CLINICAL IMAGE

Diagnostic workup of a patient with severe hypercalcemia and a history of malignancy

Barbara Bromińska, Ewa Milewska, Ewelina Szczepanek-Parulska, Rafał Czepczyński, Marek Ruchała

Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland

Hypercalcemia is a relatively frequent clinical issue. Hyperparathyroidism and malignancy are the most common causes of this condition, accounting for 90% of cases.[1]

A 64-year-old woman consulted an oncologist because of weight loss, bone pain, and depression. Twenty years before, she underwent mastectomy with adjuvant chemotherapy due to breast cancer and hysterectomy for cervical cancer. During the index visit, 18F-fluorodeoxyglucose positron emission tomography / computed tomography was performed (FIGURE 1A–1C).

The patient was referred to the Department of Endocrinology. On admission, she complained of bone pain, weight loss, and depressed mood. She was on a wheelchair and was using transdermal opioid analgesics due to bone pain and difficulties with moving. Her medical history included nephrolithiasis, untreated osteoporosis, previous bilateral alloplasty of the hip joint, and a history of fracture of the left clavicle, proximal epiphysis, and diaphysis of the left humerus.

Laboratory tests revealed severe hypercalcemia (16.64 mg/dl; reference range, 8.8–10.2 mg/dl), hypophosphatemia (2.51 mg/dl; reference range, 2.7–4.5 mg/dl), and increased levels of parathyroid hormone (PTH) (3495 pg/ml, reference range, 15–65 pg/ml). Kidney function was normal. Technetium-99m sestamibi scintigraphy and bone scintigraphy were performed (FIGURE 1D–1E). Thyroid ultrasonography revealed an oval-shaped hypoechogenic area, 16 × 13 mm in size, localized on the posterior wall, in the lower pole of the right thyroid lobe. We performed fine-needle aspiration biopsy with PTH washout measurement. The level of PTH was extremely high (>5000 pg/ml), which was suggestive of parathyroid adenoma. The level of methoxycatecholamines in a 24-hour urine sample was within the reference range. To exclude genetic causes, blood samples were collected for identification of potential mutations in the *MEN1* and *RET* genes.

Due to the risk of parathyroid cancer and life-threatening hypercalcemia, after a few days of conservative treatment involving intensive hydration and administration of loop diuretics and intravenous bisphosphonates, the patient was transferred to the Department of Endocrinological Surgery and operated on. Directly after

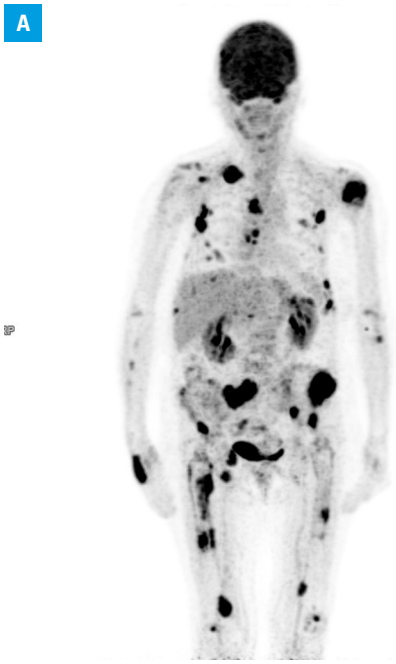
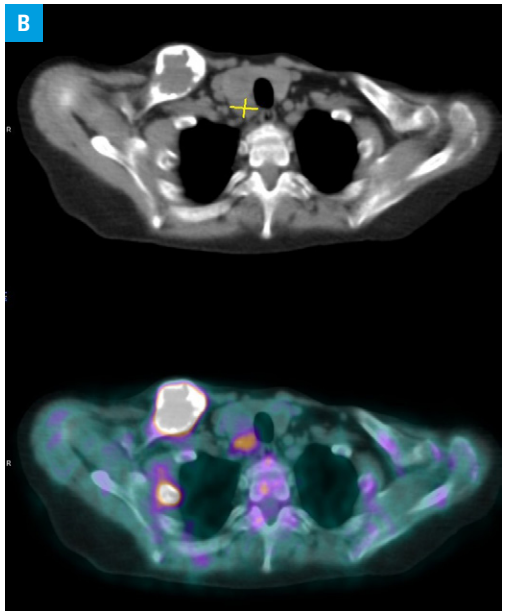
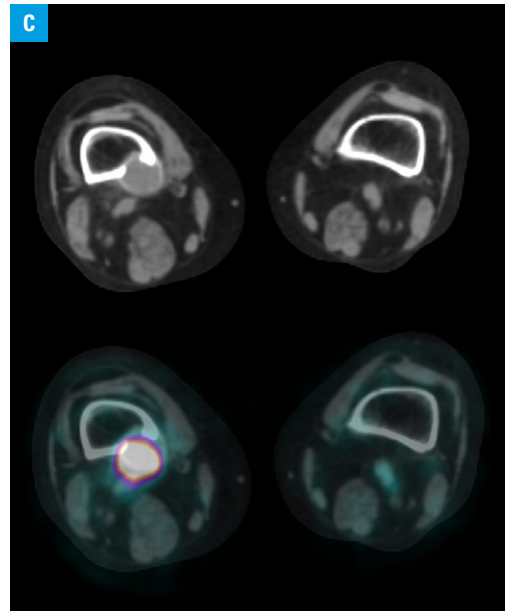


