AACE Clinical Case Rep. 10 (2024) 113–114

Clinical Case Reports™
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Visual Vignette

A Vertebral Fracture Unmasking Systemic Mastocytosis in a 29-Year-Old Man

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ARTICLE INFO

Article history:
Received 10 February 2024
Accepted 14 February 2024
Available online 19 February 2024

Case Presentation

A 29-year-old man presented to the endocrinology clinic after sustaining a T3 vertebral burst fracture from a ground-level fall. The magnetic resonance imaging revealed a T3 burst fracture deformity, compression deformities of 4 other vertebral bodies, and multilevel diffuse marrow enhancement (Fig. 1). The dual x-ray absorptiometry scan showed both T-scores and Z-scores of −4.2 lumbar spine, −2.5 femoral neck, −1.8 total hip, and −1.6 distal forearm. His medical history was significant for reflux, headaches, irritable bowel syndrome, and severe allergic reactions to tilapia and crab, which manifested as syncope. He denied fatigue, weight gain, cold intolerance, gluten sensitivity, kidney stones, nausea, and glucocorticoid use. The physical examination was unremarkable without rash. Laboratory evaluations revealed a normal thyroid stimulating hormone level, celiac panel, blood count, comprehensive metabolic panel, parathyroid hormone level, 25-OH vitamin D level, and 24-hour urine calcium level. The basal serum tryptase was 16.5 ng/mL (reference range <11.5 ng/mL) and the tryptase genotype was normal (2 α 2 β). A bone marrow biopsy was obtained (Fig. 2).

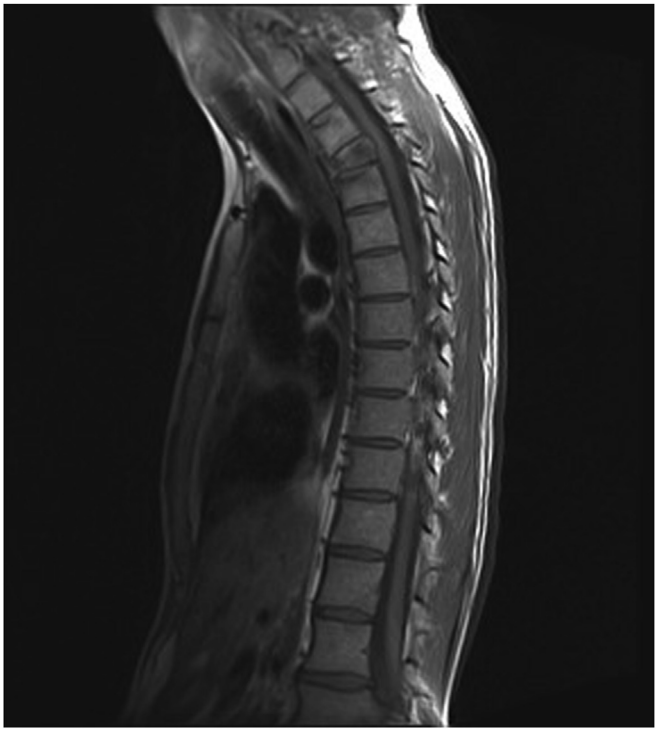

Fig. 1. The MRI shows a T3 burst fracture with multilevel enhancing marrow signal lesions.

What is the diagnosis?

Answer

Osteoporosis secondary to systemic mastocytosis. The bone marrow biopsy revealed numerous aggregates of spindled mast cells (MCs) that demonstrated positive immunohistochemical staining for CD117, tryptase, and CD25 (Fig. 2). The *KIT* p.D816V mutation was detected in the aspirate at 0.07% variant allele frequency. Therefore, this patient met the 2017 WHO criteria for systemic mastocytosis (SM).[1] Mastocytosis is a group of rare myeloid neoplasms that results in abnormal accumulation and expansion of neoplastic MCs within one or more organs. There are 3 types of mastocytosis including cutaneous mastocytosis, MC sarcoma, and SM. Systemic mastocytosis subtypes are: indolent SM, smoldering SM, aggressive SM, SM with an associated myeloid neoplasm, and MC leukemia. Patients with all

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https://doi.org/10.1016/j.aace.2024.02.003

