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Case Report

Deciphering the Origin of Diffuse Skeletal Lesions Mimicking Malignancy: The Diagnostic Power of an Integrative Multidisciplinary Approach in Systemic Sarcoidosis with Osseous Involvement

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Abstract

Background: *Diffuse lytic skeletal lesions in adults typically raise immediate concern for disseminated malignancy, particularly multiple myeloma or metastatic carcinoma. Sarcoidosis, a multisystem granulomatous disorder known as "the great mimicker," can radiographically and metabolically resemble advanced cancer. Axial skeletal involvement, historically considered rare, is increasingly recognized with modern imaging.*

Case Presentation: *A 48-year-old man presented with progressive musculoskeletal pain without constitutional symptoms. MRI skull, spines and pelvis demonstrated multiple poorly circumscribed lesions concerning for metastases. 18F-FDG PET/CT revealed widespread hypermetabolic lytic lesions (SUVmax up to 10.58) and multisystem lymphadenopathy. Extensive laboratory evaluation including SPEP, serum free light chains, tumour markers, and bone marrow biopsy, showed no evidence of malignancy. Two subsequent core biopsies to the humerus and supraclavicular lymph node were nondiagnostic.*

Multidisciplinary Intervention: *Following an MDT review, the team proceeded with mediastinoscopy to obtain high-volume tissue. Histopathology demonstrated "multiple, coalescing, non-caseating epithelioid granulomas" with Langhans-type giant cells, and molecular studies excluded tuberculosis.*

Conclusion: *This case highlights the profound diagnostic overlap between sarcoidosis and metastatic malignancy, the non-specificity of high SUVmax values, and the essential role of MDT-guided biopsy selection and involvement. Early recognition prevents inappropriate oncologic treatment and enables timely inflammatory control.*

Keywords: *Sarcoidosis; Osseous Sarcoidosis; Cancer of Unknown Primary; PET/CT; Mediastinoscopy; Multidisciplinary Team.*

Introduction

Diffuse skeletal lesions in adults are most associated with metastatic carcinoma or multiple myeloma[16]. Sarcoidosis, however, remains one of the most challenging mimickers in clinical medicine[22]. It is characterized by non-caseating granulomas composed of macrophages, epithelioid histiocytes, and $CD4^+$ T-cells[22]. Although over 90% of patients exhibit intrathoracic involvement[2], extrapulmonary manifestations, including osseous disease, are increasingly recognized with advanced imaging[1112].

Historically, osseous sarcoidosis was reported in only 1–13% of cases[20], typically affecting small tubular bones. Modern MRI and PET/CT studies reveal more frequent axial involvement[1112], often mimicking metastatic disease. FDG uptake reflects glycolytic activity rather than malignancy and activated macrophages within granulomas can produce SUVmax values exceeding 10[12].

Sarcoidosis mimicking cancer of unknown primary (CUP) is well documented[34]. Multidisciplinary evaluation is essential to avoid anchoring bias and unnecessary oncologic interventions[918].

Case Presentation

A 48-year-old man with no chronic respiratory or immunosuppressive history presented at the orthopaedics surgical department with subacute musculoskeletal pain involving the shoulders, right hip, and spine. He denied weight loss, night sweats, or fevers.

Initial Imaging

MRI of the lumbar spine and pelvis revealed “poorly circumscribed foci with high T2 and low T1 signal” in the pelvis, symptomatic left iliac spine (Figure 1) and vertebral bodies, features concerning for metastatic disease[11]. Furthermore, imaging demonstrated “punched-out” lytic lesions, prompting urgent malignancy workup and involvement of the oncology division. At this point the differential diagnosis was multiple myeloma and cancer of unknown primary (CUP).

Laboratory Evaluation

Given the suspicion for multiple myeloma and occult solid primary malignancy, the patient underwent comprehensive testing:

- Serum Protein Electrophoresis (SPEP): Negative
- Urine Bence-Jones proteins: Negative

- Serum free light chains: Normal
- Calcium and creatinine: Normal
- PSA, CEA, CA 19-9: Normal

The first four findings did not meet CRAB criteria for myeloma[16].