FIGURE 1 **A** – maximum intensity projection image of 18F-fluorodeoxyglucose positron emission tomography coregistered with computed tomography (18F-FDG PET/CT) showing multiple FDG avid foci in the skeleton. A lesion on the posterior wall of the right thyroid lobe was visible (maximum standardized uptake value [SUV_{max}], 4.3). Additionally, bilateral adrenal tumors were visualized; the one in the right adrenal gland (sized 3.5 × 2.7 cm) presented an increased glucose uptake (SUV_{max}, 5.3). Otherwise, there were no signs of cancer recurrence.

Correspondence to:
Barbara Bromińska, MD, PhD, Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, ul. Przybyszewskiego 49, 60-355 Poznań, Poland, phone: +48 61 869 13 33, email: barbarabrominska@ump.edu.pl
Received: April 20, 2021.
Revision accepted: May 16, 2021.
Published online: May 21, 2021.
Pol Arch Intern Med. 2021; 131 (7-8): 727-729
doi:10.20452/pamw.16003





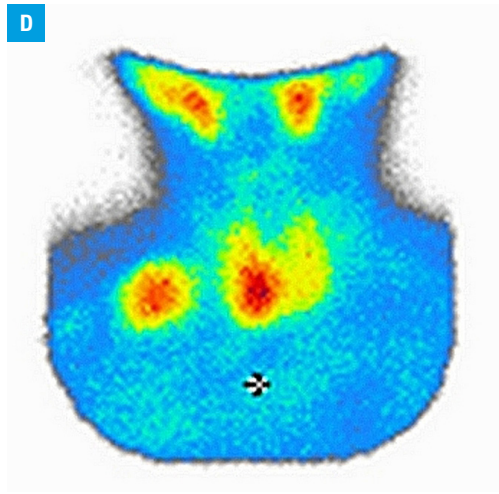
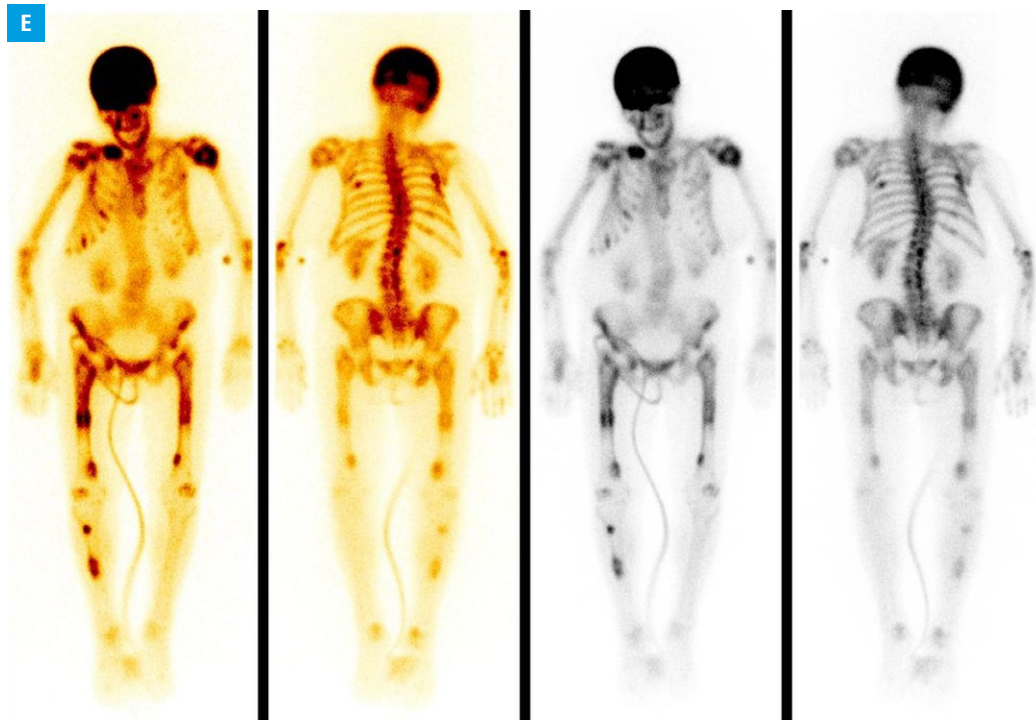


