SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2022; 39 (3); e2022034 DOI: 10.36141/svdld.v39i3.8744

Unusual bone localization of sarcoidosis mimicking metastatic lesions: case report and review of literature

Besma Hamdi[1,5], Emna Ben Jemia[1,5], Monia Attia[2,5], Ikbel Khalfallah[1,5], Hend Riahi[4,5], Anissa Berraies[1,5], Mohamed Faouzi Ladeb[4,5], Soumaya Rammeh[3,5], Agnes Hamzaoui[1,5]

[1]Pulmonology Departement Diseases, Abderrahmen Mami Hospital, Ariana 2080, Tunisia; [2]Medical Imaging Departement, Abderrahmen Mami Hospital, Ariana 2080, Tunisia; [3]Anatomopathologic Departement, Charle Nichole Hospital, Tunisia; [4]Medical Imaging Departement, Kassab Orthopedic Institute; Ksar Said, Tunisia; [5]University of Tunis El Manar, Faculty of Medicine of Tunis, Tunis 1007, Tunisia

Abstract. Sarcoidosis is a multisystem disease of unknown origin. Diagnosis remains challenging, based on organ site involvement, histological confirmation of non-caseating granuloma and an appropriate clinical syndrome. Granulomatous bone involvement is rare and may be ignored because it is usually asymptomatic. Vertebrae, ribs and skull localizations are rarely reported. We described an interesting case of a woman with chronic and multiorgan sarcoidosis with unusual bone localizations.

Key words: Sarcoidosis, Bone lesions, Radiographic imaging, Granuloma

Introduction

Sarcoidosis is a granulomatous disease of unknown aetiology which may affect any organ (1). Lungs, lymph nodes, skin and eyes are the most commonly affected organs. Bone localisations usually interest phalange of the hands and feet and it is rare to see other sites in the cranio-caudal axis. It is necessary to eliminate other diagnosis, such as malignancy and other granulomatous infections.

Case presentation

After an oral consent, we present the case of a 58-year-old Tunisian woman, with a history of arterial hypertension and diabetes mellitus who was admitted for weight loss (20 kg), dyspnoea, dry cough and back pain evolving since two years. Physical examination revealed an isolated left subclavicular lymphadenopathy and frontal swelling with no other abnormalities.

Investigations

Chest radiograph showed bilateral interstitial involvement predominating in the bases (figure 1).

Laboratory investigations showed a normal calcemia, a high level of alkaline phosphatase and gamma glutamyl transferase as well as high level of inflammatory parameters. A computed tomography (CT) scan was realized and showed micronodules with lymphatic distribution in both lungs along with clavicular, mediastinal and abdominal lymph nodes. Liver was dysmorphic and micronodular with perihepatic adenomegaly discretely compressing intrahepatic bile ducts.

Moreover, the computed tomography of the body revealed a multiple mixed, lytic and sclerotic bone le-

Received: 8 February 2019
Accepted after revision: 21 September 2022
Correspondence: Dr Hamdi Besma
Pulmonology Departement Diseases, Abderrahmen Mami Hospital, Ariana 2080, Tunisia
Tel: 0021698478856
E-mail: h_besma@yahoo.fr

