Netherlands
The Journal of Medicine

CASE REPORT

Sarcoidosis mimicking metastatic disease: a case report and review of the literature

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ABSTRACT

Osseous and in particular vertebral sarcoidosis is exceedingly rare and a difficult diagnosis to establish because it may simulate many diseases, including even metastatic malignancy. We present a patient with lesions in bones, lungs and lymph nodes, mimicking the presence of extensive metastatic disease. Our case emphasises the importance of histological evidence before the diagnosis of osseous sarcoidosis can be made with confidence.

KEYWORDS

Besnier-Boeck-Schaumann, hypercalcaemia, vertebral, sarcoidosis

INTRODUCTION

Sarcoidosis is a chronic granulomatous multisystem disease of unknown aetiology, which usually affects young adults. The diagnosis of sarcoidosis is made by a combination of clinical, radiological and histological findings. Symptoms are weight loss, fatigue, fever, night sweats, coughing and shortness of breath. On the X-ray of the chest a spectrum of abnormalities can be seen varying from lymphadenopathy to extensive parenchymal destruction.

However, histological proof with noncaseating granulomata remains the hallmark of this disease. The diagnosis is sometimes difficult to establish, because sarcoidosis may simulate many diseases, including even metastatic malignancies. We present a patient with lesions in bones, lungs and lymph nodes, mimicking the presence of extensive metastatic disease.

CASE REPORT

A 61-year-old asymptomatic white male, working as a carpenter, was referred to our hospital with renal function impairment, with a creatinine of 123 μmol/ (70-110 μmol/) which was found on a routine check-up in June 2004. Physical examination showed no abnormalities. Routine laboratory tests showed a creatinine of 111 μmol/l, creatinine clearance 91 ml/min, a calcium of 3.15 mmol/l (2.20-2.60 mmol/l), with a normal albumin value of 41 g/l (34-48 g/l), serum phosphate concentration of 0.94 mmol/l (0.75-1.45 mmol/l) and an erythrocyte sedimentation rate of 37 mm/h (0-20 mm/h). Further laboratory tests showed a parathormone <0.4 pmol/l (0.6-4.2 pmol/l), 25-hydroxy vitamin D concentration of 68 nmol/l (25-160 nmol/l), thyroid-stimuating hormone of 1.5 mU/l (0.3-4.0 mU/l), normal angiotensin-converting enzyme level of 48 U/l (12-68 U/l) and normal serum protein electrophoresis. A chest X-ray revealed multiple pulmonary nodules in the right lower lobe and broadening of the mediastinum, suspicious for pulmonary metastases and extensive mediastinal lymphadenopathy (*figure 1*). A Tc-99m HDP whole-body bone scan revealed numerous hot spots, mainly axial, which was highly suggestive of extensive metastatic disease (*figure 2*). Total spine magnetic resonance imaging (MRI) showed abnormal marrow signal intensity within several vertebral bodies (*figure 3 A-B*), without radiological signs of cord compression. Extensive bone lesions were also observed in both iliac bones (*figure 3 C-D*), acetabulum and proximal femurs. All of these findings were highly suggestive of metastatic disease. Further work-up included a computed tomography (CT) scan of the chest and abdomen, which showed multiple lung lesions and enlarged mediastinal lymph nodes, suggesting extensive lung and lymph node metastases (*figure 4*). In the abdomen enlarged lymph nodes were mainly found along the aorta and the iliac artery. A lesion in the spleen was observed, suggesting spleen metastasis. Bone biopsy of the iliac

Figure 1. *Chest radiograph revealing reticulonodular interstitial disease in the lower lobes, hilar lymphadenopathy and broadening of the mediastinum*

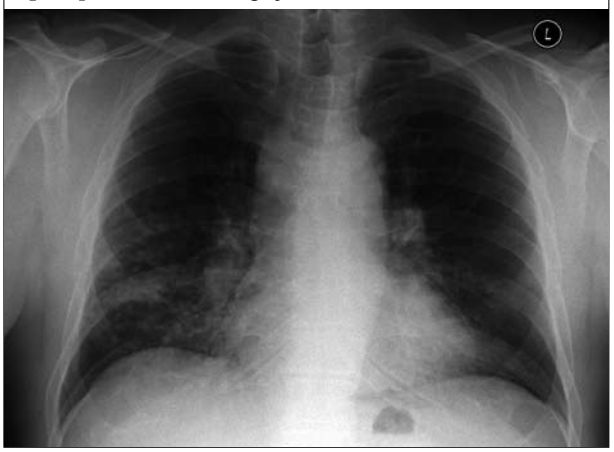


Figure 2. *Tc-99m HDP bone scintigraphy showing multiple focal areas of abnormal radiotracer accumulation mainly in the axial skeleton, but also in the left shoulder region, both iliac bones, hips and left ankle*