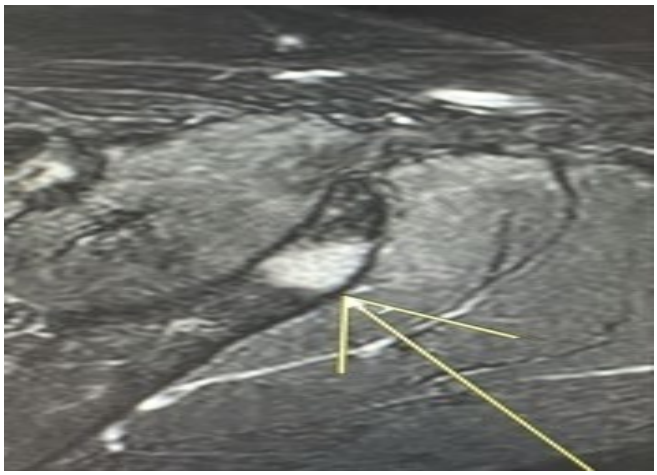

Figure1: MRI pelvis showing lytic lesion left iliac spine

In addition, a bone marrow aspirate was performed which showed <5% plasma cells, below the 10% threshold for myeloma[16]and no evidence of metastatic carcinoma as supported by the above biochemistry investigations. In a further diagnostic workup, a targeted biopsy of the right humerus was nondiagnostic, as illustrated in Figure 2, consistent with reports that osseous sarcoidosis often yields insufficient material with needle sampling[19].

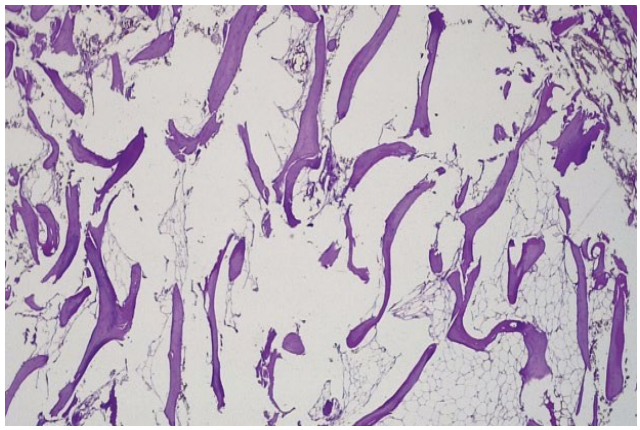

Figure 2: Humerus bone biopsy, non-diagnostic

Furthermore, an advanced imaging in FDG-PET/CT scan was suggested by the surgical oncology team, to establish whether the lytic lesions are not malignancy of unknown primary.

^18F-FDG PET/CT demonstrated, Figure 3:

- Symmetric hilar lymphadenopathy including the supraclavicular lymph nodes (SUVmax 6.98–7.38)
- Intense abdominal nodes (SUVmax 12–14)
- Multiple hypermetabolic lytic skeletal lesions, showing the left symptomatic iliac spine with intense (SUVmax up to 10.58)