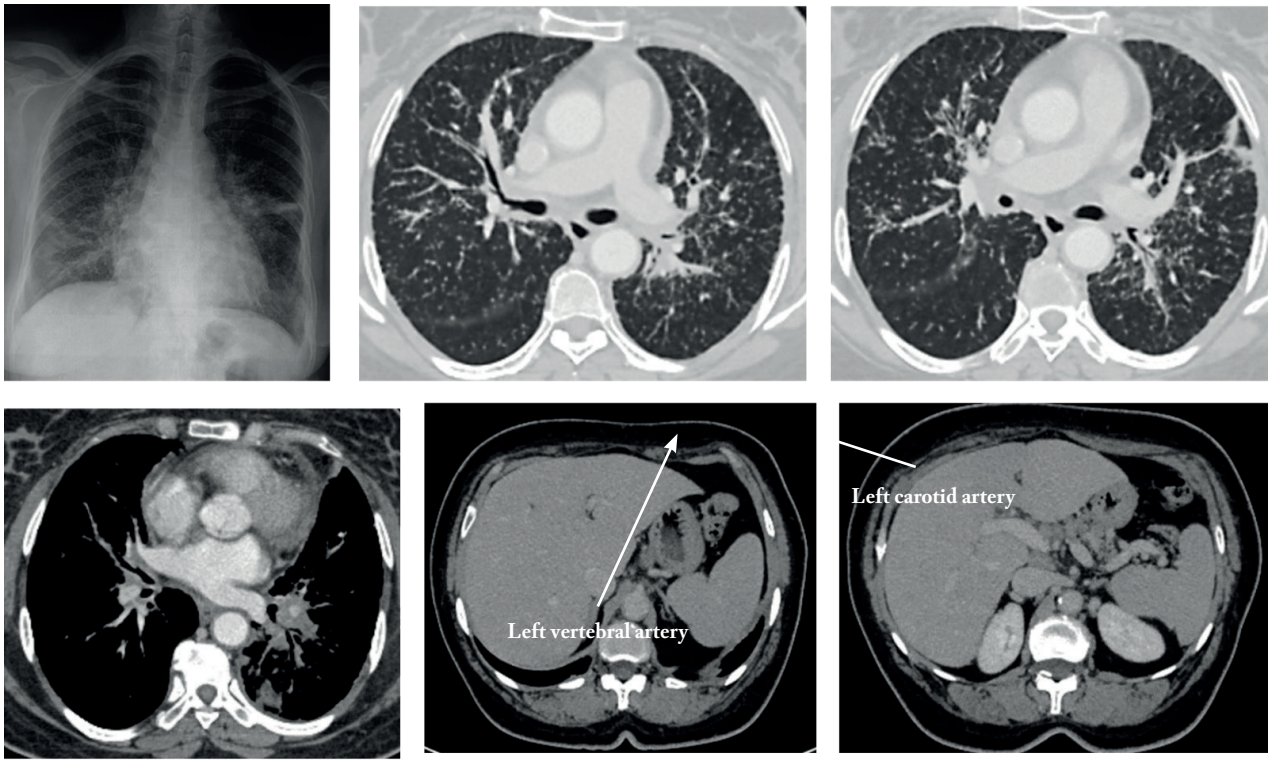

Figure 1. Chest radiography showing bilateral interstitial syndrome predominating in the bases. A computed tomography (CT) scan: micronodules with lymphatic distribution in both lungs with clavicular, mediastinal and abdominal lymph nodes and dysmorphic micronodular liver

sions with with suspicious signs of malignancy in 7th cervical vertebrae, thoracic vertebrae (8, 9, 11), 1st and 2nd Sacral vertebra, 6th,9th, tenth right ribs, costal cartilage of the 6th left ribs and a lytic lesion of the frontal bone (figure 2). These findings were suggestive of one of many oncologic processes, with differential diagnoses including metastases or tuberculosis.

These lesions are hypointense on T1 sequence, hypointense surrounded by an hyperintense border on STIR sequence and are mildly enhanced after gadolinium injection (figure 3).

Bone malignancy was the most likely diagnosis.

Flexible bronchoscopy showed inflammatory mucosa and biopsies were negative. Lymphocytosis was found in the bronchoalveolar lavage analysis (lymphocyte count: 46%) with a slight increase in CD4/CD8 ratio (2.4).

Investigations for tuberculosis (Ziehl–Neelsen stain and culture) were negative including tuberculin skin test and mycobacterial stains.

Node biopsy of the sub clavicular adenopathy was done and revealed granulomatous inflammation without caseous necrosis

Considering clinical presentation, radiological imaging, biological parameters and histological data the diagnosis of multisystem sarcoidosis was retained.

As the patient presented an altered general state with aggressive osseous lesions in CT, histological confirmation of bone lesions was needed. Costovertebral biopsy dismissed the diagnosis of malignancy and confirmed the granulomatous inflammation without caseous necrosis (figures 4, 5).

The other lesions (lung, lymph nodes skin and liver) were not biopsied.

Finally, the diagnosis of systemic sarcoidosis with bone involvement was confirmed.

