Isolated Sacral Sarcoidosis a Hidden Cause of Sciatica: Case Report and Brief Review of the Literature

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Abstract- Bone involvement in sarcoidosis is rare; its estimated prevalence ranges between 3 and 13%. Osseous lesions usually occur in the phalanges of the hands and feet. Involvement of the axial skeleton is more uncommon. Osseous involvement may be asymptomatic. It is often incidentally discovered on imaging modalities. Radiological techniques can reveal sclerotic and/or destructive lesions. We present a case of a 61-year-old woman in whom osseous sarcoidosis of the sacrum was revealed by back pain and sciatica. To our knowledge, only one isolated case of sacral sarcoidosis has been reported in the literature. Sarcoid bone lesions can be present at disease onset without pulmonary involvement. A biopsy is often required in order to eliminate other conditions, especially malignancy. Treatment is not specific and also not needed in a significant number of cases.

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Keywords: Osseous sarcoidosis; Sarcoidosis; Back pain; Granuloma; Bone marrow biopsy

Introduction

Sarcoidosis is a multisystem inflammatory disease of unknown etiology. It is characterized by the formation of noncaseating granulomas infiltrating affected organs (1). The disease is extremely heterogeneous, which makes it usually a diagnosis of exclusion (2). Although lungs and lymphatic system are the most affected organs in sarcoidosis, multiple organ systems can be involved (1,3). However, bone involvement in sarcoidosis is rare (3% to 13%) (3-6), and involvement in sacrum is even rarer (7,8). Since osseous sarcoidosis is often asymptomatic, its prevalence may be underestimated (9). Bone involvement is often associated with cutaneous lesions (10). Any bone may be affected in osseous sarcoidosis. Bilateral involvement of the tubular bones of the hands and feet (Juggling osteitis) is the most frequent site of involvement in bone sarcoidosis (4). However, reports of sacral involvement are rare but do exist (5,11,12). We present a case of isolated sacral sarcoidosis revealed by lombosciatica.

Case Report

A 61-year-old woman with no significant health problems presented with a one-year history of worsening mechanic low back pain and bilateral intermittent sciatica. No other symptoms were present (fever, weight loss, dyspnea, visual disturbances, or skin changes). Osteoarticular examination showed reproducible sacroiliac pain with Tripod's maneuver. The range of motion in the lumbar spine was decreased. Neither lymphadenopathy nor skin changes were detected. The remainder of her physical examination, including lung examination, was normal. Initial laboratory results included a normal blood count except lymphopenia of 1070/mm^2, no biological inflammatory syndrome, and normal liver and renal function tests. Chest and spine Radiography was unremarkable. Radiography of the pelvis and sacrum showed sacral and bilateral iliac

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sclerosis with normal joint space. Magnetic Resonance Imaging (MRI) of the lumbosacral spine showed facet joint osteoarthritis associated with lumbar spinal stenosis and bilateral sacral edema with linear reticular images (Figure 1). In light of these findings, a bone biopsy of the iliac crest was performed. The anatomopathological report disclosed an epithelioid and gigantocellular granulomatous reaction without caseum. Stains for acid fast bacilli were negative.

Serum calcium, phosphorus, vitamin D, and 24-hour urine calcium were normal. Tuberculin skin test and the QuantiFERON-TB Gold test were negative. Furthermore, Syphilis, Lyme and HIV serology, antinuclear antibody (ANA) and anti-neutrophil cytoplasmic antibody (ANCA) were all negative. Accessory salivary gland biopsy was normal. Hematological malignancy was also ruled out (normal serum protein electrophoresis, normal serum and urine immunoelectrophoresis). A thoraco-abdominal and pelvic CT scan showed infracentimetric coelio-mesenteric nodes without adenomegaly. An angiotensin converting enzyme level was drawn and was within normal limits. Ophthalmological examination showed minimal dry eye syndrome with no uveitis. Bronchoalveolar lavage with biopsies and echocardiography didn't demonstrate granulomatous infiltration. The diagnosis of isolated sacral sarcoidosis was confirmed. The patient was treated with paracetamol and celecoxib and monitored every 3 months. Symptoms were decreasing and pain relief was reported. At 24 months follow-up, she only complained of sciatica flare-ups.