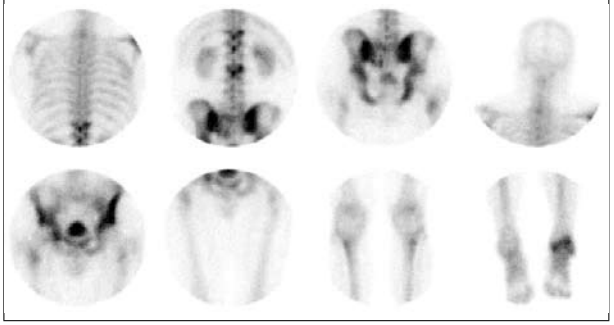
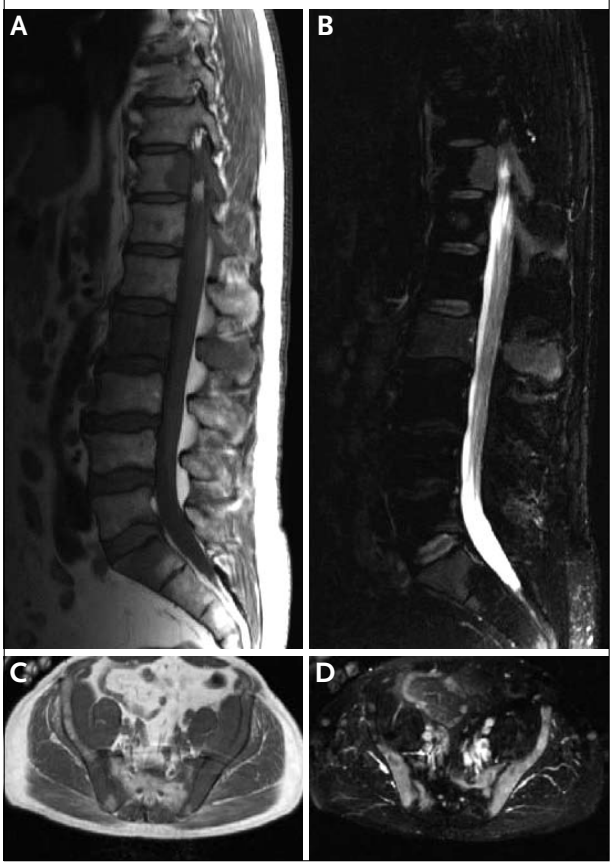
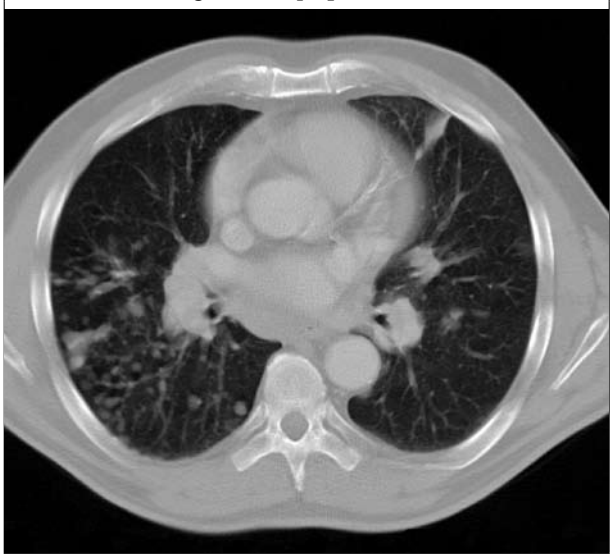


Figure 3. *A) Sagittal T1-weighted MRI showing multiple low signal lesions in the vertebral bodies and enlarged abdominal lymph nodes, B) T2-weighted sequences showing hyperintensive vertebral lesions, C) Axial T1-weighted MRI demonstrating hypointense lesions in both iliac bones and D) The iliac lesions have a high signal intensity in T2-weighted sequences*



bone demonstrated the presence of epithelioid granulomas and giant cells (*figure 5*). The same was found in biopsy specimens of peripheral lung tissue. Polymerase chain reaction on mycobacteria was negative. These pathological findings were consistent with sarcoidosis and because of the hypercalcaemia, treatment followed with prednisolone 20 mg/day. After six months of treatment the patient is still asymptomatic while calcium and renal function have normalised. A second MRI of the spine showed an amelioration in signal intensity without, however, a decrease in the number and volume of the lesions.

