CASE REPORT

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A Rare Cause of Bone Pain in an Older Adult with Pulmonary Sarcoidosis

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Abstract

The pathophysiology of sarcoidosis includes defective T cells and macrophages, which lead to the formation of granulomas. On the other hand, increased turnover of osteoclasts has been observed in Paget's disease, where osteoclasts are a member of the macrophage family. There may be a common intrinsic factor associated with the vitamin D receptor gene receptor that triggers the defective activation of macrophages in both disorders. More than half of patients with Paget's disease are asymptomatic; thus, the coexistence of the two disorders may go unnoticed. To the best of our knowledge, the coexistence of Paget's disease and pulmonary sarcoidosis in the same patient has not been previously reported. Whether bisphosphonate can be used for the treatment of osseos sarcoidosis is a subject for future research. Herein, we report a case of Paget's disease in an older patient with pulmonary sarcoidosis.

Keywords: Bone disease, bone pain, clinical geriatrics, pain, sarcoidosis

Introduction

Paget's disease cause of that fracture and deformity osteoarthritis, neuropathy, bone tumor (1%), is presentation symptomatic or asymptomatic on especially calvarium, pelvis, ekstremite and vertebrae bones. Due to increase malignancy cases, the clinician often miss the main reason of symptom. Because malignancy screening been important step in examination for especially some symptoms and nobody want miss malignancy. We present a case report about paget disease that second most common bone disease in elderly. Consent forms have been obtained from the patient for case presentation.

Case Report

A 78-year-old-female presented to the geriatrics outpatient clinic with headache and pain in her right upper arm dating four years back. The patient described a constant, throbbing pain on both sides of the head. The pain in the right arm radiated to the right shoulder. On a scale from 0 to 10, the patient rated the pain as 4. Five years before the current presentation, the patient was diagnosed with pulmonary sarcoidosis in the pulmonary medicine clinic of the same hospital. The patient was not taking steroids because she had stage II disease characterized by bilateral hilar lymphadenopathy and pulmonary infiltrates with mildly abnormal lung function. Other medical history included hypertension and benign paroxysmal positional vertigo. Her medications included betahistine dihydrochloride, candesartan, and cilexetil. The family history included a younger brother diagnosed with laryngeal carcinoma and a younger sister with glioblastoma multiforme. Her right upper arm was sensitive to palpation.

Plain radiograph of the right humerus shows osseous expansion (Figure 1A). Plain radiograph and computed tomography (CT) of the head revealed several hypodense lesions in the skull (Figures 1B, 2A). Whole-body fluorodeoxyglucose positron emission tomography (PET)-CT detected heterogeneous lesions in the calvarial bones and T5 vertebral body (maximum standardized uptake value: 2.5). Bone scintigraphy revealed increased diffuse osteoblastic activity in the calvarial bones, right humeral head, and right aspect of the T11 vertebral body.

The patient was diagnosed with polyostotic Paget's disease based on diagnostic radiological findings and elevated serum

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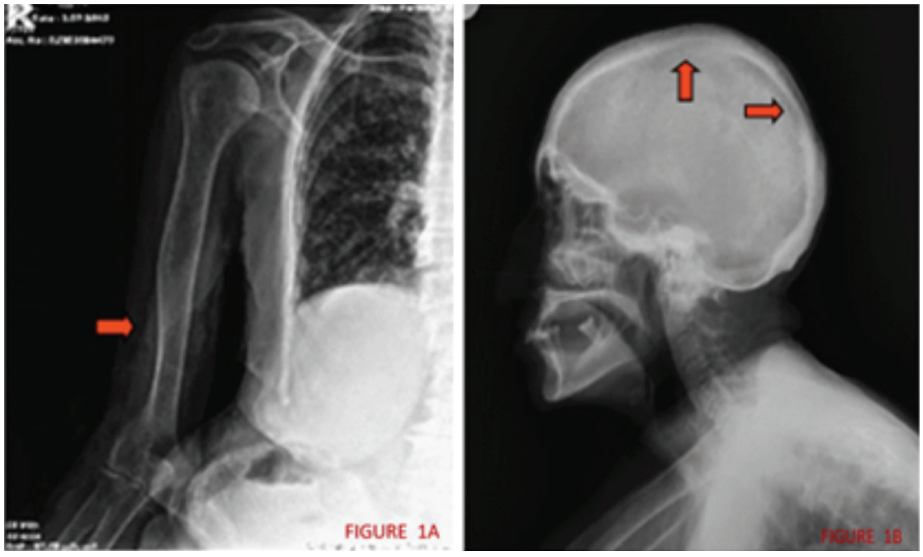

Figure 1A. Plain radiograph of the right humerus, **Figure 1B**. Plain radiograph of the head

