End-stage skeletal manifestations of severe hyperparathyroidism

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A 58-YEAR-OLD RUSSIAN FEMALE COMPLAINED of 2 years of back pain. A magnetic resonance imaging scan obtained as part of a neurosurgical evaluation revealed lumbar degenerative disc disease, for which she underwent 2-level lumbar decompression. Her symptoms worsened and did not improve after 6 months of maximal medical management. A repeat magnetic resonance imaging scan revealed multiple masses within her lumbar spine and sacrum. An internal medicine consultation revealed a strong family history of cancer. Biochemical testing revealed an elevated serum calcium level (13.4 mg/dL; normal 8.4-10.2 mg/dL); therefore, a workup for metastatic cancer was initiated. A bone scan showed multiple areas of increased uptake in the skull, and thoracic and lumbar spine (Fig 1). A computed tomography–guided biopsy of a right sacral lytic lesion revealed extensive fibrosis, with no residual normal bone marrow, which was consistent with severe osteitis fibrosa cystica (Fig 2). Further biochemical workup confirmed a markedly elevated parathyroid hormone level (1256 pg/mL; normal, 10-60 pg/mL) and a normal parathyroid hormone-related peptide (< 0.4 pmol/L; normal, < 1.3 pmol/L). An operation was decided on at this time for the diagnosis of hyperparathyroid crisis. The patient reported nausea and vomiting, constipation, polydypsia, polyuria, and fatigue. Further biochemistry revealed a chloride to phosphorus ratio of over 50 (chloride = 112 mmol/L; normal, 96-108 mmol/L; phosphorus = 2.2 mg/dL; normal, 2.7-4.5 mg/dL), an alkaline phosphatase of 791 U/L (normal, 39-117 U/L) and a normal serum protein electrophoresis. She also had an elevated creatinine level and reduced creatinine clearance, as well as calcium deposits in her kidneys—all consistent with hypercalcemic nephropathy. A left neck mass noted on physical examination was confirmed by computed tomography scan to be a 2-cm tumor behind the thyroid suspicious for parathyroid carcinoma. A parathyroidectomy with left thyroid lobectomy was performed. Pathological findings revealed a large parathyroid adenoma without evidence of malignancy. The patient's postoperative course was remarkable for hungry bone syndrome. Six weeks after the operation, the patient was markedly improved and stated she was "back to normal."

DISCUSSION

Primary hyperparathyroidism was originally described as a disease of "bones and stones," and 50 years ago radiologists and endocrinologists were well versed in the radiologic signs of this disease. Historically, the incidence of clinically evident bone disease was 15%; however, the advent of serum autoanalyzers has dramatically changed the phenotype of patients presenting with hyperparathyroidism.[1] Primary hyperparathyroidism is now most commonly diagnosed before overt symptoms, and clinically evident bone disease is distinctly uncommon.

As in this patient, reports of clinically evident bone disease secondary to primary hyperparathyroidism typically occur in immigrants from areas with limited access to health care. Osteitis fibrosa cystica is the most severe form of this disease and consists of bone cysts, osteoporosis, and brown tumors, which result from excessive osteoclast-mediated bone resorption.[2] These skeletal changes most commonly present as pain; however, pathologic fractures and skeletal deformity are not infrequent complications. In fact, paraplegia, secondary to vertebral collapse, is at the severe end of the spectrum.[3] Similarly, our patient required a thoracic-lumbar-sacral orthotic brace for severe destruction of the thoracic and lumbar spine.

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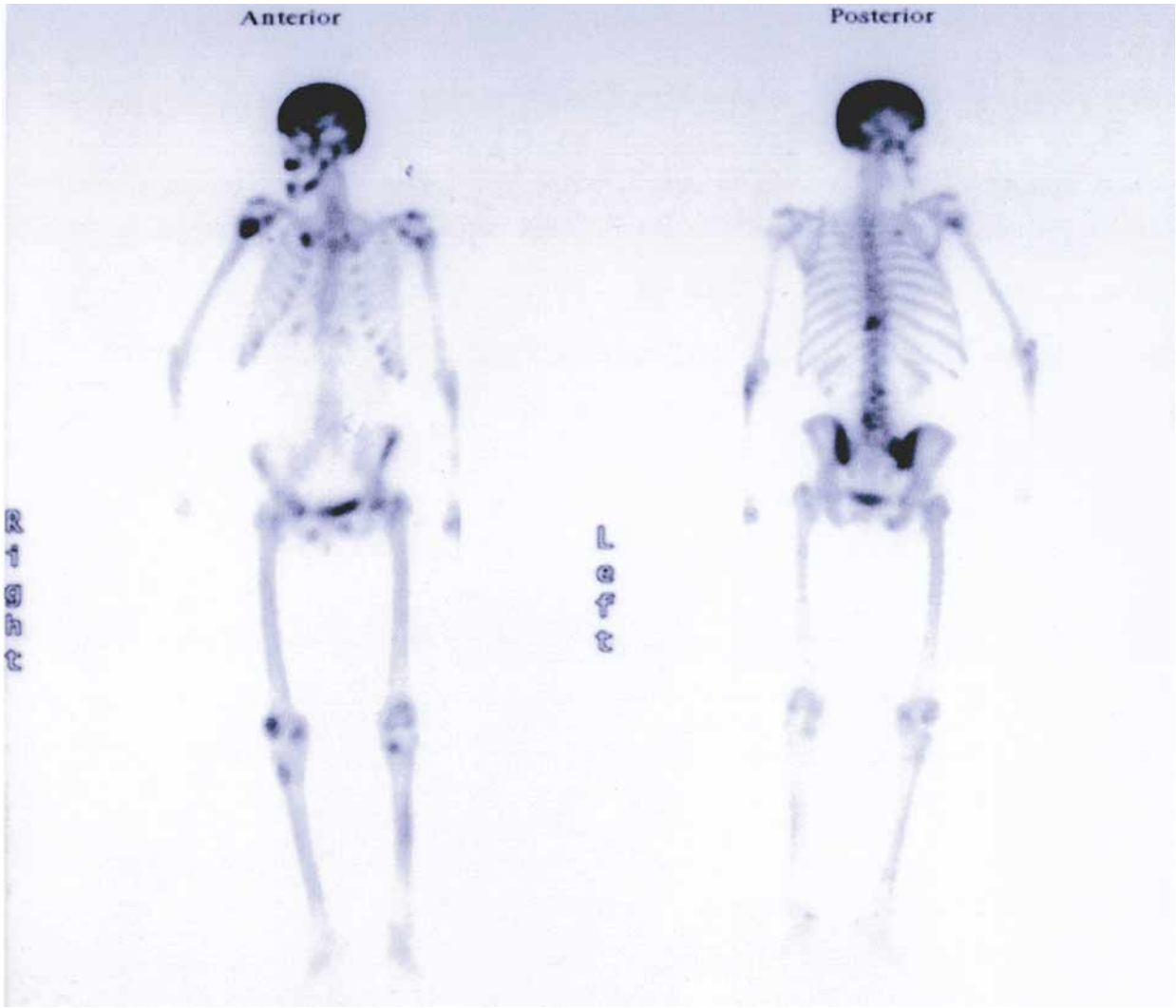

