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From Malignancy to Sarcoidosis: Two Surprising Cases

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1. Abstract

1.1. Background

Sarcoidosis is a multisystem granulomatous disease of unknown etiology, which can occasionally manifest as sarcoid-like reactions in patients with a history of malignancy. These reactions may pose significant diagnostic challenges, particularly in distinguishing them from metastatic disease in oncology patients. We present two illustrative cases from our clinic that highlight the clinical and radiological complexities of differentiating sarcoidosis from metastatic disease in cancer survivors. Detailed clinical histories, imaging findings, histopathological results, and treatment approaches were reviewed.

1.2. Case Presentation

The first case involved a 48-year-old woman with a history of early-stage breast cancer, who developed bilateral hilar and mediastinal lymphadenopathy with hypermetabolic lesions in the lungs and spleen. Endobronchial ultrasound-guided biopsy revealed non-necrotizing granulomatous inflammation consistent with sarcoidosis.

The second case concerned a 42-year-old male with COPD and occupational exposure, presenting with a pulmonary mass and widespread lymphadenopathy. Histopathological examination of lymph node and lung biopsies demonstrated non-caseating granulomas, leading to a diagnosis of sarcoidosis. Both patients were treated with low-dose corticosteroids and remain under follow-up.

1.3. Conclusions

These cases emphasize the importance of including sarcoidosis or sarcoid-like reactions in the differential diagnosis of FDG-avid lymphadenopathy in cancer survivors. Accurate diagnosis, achieved through multidisciplinary evaluation and histopathological confirmation, is essential to avoid misdiagnosis and prevent unnecessary treatments.

2. Introduction

Sarcoidosis is a systemic granulomatous disorder with an unknown cause, marked by the presence of non-caseating granulomas in multiple organs, mainly involving the lungs and lymph nodes. Although the precise etiology remains unclear, it is widely thought that sarcoidosis results from an exaggerated immune response to unidentified agents in individuals with a genetic predisposition [1].

A growing body of case reports and studies has documented instances of sarcoidosis or sarcoid-like reactions occurring in patients with prior malignancies. Although this is uncommon, it creates a diagnostic challenge because radiological features-such as mediastinal lymph node enlargement or lung nodules-can easily be mistaken for metastatic spread or tumor recurrence rather than sarcoidosis [2,3].

Certain cancers, especially breast cancer, lymphoma, and testicular cancer, have been frequently linked with sarcoidosis or sarcoid-like granulomatous responses [2,4]. For example, Brincker was among the pioneers to propose a potential connection between malignancy and sarcoidosis, suggesting that the disease may develop as an immune reaction triggered by tumor antigens or effects of cancer treatments [3]. More recent research has shown increased rates of sarcoidosis after therapies such as chemotherapy, immunotherapy, or radiation, lending support to the idea that malignancy and its treatment could be potential inducers [5,6].

Despite these findings, the exact nature of the relationship between sarcoidosis and cancer remains unclear, and distinguishing true sarcoidosis from sarcoid-like reactions continues to be a significant clinical challenge. It is crucial to consider sarcoidosis in the differential diagnosis when imaging or clinical symptoms mimic metastatic disease, as misdiagnosis can lead to inappropriate treatments or delayed care [7].

This article presents two notable cases of sarcoidosis, highlighting the diagnostic complexities and clinical importance of recognizing this rare association.

3. Cases

3.1. Case 1

A 48-year-old woman with no known comorbidities underwent breast-conserving surgery in 2016 after being diagnosed with hormone receptor-positive, HER-2 negative, Luminal A subtype breast cancer. The patient, classified as having early-stage breast cancer, received radiotherapy targeting the primary tumor. She did not receive adjuvant chemotherapy but was treated with tamoxifen for 5 years, followed by 8 years of aromatase inhibitor therapy and continued with annual follow-ups.

In January 2025, a thoracic CT—ordered due to hilar lymphadenopathy observed on a PA chest radiograph—revealed bilateral hilar lymphadenopathy (Figure 1). Given the differential diagnoses, including lymphoproliferative disease, sarcoidosis, and metastatic disease, a PET-CT scan was performed. The PET-CT demonstrated hypermetabolic lymph nodes in the mediastinum and both hilar regions (right hilar SUVmax: 13) (Figure 2). Additionally, there were non-metabolic nodular opacities in both lung parenchyma and hypermetabolic foci in the spleen (early SUVmax: 4.5; late SUVmax: 6.2), which could not be precisely quantified on CT. Abdominal MRI revealed multiple hypointense nodular lesions in the spleen.

