Episode 40

Problem Representation
A 46-year-old woman with advanced HIV infection on antiretrovirals presented with dyspnea and anterior thigh pain, found to have hilar lymphadenopathy and diffuse lytic bone lesions on imaging.

Schemas
The CPSer's schema for granulomatous inflammation identifies infections, autoimmune diseases, and cancer as the most common cause of granulomas on histopathology. Less common causes include immunodeficiency syndromes, medications, and reactions to foreign bodies.

Diagnosis
Empiric antifungal therapy was started for presumed blastomycosis. Biopsy of one of the bony lesions, however, revealed noncaseating granulomas on histopathology with negative cultures and staining for mycobacteria and fungi. Given the hilar adenopathy, negative cultures/stains, and noncaseating granulomas, the patient was diagnosed with extrapulmonary sarcoidosis. She was treated with steroids and had improvement in her symptoms!

Teaching points

- As Dr. Chris Jackson points out, the presence of bone lesions doesn't always implicate cancer. Broadly speaking, bone lesions on imaging[1] can be caused by benign primary bony disease, malignancies (either primary or secondary), infections, inflammatory conditions, or endocrinopathies (e.g. hyperparathyroidism).
- The musculoskeletal manifestations[2] of sarcoidosis include arthritis, myopathy, and bone lesions. Bone lesions can appear lytic or sclerotic on imaging and most frequently involve the proximal/middle phalanges and axial skeleton. These are most often asymptomatic and only discovered incidentally. Notably, serum alkaline phosphatase levels are not typically elevated even with extensive bony disease (similar to multiple myeloma).
- Autoimmune diseases (ADs), while rare overall, can occur in persons living with HIV (PLWH). In a retrospective study[3] of PLWH, the most common ADs were immune thrombocytopenia (ITP), inflammatory myopathies, sarcoidosis, and guillain-barre syndrome. With the exception of ITP, ADs most commonly occurred in patients with good response to antiretroviral medications or during immune reconstitution. In patients with lower CD4 counts[4] (i.e. < 200/uL), infectious or malignant causes of granulomas should be prioritized over sarcoidosis, however.

Clinical Reasoning Pearl

Many disease processes wax and wane in their manifestations. As such, it can occasionally appear that a patient "responds" to a given intervention when, in fact, this intervention exerted no effect.

<u>For example:</u>
By being skeptical about the patient's possible "response" to amphotericin, Rabih was able to keep his differential diagnosis broad and ultimately favor sarcoidosis.

References

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2. Bechman K, Christidis D, Walsh S, Birring SS, Galloway J. A review of the musculoskeletal manifestations of sarcoidosis. Rheumatology (Oxford). 2018 May 1;57(5):777-783.
3. Virot E, Duclos A, Adelaide L, Miailhes P, Hot A, Ferry T, Seve P. Autoimmune diseases and HIV infection: A cross-sectional study. Medicine (Baltimore). 2017 Jan;96(4):e5769.
4. Morris DG, Jasmer RM, Huang L, Gotway MB, Nishimura S, King TE Jr. Sarcoidosis following HIV infection: evidence for CD4+ lymphocyte dependence. Chest. 2003 Sep;124(3):929-35.