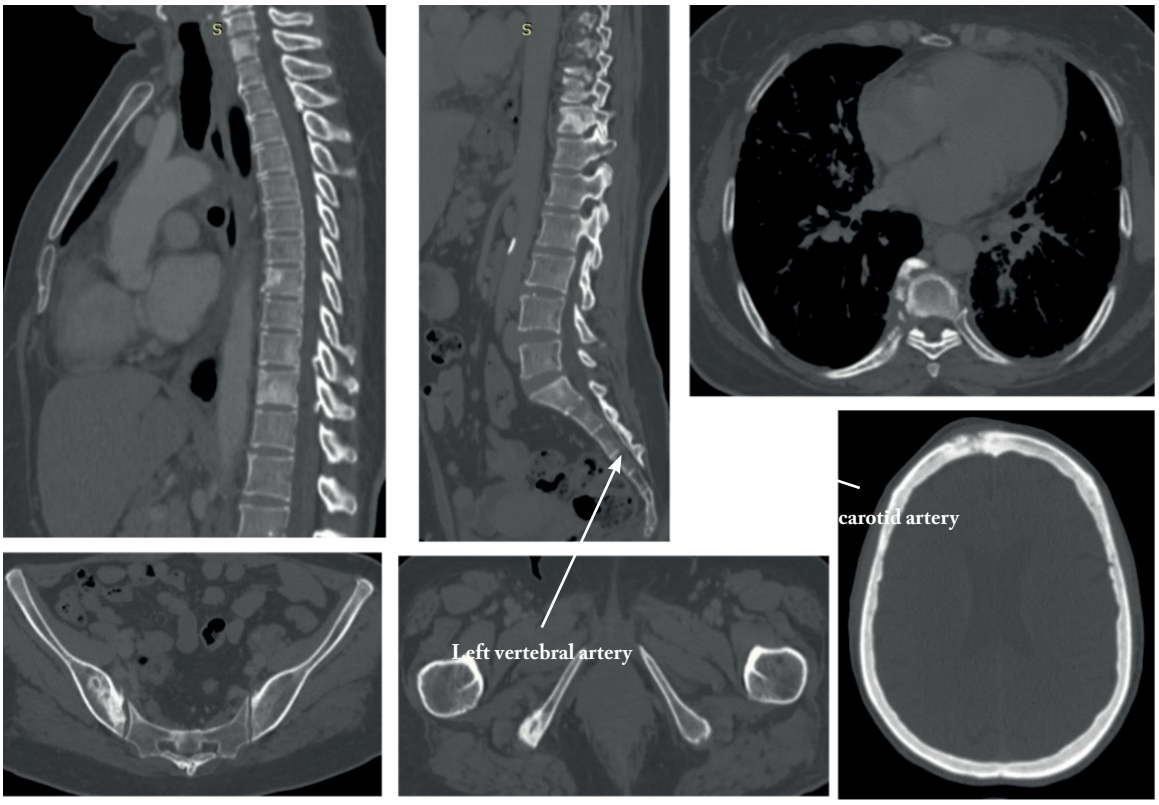

Figure 2. A computed tomography (CT) scan: multiple lytic, sclerotic and mixed bone lesions of C7,D8,D9,D11,S1 vertebra and iliac bone. Aggressive lytic lesion of frontal bone and 6th right rib.

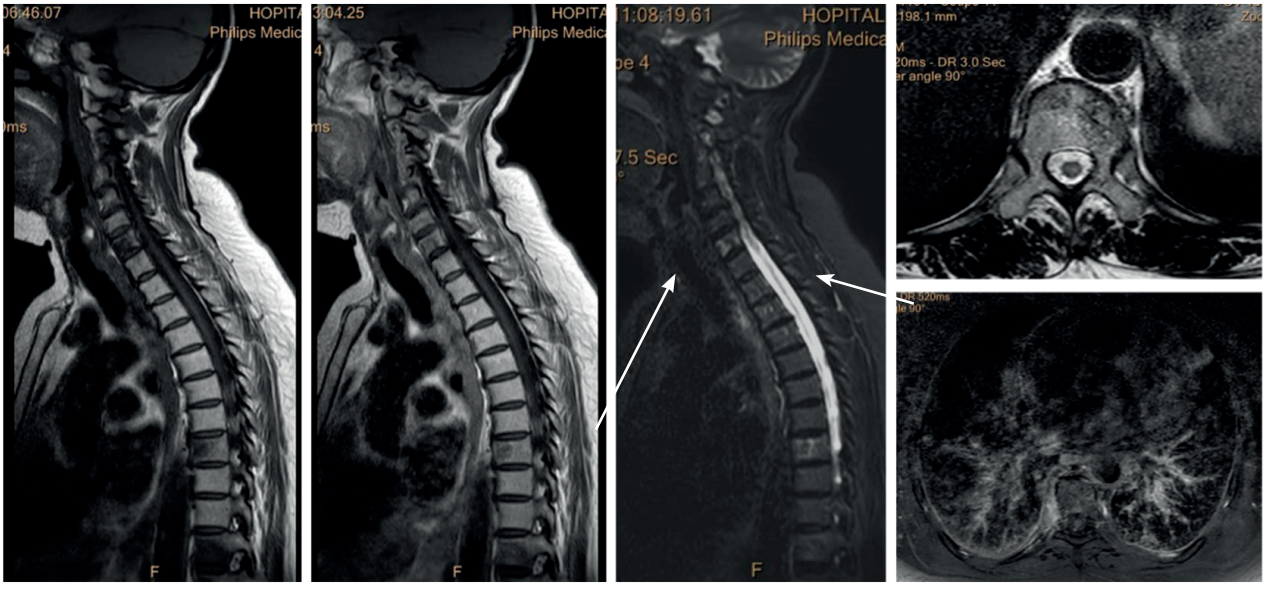

Figure 3. MRI sequences:T1,Stir,T1 after gadolinium injection: multiple infiltrative bone lesions hypointense on T1, hypointense on STIR surrounded by an hyperintense border. These lesions are mildly enhanced after gadolinium injection