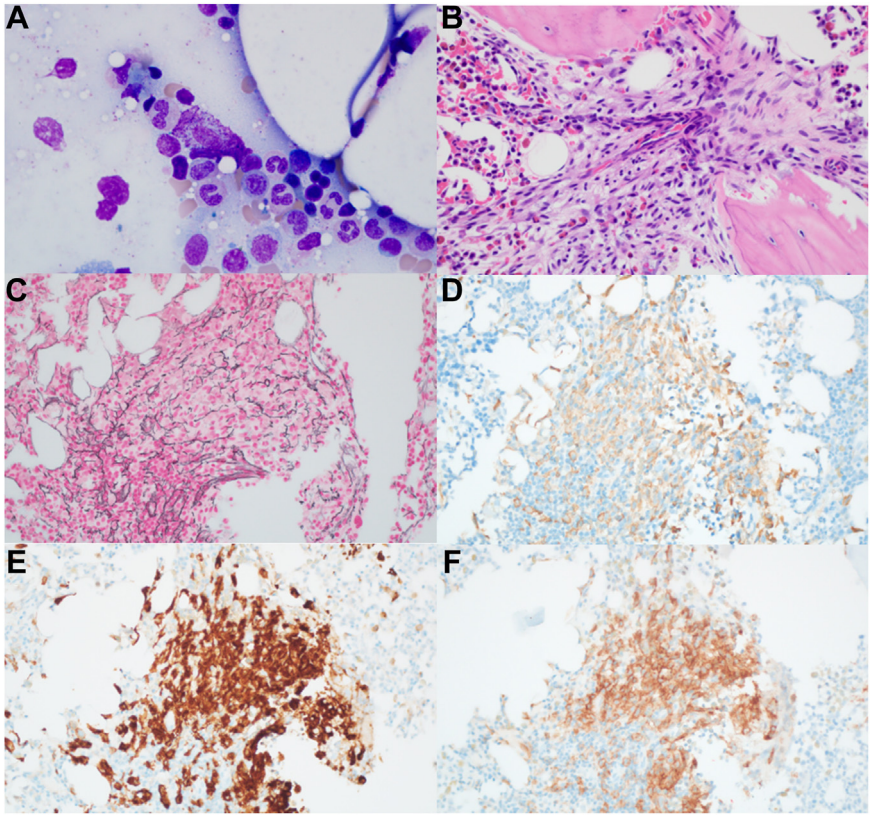

Fig. 2. *A*, Wright-Giemsa staining of the aspirate demonstrates atypical, spindled mast cells (original magnification 1000×). *B*, Hematoxylin and Eosin staining with aggregates of greater than 15 spindled mast cells (original magnification 400×). *C*, Reticulin special staining highlights increased reticulin around the spindled mast cells (original magnification 400×). *D*, Immunohistochemical staining for Tryptase highlights the spindled mast cells (original magnification 400×). *E*, Immunohistochemical staining for CD117 highlights spindled mast cells and CD117 positive precursor cells (original magnification 400×). *F*, Immunohistochemical staining for CD25 shows aberrant expression in the atypical mast cells (original magnification 400×).

subtypes of SM are at risk of osteoporosis and low-trauma fractures.[2] Patients who present with diffuse reddish-brown macules (termed mastocytosis-in-the-skin), anaphylaxis associated with cardiovascular collapse,[3] pathologic fractures, or a combination of these should be screened for SM.

The pathophysiology of mastocytosis bone disease is poorly understood but may occur through the activation of osteoclasts from MC mediators including histamine, tryptase, inter leukin-6, inter leukin-1, and tumor necrosis factor-α. The patient was started on a recently Food and Drug Administration-approved *KIT* p.D816V selective tyrosine kinase inhibitor called avapritinib for indolent SM. He also began infusions of zoledronic acid for osteoporosis. There is little data to guide how to prevent or manage osteoporosis in SM. It is also not known whether tyrosine kinase inhibitors might prevent or reverse bone damage. This case highlights SM in the differential for pathologic fracture and the need to study bone health in these patients.

Disclosure

The authors have no conflicts of interest to disclose.

Acknowledgments

Patient consent was obtained. The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or the U.S. Government.

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