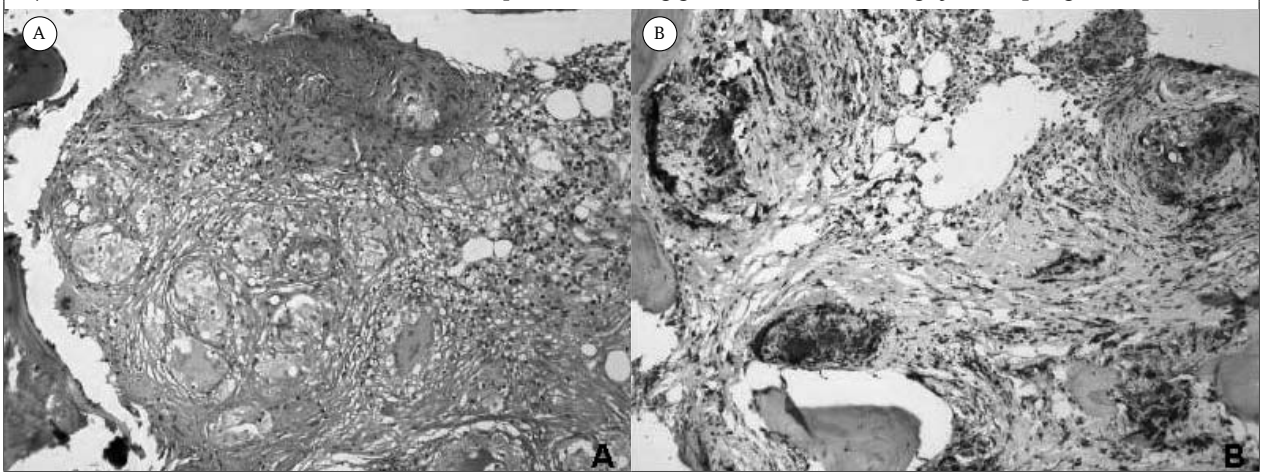
Figure 4. *CT scan of the chest showing multiple lung lesions and enlarged hilar lymph nodes*



DISCUSSION

Sarcoidosis is a multisystem disorder characterised by noncaseating granulomatous infiltration. The most common sites of involvement are lungs and lymph nodes, while other organs such as spleen, liver, skin, eyes, muscles, bones, central nervous system and salivary

Figure 5. *A) Bone marrow biopsy from the iliac bone stained with periodic acid-Schiff (PAS), showing multiple epithelioid granulomata and giant cells*
B) section stained with an anti-CD68 antibody demonstrating granulomata consisting of macrophages



glands are less frequently involved.[1] With this variety of organs involved, sarcoidosis can mimic other diseases. In our case, the patient was thought to have disseminated metastatic malignancy, based on bone scintigraphy, MRI and chest plus abdominal CT suggesting bone, lung, lymph node and spleen metastasis. In 2003 Haluska *et al.* presented a similar patient who was presumed to have widespread metastatic melanoma; vertebral MRI lesions suggested metastatic neoplasm. However, these lesions turned out to be nonnecrotising granulomas consistent with sarcoidosis.[2] Ludwig *et al.* reported a patient presenting with low back pain, who was also thought to have metastatic skeletal disease based on MRI, bone scintigraphy chest CT and FDG-PET imaging, which also turned out to be sarcoidosis.[3] A similar case was also reported by Mangino *et al.*[4]

Osseous involvement is relatively uncommon in sarcoidosis. The incidence varies from 1 to 13%.[5] Most cases of osseous sarcoidosis occur in the long bones of the hands and feet.[6] Vertebral involvement in sarcoidosis is exceedingly rare with less than 30 cases reported.[4] A consistent feature of previous reports of vertebral sarcoidosis is back pain,[7,8] but our case shows that extensive vertebral bone lesions can be present without symptoms, with hypercalcaemia as sole abnormality. Granulomas in sarcoidosis provide a nonrenal source of 1,25-dihydroxy-vitamin D3, which has been demonstrated in lymph nodes and in alveolar macrophages. This hyperproduction may result in enhanced intestinal calcium absorption leading to hypercalcaemia.[9] In our case, however, the vitamin D concentration was normal, so the hypercalcaemia in our patient was most likely due to the observed bone lesions.