FIGURE 1 **B**, **C** – fused 18F-FDG PET/CT images showing FDG avid lesions in the right clavicle and the nearby lower pole of the right thyroid lobe (marked by the cross) (**B**) and a hypermetabolic area in the right femur (**C**); **D** – technetium-99m (99mTc) sestamibi parathyroid scintigraphy showing a hypermetabolic area in the lower pole of the right thyroid lobe and an increased radioisotope uptake in the right clavicle after a fracture. **E** – 99mTc bone scintigraphy depicting an intense tracer uptake in the skull, right clavicle, proximal parts of the left humerus and right forearm, ribs, femurs, right calf, and heels



parathyroidectomy, the serum concentration of PTH decreased from 2340 pg/ml to 308 pg/ml and returned to reference values in the consecutive days. Genetic tests revealed that the patient was a carrier of the p.(S649L) variant (VCV000024928.11) in the transmembrane domain of the *RET* gene, which might be a factor predisposing to medullary thyroid carcinoma or multiple endocrine neoplasia type 2 syndrome.[2,3] Family members, though asymptomatic, were notified and referred for genetic testing.

Brown tumors are benign bone lesions that develop as a consequence of excessive osteoclastic activity and bone remodeling. They are present in approximately 1% of patients with hyperparathyroidism. Radiological images of brown tumors are rare and highly variable.[4] Irregular contour and multiplicity of these lesions may mimic metastases to the skeleton.[5] Due to the fact that our patient had a previous history of uterine and breast malignancy, she was firstly suspected of neoplastic disease.

To conclude, in the presented case the initial symptoms suggested recurrence of cancer. During the diagnostic workup we found out that the patient had a very rare complication of hyperparathyroidism—brown tumors. Additionally, we discovered that she was a carrier of the rare p.(S649L) variant of the *RET* gene. This case emphasizes the importance of a multidisciplinary approach to the patient. Adequate and quick diagnosis was established thanks to the cooperation between members of a team of specialists, including an endocrinologist, surgeon, geneticist, oncologist, and a nuclear medicine specialist.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Bromińska B, Milewska E, Szczepanek-Parulska E, et al. Diagnostic workup of a patient with severe hypercalcemia and a history of malignancy. Pol Arch Intern Med. 2021; 131: 727-729. doi:10.20452/pamw.16003

REFERENCES

1 Zagzag J, Hu MI, Fisher SB, Perrier ND. Hypercalcemia and cancer: differential diagnosis and treatment. CA Cancer J Clin. 2018; 68: 377-386.

2 Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015; 17: 405-424.

3 ClinVar Database. https://www.ncbi.nlm.nih.gov/clinvar/. Accessed April 10, 2021.

4 Syed H, Khan A. Primary hyperparathyroidism: diagnosis and management. Pol Arch Intern Med. 2017; 127: 438-441.

5 Cyranska-Chyrek E, Szczepanek-Parulska E, Markuszewski J, et al. Sudden hip pain in a young woman. Am J Med. 2017; 130: e379-e381.