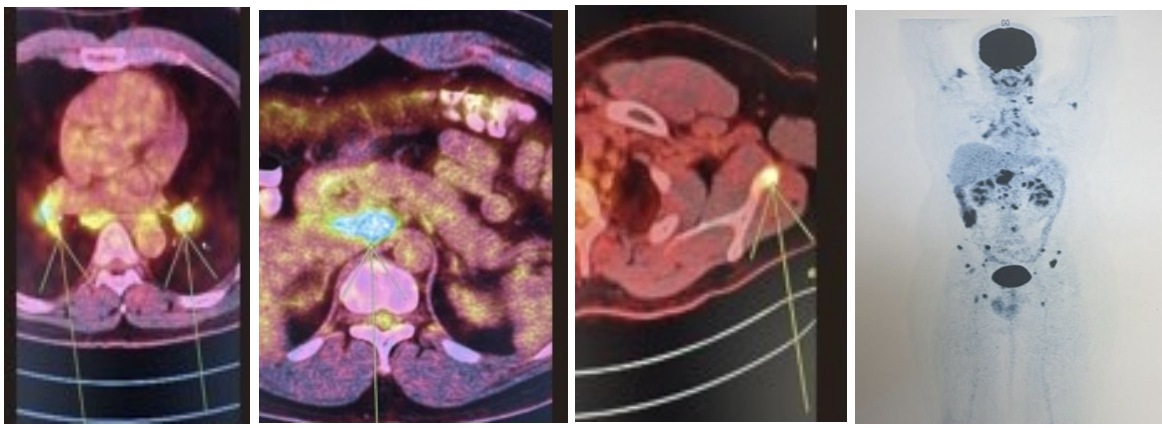

Figure 3: PET/CT imaging showing diffuse SUV uptake in the skeletal system and lymph nodes

Sarcoidosis is known to produce SUVmax values ranging from 2.5 to >20[12], overlapping with malignancy[11]. Symmetric hilar involvement favoured a granulomatous process[22]. However, there was no conclusive evidence to support the diagnosis. It is for this reason that the team recommended an ultrasound-guided biopsy, Figure 4, that yielded insufficient tissue.

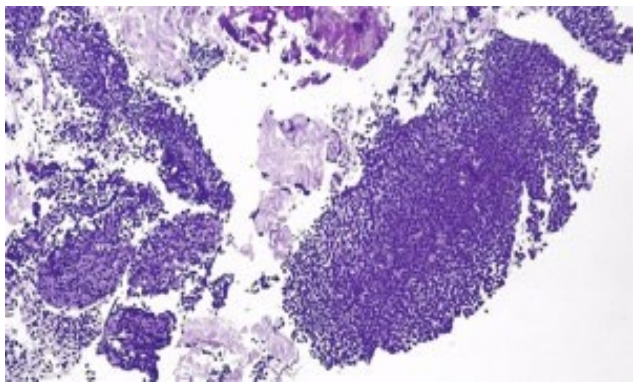

Figure 4: Core biopsy of the supraclavicular lymph node

After three nondiagnostic biopsies, namely, bone marrow biopsy, humerus bone biopsy and supraclavicular lymph node, an MDT discussion involving Orthopaedics, Oncology, General Surgery, Pathologist, Radiologist and Thoracic Surgery recommended mediastinoscopy. Although EBUS is effective for sarcoidosis, mediastinoscopy remains the gold standard when high-volume tissue is required to exclude lymphoma[14].

Definitive Diagnosis

Histopathology

Mediastinal lymph node tissue demonstrated:

- Complete architectural effacement
- Multiple coalescing non-caseating epithelioid granulomas
- Langhans-type giant cells
- Dense fibrosis and hyalinization

These findings are characteristic of sarcoidosis[22], as shown below in Figure 5.