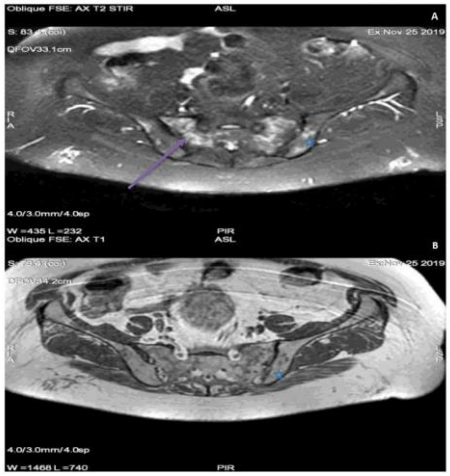

Figure 1. (A) Axial T2-weighted STIR fat SATURATED, (B) axial T1-weighted MRI images demonstrated indistinct lesions on bilateral iliac bone (star) and particularly midsacral area (arrow). These lesions were hypo intense on T1- weighted and hyperintense on fat-saturated images with respect of sacroiliac joints

Discussion

We report a case of isolated sacral sarcoidosis with no evidence of pulmonary involvement. The incidence of osseous sarcoidosis ranged from 3% to 13% (3-6). When the present, bone disease is more common in the small tubular bones of the appendicular skeleton (4). Skeletal lesions of sarcoidosis are often asymptomatic. Thus, estimations of the incidence of sarcoid bone may be falsely low (9,13). The most common locus of symptomatic osseous sarcoidosis is the vertebrae, for which a dozen of cases have been reported (14-21). The sacrum is a rare site of involvement. We reviewed the literature in order to identify cases of osseous sarcoidosis with sacral involvement. (Table 1) summarizes the main studies conducted on osseous sarcoidosis with involvement of the sacrum. Up to 70 osseous sarcoidosis with sacral involvement have been described (Table 1). An isolated case of sacral sarcoidosis has been reported by Garwood *et al.*, (11).

Pain is often a prominent feature of axial skeletal sarcoidosis, and it can be the initial sign of the disease, as in our case (22). Although most patients have evidence of lung involvement or lymphadenopathy, the bone disease may occur without common manifestations of sarcoidosis (11). The diagnosis of sarcoidosis is rarely made as a result of the evaluation of bone lesions, which often escape notice or are overshadowed by the systemic involvement of the disease (23).

Radiographs of the hands and feet may be used to help establish the diagnosis of osseous sarcoidosis. The lesions usually appear in the phalanges of the hands and feet and are often multifocal and lytic (24,25).

Osseous sarcoidosis has a variety of radiological patterns: lytic lesions (also called bone cysts), permeative lesions resulting in a reticular or lace-like pattern usually accompanied by soft tissue swelling, destructive lesions resulting in a sequestrum (7). Fractures are rare but may occur in the case of extensive lytic lesions (7). However, periostitis is uncommon (7). Lesions may be predominantly lytic, sclerotic, or a mixture of the two (26). Lytic lesions can simulate metastases (9). Our patient's MRI showed bilateral sacral edema with linear reticular images.

Plain radiography cannot reliably reflect early bone lesions, especially when lesions are small (12). Reports have highlighted the use of advanced imaging such as bone scintigraphy (27,28), computed axial tomography (29), or MRI (27,30) in establishing the diagnosis of bone sarcoidosis. Bone scintigraphy was considered a sensitive method of detecting bone involvement in sarcoidosis;

however, the increased uptake is not specific and cannot differentiate bone sclerosis from metastasis (27). Recently, MRI has been considered the most sensitive modality in the detection of the axial skeleton and bone marrow involvement (30-32). It improves the detection of Musculoskeletal involvement in sarcoidosis patients, thus revealing disease not seen at conventional radiography (30). Granulomatous infiltration of the bone marrow results in abnormal signals on MRI. The lesions are usually hypointense on T1-weighted imaging, hyperintense on T2-weighted and STIR imaging, and show enhancement after contrast administration (12). MRI Was the most widely used diagnostic imaging modality in the literature (Table 1).

Diagnosis of sarcoidosis is relatively easy when the patient presents with multisystem features of the disease. However, it may be difficult to establish the diagnosis if the bone lesions occur in the absence of typical pulmonary and systemic typical manifestations of sarcoidosis as in our patient. The differential diagnosis of sarcoidosis of the bones should always include malignancy such as bone metastasis, myeloma, lymphoma, fungal and mycobacterial infections such as tuberculosis, histoplasmosis, and coccidiomycosis, bone metabolic diseases such as osteopetrosis, Paget's disease, and hyperparathyroidism, and bone tumors (7,33). A bone biopsy is often needed to demonstrate the presence of noncaseating granuloma and exclude tuberculosis and other conditions by appropriate laboratory tests and cultures (34). More than 50% of patients with known sarcoidosis have bone marrow granulomas (35). Higher incidence of extrapulmonary involvement, lymphopenia, thrombopenia, or anemia have been reported in patients with bone involvement than those without involvement (36). Our patient had lymphopenia associated with bone disease. Granulomatous infiltration of the bone marrow may be the cause of lymphopenia.