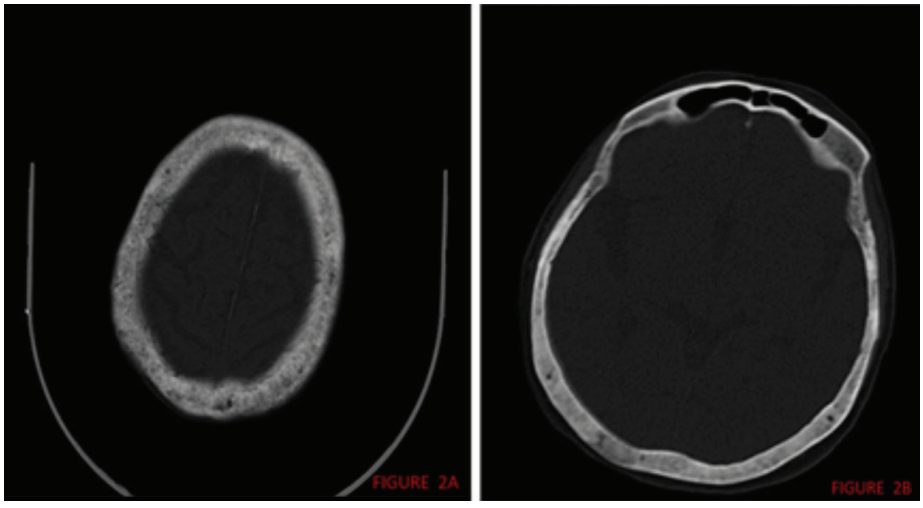

Figure 2A. Cranial CT before treatment, **Figure 2B**. Cranial CT after treatment

alkaline phosphatase (ALP). Treatment with intravenous yearly zoledronic acid therapy was initiated along with oral nutritional supplements for malnutrition. At follow-up, the patient reported no headache or bone pain. Follow-up cranial CT after treatment with zoledronic acid showed complete resolution of the cranial lesions (Figure 2B).

Discussion

Sarcoidosis is a multi-system inflammatory disorder with a complex pathophysiology. Unknown antigens trigger a cell-mediated immune response that leads to the accumulation of T cells and macrophages, followed by the formation of granulomas. Demaria et al. (1) reported bone involvement in sarcoidosis to be 14%. The relationship between macrophage activation and vitamin D metabolism has been proposed as the pathophysiological mechanism underlying sarcoidosis (2). The first-line treatment for bone involvement in sarcoidosis is steroids (3).

Paget's disease is a chronic bone disease affecting either single or multiple bones. The prevalence of this condition is relatively low in Africa and Asia compared with Europe and the United States (4). The treatment aims to suppress osteoclasts and osteoblasts with bisphosphonate therapy (5). Kurihara et al. (6) showed that osteoclasts in Paget's disease have increased vitamin D3 receptor sensitivity, which may be associated with higher vitamin D receptor (VDR) gene expression. Moreover, Ishizuka et al. (7) reported that bone resorption in Paget's disease can be prevented using vitamin D antagonists.

VDR is a regulatory transcription gene that belongs to the nuclear receptor family. VDR plays a role in cell proliferation, differentiation, immune response, and ligand-dependent pathways including the calcium-phosphorus balance, in the body. The effect of vitamin D3-VDR signaling on the immune system is increasingly recognized, as VDR expression and activity play important roles in both T cell development and

differentiation (8). VDR shows sequence similarity to steroid and thyroid hormone receptors (9). Interestingly, glucocorticoids, the first-line therapy for sarcoidosis, have been shown to reduce VDR gene expression (10).

Initially, the differential diagnoses of our patient's bone lesions included malignant bone metastases, multiple myeloma, bone involvement of sarcoidosis, and metabolic bone diseases. Normal immunofixation electrophoresis and whole body PET-CT scan exonerate metastatic malignancies and multiple myeloma. Noy et al. (11) also excluded similar differential diagnoses in the cases they presented.

Bone involvement in sarcoidosis mostly occurs in the form of lytic and sclerotic lesions (12,13). However, our patient exhibited osteoblastic changes on imaging, which decreased the suspicion of osseous sarcoidosis. No granular lesions were observed in the liver relating to the patient's sarcoidosis, and liver enzymes other than ALP were within the normal reference range. We therefore arrived at the diagnosis of Paget's disease in this older patient with sarcoidosis.

Conclusion

The etiologies of Paget's disease and sarcoidosis are not well-defined. The pathophysiology of sarcoidosis includes defective T cells and macrophages, which lead to the formation of granulomas (3). On the other hand, increased turnover of osteoclasts has been observed in Paget's disease (14), where osteoclasts are a member of the macrophage family. There may be a common intrinsic factor associated with the VDR gene receptor that triggers the defective activation of macrophages in both disorders. More than half of patients with Paget's disease are asymptomatic; thus, the coexistence of the two disorders may remain unnoticed. Whether bisphosphonates can be used in the treatment of osseous sarcoidosis is a topic for future research.

Ethics

Informed Consent: Consent forms have been obtained from the patient for case presentation.

Authorship Contributions

Design: T.T., Data Collection or Processing: T.T., B.C., Analysis or Interpretation: N.Ş.D.,Ç.A., A.T., Literature Search: B.C., Writing: T.T.

Conflict of Interest: Aslı Tufan is Associate Editor in European Journal of Geriatrics and Gerontology. She had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Other authors have nothing to disclose.

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