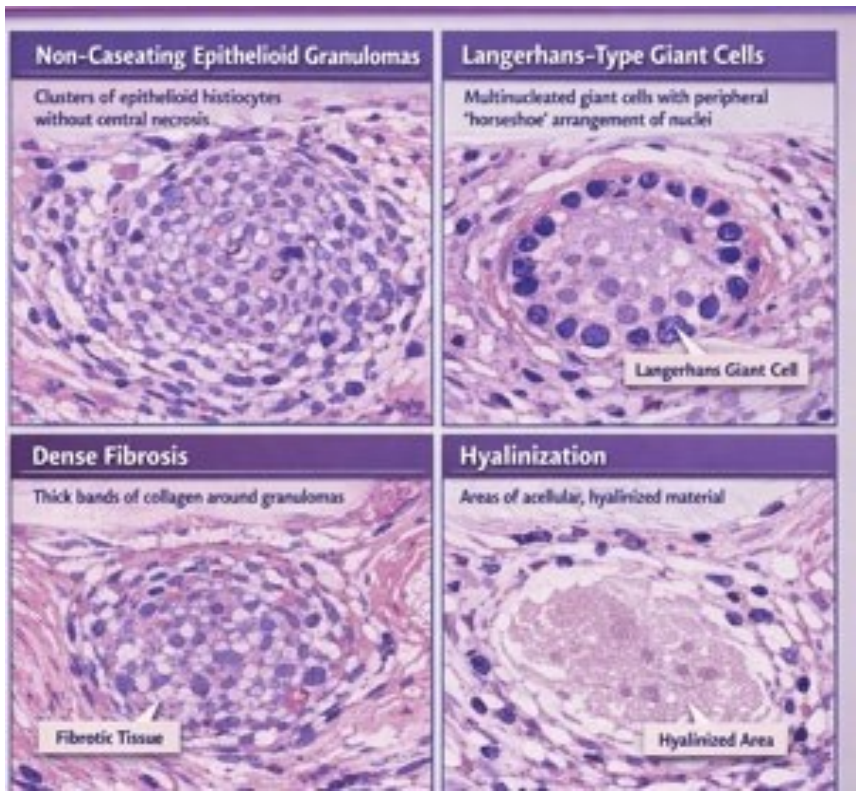

Figure 5: Histopathology slide images confirming sarcoidosis, Courtesy Ampath Laboratory Services.

To further exclude any infectious aetiology and in the South African context of tuberculosis (TB), the American Thoracic Society (ATS) guidelines emphasize the necessity of excluding tuberculosis in granulomatous disease[5] as shown below and negative results for TB

- ZN stain: Negative
- PAS-D: Negative
- TB PCR: Negative
- TB culture: No growth

A final diagnosis of Systemic Sarcoidosis with Extensive Osseous Manifestation was established. Interestingly, further laboratory test of Absolute Eosinophil Count (AEC), a biomarker of inflammatory conditions, was within normal limits.

Discussion

Osseous sarcoidosis can produce lytic lesions indistinguishable from metastatic disease or myeloma[10,19]. Granulomatous inflammation disrupts osteoblast–osteoclast balance, thereby promoting osteolysis[21].

High SUVmax values are not specific for malignancy. Sarcoidosis can produce values >10 or even >20[12], overlapping with aggressive tumors[11]. Symmetric hilar nodes and peri lymphatic lung nodules favour sarcoidosis[22].

Fragmented care is a known barrier in sarcoidosis management[9,18]. MDT-guided selection of mediastinoscopy improved diagnostic yield in this case study and prevented misdiagnosis, consistent with large cohort experience[8].

With further referral and intervention of the Specialist Physicians, the patient was initiated on corticosteroids. Corticosteroids remain first-line therapy for symptomatic sarcoidosis[6]. After a week of treatment, the patient showed early symptomatic improvement especially the pelvic pains that hindered mobility and quality of life.

Long-term management considerations include:

- Prednisone tapering over 6–8 weeks to a maintenance dose of 5–10 mg[1]
- Bone health monitoring, including BMD testing[21]
- Steroid-sparing agents such as methotrexate or TNF-α inhibitors for refractory disease[17]
- Infliximab, which has demonstrated efficacy in refractory vertebral sarcoidosis[7]

Conclusion

This case underscores the diagnostic complexity of systemic sarcoidosis presenting with diffuse lytic skeletal lesions. High SUVmax values, extensive bone involvement, and multisystem lymphadenopathy can strongly mimic metastatic malignancy. When initial biopsies are nondiagnostic, MDT-guided selection of high-yield surgical targets is essential. Early recognition prevents inappropriate oncologic treatment and enables effective inflammatory control.

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