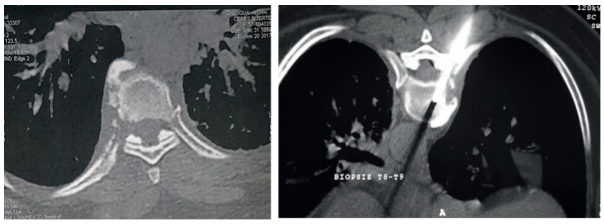

Figure 4. Costo-vertebral biopsy (6th right rib)

Pre therapeutic investigations

At the time of diagnosis, pulmonary function tests showed a forced expiratory volume in 1 s (FEV1): 1.05 L (51% of predicted) and FEV1/forced vital capacity (FVC): 55%. Six-minute walking distance (TM6) was 454m (65% of predicted value) without any impact neither on peripheral oxygen saturation nor on dyspnoea class: 2 (Borg scale).

Treatment

As the patient was symptomatic (dyspnoea, dry cough, weight loss,) along with abnormal pulmonary function tests, we decided to start oral prednisone 0.5mg/kg/day. After two months an excellent response to treatment was observed. In fact, the frontal swelling disappeared in the 3rd day of treatment and functional explorations showed an improvement of TM6 (79% of predicted value), FEV1 (from 51% to 73%), FVC (from 78% to 80%) and FEV1/FVC (from 55% to 72%).

Glucocorticoid-based treatment was maintained for a total of 18 months without a vitamin D supplementation. The patient was followed for 3 years. Her back pain gradually decreased. There was no progression or involvement of other bones or new skin lesions.

Discussion

We reported a rare case of a woman with chronic and multifocal sarcoidosis with unusual and symptomatic bone localizations mimicking metastatic lesions.

Sarcoidosis is a multisystemic disease of unknown aetiology. The epidemiology remains poorly defined. Cases are reported worldwide in all races and sexes, but young adults and people of black ethnicity seem to be at greater risk. It most frequently affects lungs, lymph nodes, skin, and eyes (1). Musculoskeletal manifestations are seen in 25% to 30% of patients (2). Symptoms severity is variable, ranging from arthralgia to severe back pain due to destructive bone lesions.

Bone involvement is rare with a reported incidence between 1 and 14 % (3). Small bones of the hand and feet represent the first bone target according to previous studies (3). However, the use of the magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/Scan) revealed the presence of silent axial bone involvement (4). In Zhou's study, including 64 patients with osseous sarcoidosis, 59% of patients were symptomatic and the vertebrae were the most commonly affected bones (68.8% of cases), followed by pelvis (35.9%) and hand bones (15.6%) (4). Lesions were solitary or multiple and could be predominantly lytic, sclerotic or mixed. In a review of 22 patients with vertebral sarcoidosis, back pain was the principal circumstance of discovery of the disease (3). Exact incidence is unknown because of asymptomatic patients and diagnosis is generally incidental as is the case of our patient.

Diagnosis of bone sarcoidosis is a challenge for the physician. The difficulty of diagnosis is due to het-

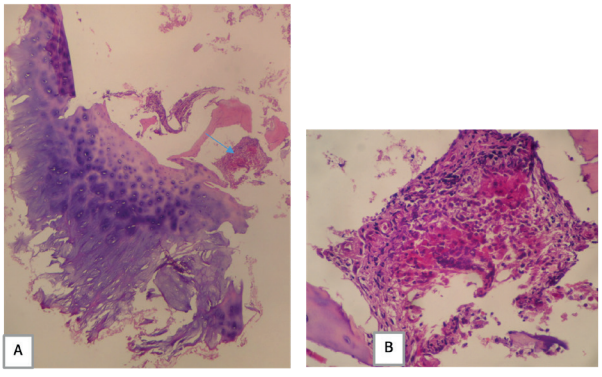

Figure 5. Histological examination of biopsy specimens from the costo-vertebra (A: hematoxylin and eosin) reveals an epithelioid granuloma and a gigantocellular granuloma in a medullary space under chondral. B: non-necrotizing granulomas compatible with bone sarcoidosis (Haematoxylin and Eosin).

erogeneous clinical features and, in some cases, to the atypical imaging presentation. In our case, despite the positivity of lymph node biopsy showing granulomatosis, neoplasia was the fear. So, we urged to perform a bone biopsy. This presentation is not exceptional, vertebral lesion with acute tetraplegy was described in a case report (5).