Based on these findings, the patient was referred for EBUS-guided lymph node sampling in February 2025. ACE levels were within the normal reference range.The EBUS biopsy revealed non-necrotizing granulomatous inflammation, supporting the diagnosis of sarcoidosis (Figure 3, 4).

The clinical-radiological evaluation concluded that the patient was considered to have a sarcoid reaction. The patient was started on low-dose corticosteroid therapy and is currently under follow-up.

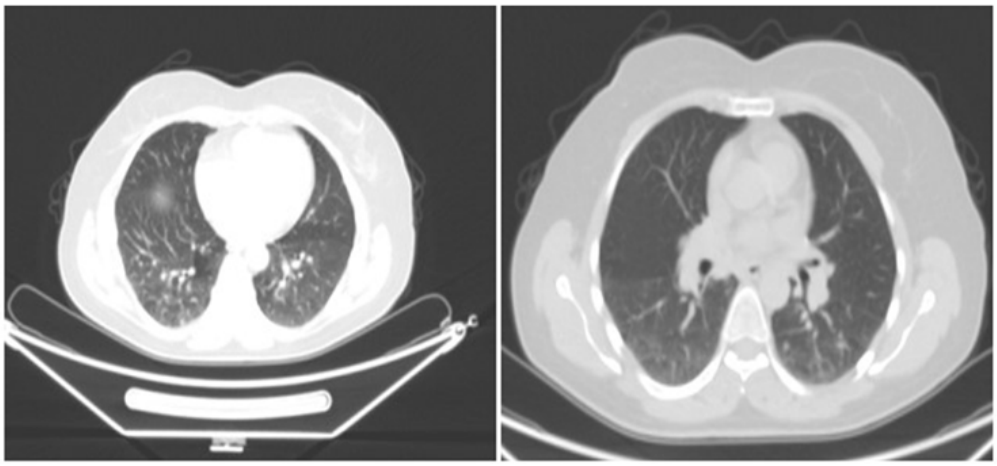

Figure 1: Case 1 Thorax CT Sections.

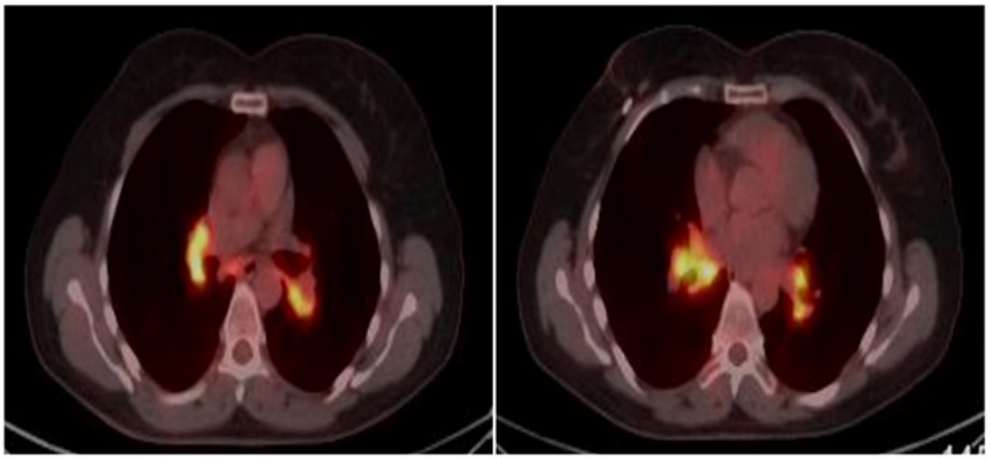

Figure 2: Case 1 PET-CT Sections.

