle dysfunction. The phase 4 is characterized by paralysis with extent associated with area involved. The time of each phase and kinetics of disease progression may vary in a wide range. The most frequent clinical symptoms of SEA are: lumbo-sacral pain (75% of cases), fever (nearly 50%) and neurological deficits (30% of cases) [1,2,4]. Difficulty with diagnosis may be caused by the fact that synchronal incidence of those three symptoms is very uncommon [8]. That may lead to incorrect diagnosis and treatment delay which results in non-reversible neurological deficit or even death.

During SEA inflammation markers such as leukocytosis, high sedimentation rate or elevated C-reactive protein level are common. However, these are not specific markers. Blood and cerebro-spinal fluid bacteriology testing is not relevant. Moreover, lumbar puncture may be a risk factor of subdural spread of infection [1,5,7,8].

In recent years MR of the spine becomes an elective diagnostic method. Magnetic resonance is a non-invasive technique showing the tissues from multiple viewpoints which is of particular importance when neurosurgical intervention is planned. Magnetic resonance helps to differentiate infective and neoplastic lesions. Multiple chest radiographs, computed tomography or radioisotope scan usually confirm intervertebral disc inflammation or osteomyelitis, usually coexistent with SEA. Notwithstanding, those techniques are not sufficiently sensitive and specific and can not replace MR scan [1,8].

Diagnostic difficulty results in misdiagnosing patients with SEA leading to a wrong diagnosis of osteitis, intervertebral disc inflammation, meningitis, urinary tract infec-

tion, sepsis or endocarditis. Quite often pain syndrome due to prolapsed intervertebral disc or degenerative joint disease, or spine tumor, transverse myelitis, demyelinating disease or spine hematoma is also diagnosed [1,2,5].

Urgent decompressive laminectomy with surgical treatment of wound and appropriate antibiotic use is an elective treatment strategy [1,2,4,7,9]. The best results may be achieved in phase 1 or 2 of SEA. In those cases complete recovery is plausible. In phase 3 skeletal muscle, sphincter muscle and sensory function improvement may be obtained. Patients in phase 4, when paralysis is present, may benefit from neurosurgical intervention unless it is performed 24–36 hours after the paralysis symptoms occur. If an informed consent is not obtained, or procedure is at a high risk of complications, or time from first paralysis symptom is more than 24–36 hours, or the entire spine is involved – conservative treatment is being performed [1]. Antibiotic use, according to microbiology of blood or fluid collected during the abscess CT guided puncture, is a key element of treatment strategy [10]. If empirical therapy is provided, activity against staphylococci including MRSA (e.g. vancomycin) and Gram-negative bacteria (III and IV generation of cephalosporin) should be considered, particularly if such infection in other organs is present. Intravenous antibiotic therapy should be maintained in SEA for at least 6 weeks [1]. Some patients are eligible to surgical treatment even if the paralysis symptoms last longer than 24–36 hours, with purpose of sepsis focus eradication which is refractory to conservative treatment epidural abscess [1]. The patient described with neurological dysfunction of a few weeks duration, belonged to that very group. Body temperature normalization and pain relief were the major results of surgical treatment. However, as presumed, neurological dysfunction was not reduced. In about 5% of cases, SEA becomes fatal. The main causes of death are uncontrolled sepsis, meningitis or concomitant diseases [1]. Moreover, the procedure of spinal surgery is associated with risk of deep vein thrombosis, concomitant infections and decubitus ulcers [11]. Those complications in immobilized patients may lead to pulmonary embolism which was probably the major cause of death in the case presented.

In summary, SEA is uncommon disease with a very serious prognosis if the appropriate diagnosis and treatment are delayed. In spite of a typical triad of symptoms (lumbar pain, fever, and neurological dysfunction) with concomitant characteristics for this disease risk factors (diabetes, purulent synovitis, urinary tract infection) presented, definitive diagnosis was made in a hospital where the patient was treated. Unfortunately, extensive infective process, retroperitoneal infiltration, prolonged neurological dysfunction, appeared to be lethal.

One should emphasize that the clinical SEA course as described above is rare. In a majority of cases all three typical symptoms are not presented. Therefore, one should be aware of that disease, especially on emergency ward when a patient with spine pain and risk factors for SEA has been admitted.

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