Fig 1. Bone scan revealing increased uptake in skull, thoracic, and lumbar spine and sacroiliac regions, initially suggesting metastatic cancer.

The most specific radiologic finding of osteitis fibrosa cystica is subperiosteal resorption of the radial aspect of the index and long fingers.[4] This pathognomonic sign and multiple lytic lesions were observed in this patient (Fig 3).

Typically, histologic changes reveal extensive cortical resorption and tunneling defects lined with osteoclasts. This patient's sacral biopsy finding demonstrates the most extreme example of hyperparathyroid bone disease, which is diffuse marrow fibrosis (Fig 2).

Currently, the only effective treatment for osteitis fibrosa cystica is localization and surgical excision of all abnormal parathyroid tissue, with subsequent calcium and vitamin D replacement. After successful surgical treatment of hyperparathyroidism, reversal of bone loss commonly occurs, although recovery to normal bone mass is

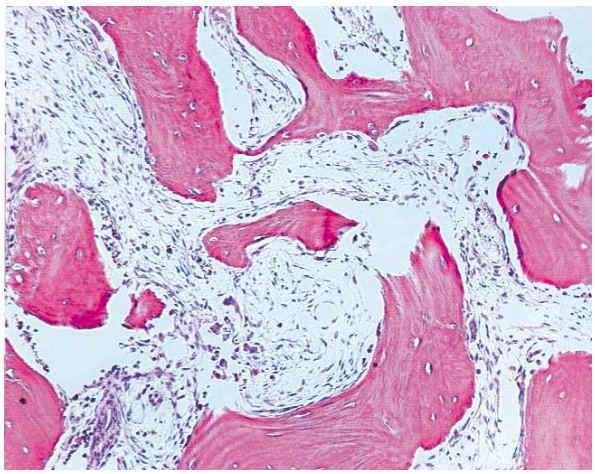

Fig 2. Biopsy specimen from sacral lytic lesion showing complete marrow fibrosis and trabecular tunneling defects typical of severe osteitis fibrosa cystica.

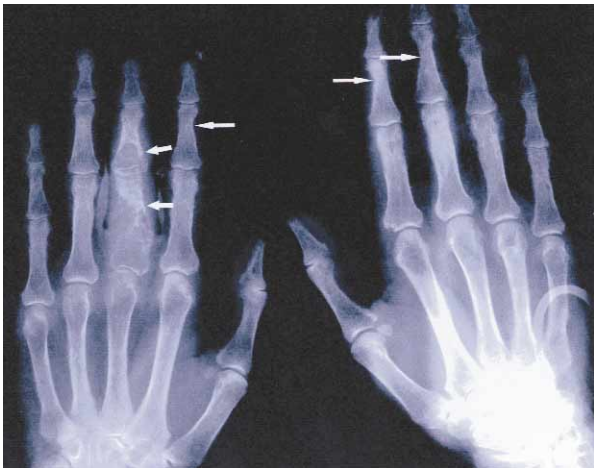

Fig 3. Plain radiograph of the patient's hands, which reveals the pathognomonic radiologic sign of osteitis fibrosa cystica, which is subperiosteal resorption of the radial aspect of the index and long fingers *(long thin arrows)*. This image also depicts cystic destruction of the proximal phalanx of the left long finger *(short, thick arrows)*.

rare. For asymptomatic or mildly symptomatic hyperparathyroidism, medical treatment options include bisphosphonates, which inhibit osteoclast bone resorption, calcimimetics, which increase the sensitivity of extracellular calcium receptors, and estrogen replacement therapy which is used for postmenopausal women.

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