The MRI findings of vertebral sarcoidosis are known to vary widely due to the variable morphology of sarcoidosis lesions. The most common findings in the literature are low signal lesions on T1-weighted images, which show enhancement with gadolinium administration. The enhancing characteristics are variable, with three patterns classically described. The first of these is a peripheral, inhomogeneous pattern, the second is a dense homogeneous pattern, and the third is a mild homogeneous enhancement such that the lesions become isointense with bone marrow following gadolinium administration. Most of the published reports describe high signal on T2-weighted and STIR images, as in the present case (6).

There are several imaging techniques that could guide the diagnosis. Several studies showed that neither PET-Scan, nor scintigraphy, nor MRI can distinguish metastatic lesions from osseous sarcoidosis (7,8). In our case, despite the positivity of lymph node biopsy showing granulomatosis, neoplasm was a haunt and we decided to realise bone biopsy.

Like the case presented, bone sarcoidosis is usually associated with multiorgan disease affecting liver, spleen, or extrathoracic lymph nodes (5). In our patient, the diagnosis of sarcoidosis has been established. However, on routine MRI, osseous sarcoidosis lesions cannot be reliably distinguished from metastatic lesions. Therefore, discussion between the radiologist and the physician is recommended to decide of follow-up or biopsy (7).

Bone scintigraphy is a sensitive indicator of the extent of osseous sarcoidosis, as well as PET scan but the specificity of both investigations is low (6), so biopsy is advisable. Granulomatous inflammation without caesium represents a strong argument for sarcoidosis but other diagnoses must be eliminated.

Level of serum calcium was not high in our patient despite the presence of lytic lesions as well as vitamin D blood testing. This finding was described in a previous study where authors did not find a significant difference of serum calcium levels between patients with or without bone sarcoidosis (4). This result may reflect different pathologic pathways compared to other diseases that affect bones such as malignancy (4).

A Task Force committee was developed by the European Respiratory Society (9) to develop new guidelines for treating sarcoidosis. The committee recommends treatment (glucocorticoids ± immunosuppressants) for pulmonary, cardiac, cutaneous and neurological involvement. Other localizations were not considered for insufficient informations in the literature to make recommendations on treatment Asymptomatic patients with stable disease do not require treatment. Bone lesions in themselves are not an indication for treatment unless they are symptomatic. As bone localisation is usually suggestive of severe sarcoidosis with multiorgan involvement, patients may require corticosteroids despite its ineffectiveness on bone architecture (2,10). In a case report, other drugs such as methotrexate has been used with favourable outcome (11). In another case, spontaneous regression was observed with clinical and radiological involution (12). No large clinical trials have been performed to compare the efficacy of corticosteroid treatment with abstention or other immunosuppressive drugs in cases of bone sarcoidosis (13).

On MRI monitoring, vertebral lesions rarely disappeared spontaneously. A detectable scare was usually observed. The presence of intralesional fat was considered as a sign of lesion involution. This finding was reported in several cases (6,14,15). It has been hypothesized that when treatment was effective, the bone marrow destroyed by the granulomatous inflammation was replaced by fatty marrow in case of an effective treatment (16). This pattern of lipomatous infiltration could be useful predicting the disease course and response to treatment but large studies confirming this finding are lacking.

Conclusion

Bone involvement in sarcoidosis is challenging because its clinical and radiographic features mimic

those of a malignancy. In cases like the one presented bone biopsy was considered necessary to confirm the diagnosis of sarcoidosis.

Funding: This research received no specific grant from any funding agency, commercial or not-for profit sectors.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Author contributions: Besma Hamdi and Emna Ben Jemia managed the patient and contributed to the writing. Anissa Berraies and Agnes Hamzaoui contributed to the review. Soumaya Rammeh contributed to the description of biopsies. Monia Attia contributed to CT scan and MRI descriptions. Hend Riahi and Mohamed Fethi Ladeb contributed to Costovertebral biopsy.

Acknowledgements: The authors declare not to have any relationship with any organization or study sponsors. We have no conflict of interest at the time of submission.

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