Bone scintigraphy has been reported rarely in vertebral sarcoidosis.[2,3,7] Although nonspecific, it may be a sensitive indicator of the extent of osseous sarcoidosis and has potential diagnostic utility in that it can localise sites for biopsy if the clinical area is not readily accessible.[7] In a few cases MRI findings in vertebral sarcoidosis have been reported.[2-5,7,8,10-12] MRI usually demonstrates multifocal lesions within the vertebrae that are hypointense (low-signal intensity) on T_1-weighted images and hyperintense (high-signal intensity) on T_2-weighted images, which enhance following contrast medium administration.[4,10] Multifocal vertebral body lesions have a broad differential diagnosis that typically includes metastatic disease (in particular prostate, breast and lung), lymphoma, myeloma, Paget's disease, osteomyelitis, renal osteodystrophy and granulomatous diseases, which stresses the need for further investigation. The rarity of osseous and in particular vertebral sarcoidosis plus its nonspecific imaging manifestations often lead to a significant delay in diagnosis.[8]

Management of bone sarcoidosis remains controversial, and randomised controlled trials have not been reported. Indications for therapy are not well defined, but pain, bone destruction and hypercalcaemia usually require treatment.[13] In our case, hypercalcaemia was the indication for therapy. Calcium can exert toxic effects on renal tubules and may lead to nephrogenic diabetes insipidus and by interstitial calcium deposition to nephrocalcinosis and chronic renal insufficiency.[9] Corticosteroids are the therapy of choice and long-term efficacy in osseous sarcoidosis has been suggested.[14] Moreover, prednisolone in relatively low doses (10-20 mg/day) is effective in rapidly correcting hypercalcaemia in sarcoidosis.[9] Symptoms are usually controlled, but radiographs may not show improvement.[15] In our case, the calcium normalised by treatment with prednisolone 20 mg/day. After 11 months a second MRI of the spine showed an amelioration in signal intensity, without, however, a decrease in the number and volume of the lesions. Rua-Figueroa *et al.* reported a change to normal signal on vertebral MRI long after a clinical response to treatment.[7]

In conclusion, osseous and in particular vertebral sarcoidosis is exceedingly rare and a difficult diagnosis to establish because of the resemblance to other diseases, including even metastatic malignancy. This case emphasises the importance of histological evidence, before the diagnosis of osseous sarcoidosis can be made with confidence.

REFERENCES

1. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med 1997;336(17):1224-34.
2. Haluska P, Luetmer PH, Inwards CY, Afessa B, Shives TC, Ingle JN. Complications of therapy and a diagnostic dilemma case. Case 3. Diagnostic dilemma: sarcoidosis simulating metastatic malignancy. J Clin Oncol 2003;21(24):4653-54.
3. Ludwig V, Fordice S, Lamar R, Martin WH, Delbeke D. Unsuspected skeletal sarcoidosis mimicking metastatic disease on FDG positron emission tomography and bone scintigraphy. Clin Nucl Med 2003;28(3):176-9.
4. Mangino D, Stover DE. Sarcoidosis presenting as metastatic bony disease. A case report and review of the literature on vertebral body sarcoidosis. Respiration 2004;71(3):292-4.
5. Jelinek JS, Mark AS, Barth WF. Sclerotic lesions of the cervical spine in sarcoidosis. Skeletal Radiol 1998;27(12):702-4.
6. Cohen NP, Gosset J, Staron RB, Levine WN. Vertebral sarcoidosis of the spine in a football player. Am J Orthop 2001;30(12):875-7.
7. Rua-Figueroa I, Gantes MA, Erausquin C, Mhaidli H, Montesdeoca A. Vertebral sarcoidosis: clinical and imaging findings. Semin Arthritis Rheum 2002;31(5):346-52.
8. Lisle D, Mitchell K, Crouch M, Windsor M. Sarcoidosis of the thoracic and lumbar spine: imaging findings with an emphasis on magnetic resonance imaging. Australas Radiol 2004;48(3):404-7.
9. Rizzato G. Clinical impact of bone and calcium metabolism changes in sarcoidosis. Thorax 1998;53(5):425-9.
10. Ginsberg LE, Williams DW, III, Stanton C. MRI of vertebral sarcoidosis. J Comput Assist Tomogr 1993;17(1):158-9.
11. Fisher AJ, Gilula LA, Kyriakos M, Holzaepfel CD. MR imaging changes of lumbar vertebral sarcoidosis. AJR Am J Roentgenol 1999;173(2):354-6.
12. Poyanli A, Poyanli O, Sencer S, Akan K, Sayrak H, Acunas B. Vertebral sarcoidosis: imaging findings. Eur Radiol 2000;10(1):92-4.
13. Bascom R, Johns CJ. The natural history and management of sarcoidosis. Adv Intern Med 1986;31:213-41.
14. Gibson GJ, Prescott RJ, Muers MF, et al. British Thoracic Society Sarcoidosis study: effects of long term corticosteroid treatment. Thorax 1996;51(3):238-47.
15. Neville E, Carstairs LS, James DG. Sarcoidosis of bone. Q J Med 1977;46(182):215-27.