Treatment of osseous sarcoidosis remains controversial and disappointing. The literature on this matter is limited since it is a rare disease. Some cases report improvement without treatment (37,38). A significant part of patients with osseous involvement have the asymptomatic non-progressive disease and don't require treatment (39). Corticosteroids may decrease pain and swelling but do not completely normalize the bone abnormality. Symptomatic relief may be obtained by colchicine, indomethacin and other nonsteroidal anti-inflammatory agents (7,9). Little data is available on alternatives to steroids, including anti-TNFalpha drugs (15,40). Empiric trials of infliximab in a patient with sarcoidosis involving the pelvis was associated with relapse of symptoms gradually after a period of four months (41). Another case reported the use of Adalimumab to treat sarcoidosis and Crohn's disease; however, the outcome was not reported (42). Therefore, clinical trials are needed to assess the efficacy of alternatives. In most patients, no chronic use of treatment is required as the outcome is often the remission of symptoms without recurrence (5).

Table 1. Results of the main studies that assessed osseous sarcoidosis with sacral involvement:

Authors/year	N	Mean age at diagnosis (years)	symptoms	Bone biopsy	Bones affected / sacrum involvement	Imaging modalities	Treatment
Sparks et al., (5)/2014	20	48.9	10 patients (50%)	4 patients	The sacrum was involved in 9 cases	13 cases: MRI 9 cases PET-CT 4 cases: CT 2 cases: X-Ray 1case: Scintigraphy	GC:6 cases MTX:4 cases HC:3 cases
Ben Hassine et al., (6)/2019	88	41	42 patients (48%)	25 patients	Pelvis (63%)	MRI: 42 (48%), PET/CT-scan: 42 (48%), X-rays: 33 (38%), Bone scan: 22 (25%) and bone scintigraphy: 16 (18%) patients	GC (54%), MTX (53%), HC (31%)
Niederhauser et al., (41)/2013	1	42	Back and pelvis pain	Yes	pelvis	MRI	GC and anti-TNFα (Infliximab)
Sakellariou et al., (43)/2011	1	46	Back pain	Yes	Lumbar spine, femur and sacrum	X-rays, CT scan, MRI	GC and MTX
Bargagli et al., (9)/2009	1	61	None	Yes	Lumbar spine, femur and sacrum	X-rays, scintigraphy, MRI	GC and MTX

Cont. Table 1

Kuzyshyn et al., (12)/2015	2	63	Lower back and leg pain	Yes	Lumbar spine, femur, humerus, scapula and sacrum	X-rays, CT scan	GC and MTX
		53	Lower back pain and right foot numbness	No	Lumbar spine, iliac bone and sacrum	CT scan, PET scan, MRI	GC
Ashamalla et al., (42)/2016	1	60	Back pain	Yes	Bilateral pelvic bones, femoral heads, and sacrum	MRI, PET scan	Anti-TNFα (Adalimumab)
Talmi et al., (44)/2008	1	48	Leg pain	Yes	Pelvis, humerus, femurs, raduis	X-Rays, PET scan	GC
Binicier et al., (26)/2008	1	55	Back pain	Yes	Iliac crests, spine, and sacrum	X-rays, MRI	GC
Garwood et al., (11)/2003	1	35	Back pain	Yes	Sacrum	MRI	GC
Resnik et al., (45)/1990	1	33	Back pain	Yes	Sacrum, iliac crests, Lumbar spine	CT scan, MRI	-
Cengiz et al., (46) / 2012	1	52	Back and right hip pain	Yes	Calvarium, thoracic spine, pelvis and sacrum	CT scan, scintigraphy	-
Zhou et al., (22)/2017	64	-	38 patients (59.4%)	42 patients (65.6%)	Pelvis (35.9%)	PET scan (50%), MRI (56%)	MTX (54.7%), HC (37.5%) and anti-TNF α (Infliximab) (23.5%)
Yachoui et al., (33)/2015	1	64	Pain in the back, neck, and pelvis	Yes	Lumbosacral spine	MRI, PET scan	MTX
Atanes et al., (47)/1991	94	47	-	No	The sacrum was involved in one patient	-	-
Kanner et al., (48)/2019	1	45	Back pain	Yes	Pelvis and lower thoracic spine	MRI	GC + MTX

N: Number; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography; CT: Computerized Tomography; GC: Glucocorticoids; MTX: Methotrexate; HC: Hydroxychloroquine; anti-TNFα: anti-Tumor Necrosis Factor-alpha

We have described a case of osseous sarcoidosis of the sacrum presenting with noncaseating granuloma and an absence of pulmonary involvement. Bone marrow biopsy is useful in establishing the diagnosis of osseous sarcoidosis. Treatment of osseous sarcoidosis is not specific. Imaging and treatment guidelines for extrapulmonary sarcoidosis are inexistent due to the lack of randomized trials. Corticosteroids may control pain and swelling but usually do not influence the course of osseous sarcoidosis. Further studies are warranted to further examine treatment options.

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