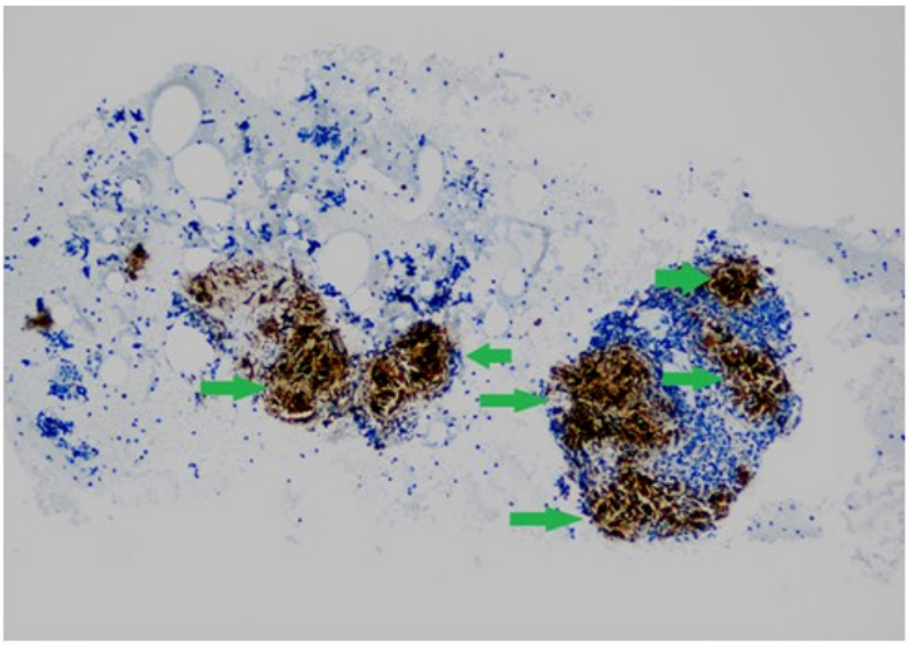

Figure 3: Hematoxylin-Eosim, x200
Sections of the lymph node show small, non-necrotizing granulomas formed by histiocytes (green arrows).

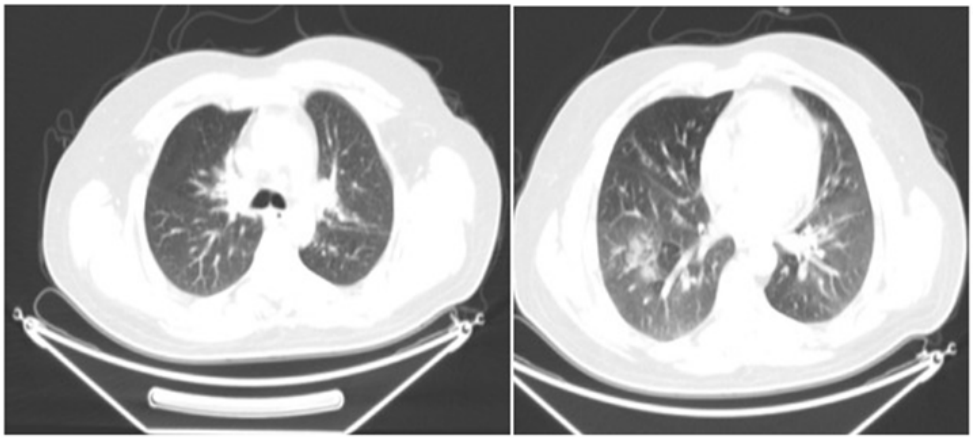

Figure 4: CD68 Immunohistochemistry, x100
Non-necrotizing granuloma formations of CD68-postive histiocytes (green arrows) are observed.

3.2. Case 2

A 42-year-old male patient with a known diagnosis of COPD presented to the pulmonology outpatient clinic with complaints of dyspnea. His medical history revealed a loss of appetite and an unintentional weight loss of approximately 20 kg over the past three months. It was noted that he had worked in the printing industry for many years with exposure to solvents. Additionally, he had a 30 pack-year smoking history.

Radiological imaging revealed multiple mediastinal lymph nodes, the largest measuring 18x11 mm, and an irregularly bordered mass lesion in the right upper lobe of the lung that could not be clearly distinguished from adjacent lymph nodes (Figure 5). Bronchoscopy was performed, which showed mucosal inflammation causing 80% narrowing of the bilateral main bronchi, along with an endobronchial lesion in the right upper lobe, from which a biopsy was taken.

On follow-up, PET-CT imaging demonstrated increased FDG uptake with a SUVmax of 3.6 in the mediastinal lymph nodes, and a SUVmax of 5.3 in the right upper lobe mass. Additionally, multiple abdominal lymph nodes were observed, the largest in the portocaval region with a SUVmax of 5.3, as well as bilateral inguinal lymphadenopathy, the largest on the left measuring 16x12 mm with a SUVmax of 12.5 (Figure 6).

An excisional biopsy of a left inguinal lymph node was performed. Histopathological analysis of both the lymph node and the bronchoscopic lung biopsy revealed non-caseating granulomatous inflammation (Figure 7). The patient was evaluated by the multidisciplinary thoracic oncology board and was started on a low-dose steroid therapy with a diagnosis of sarcoidosis. Follow-up of the patient is ongoing.

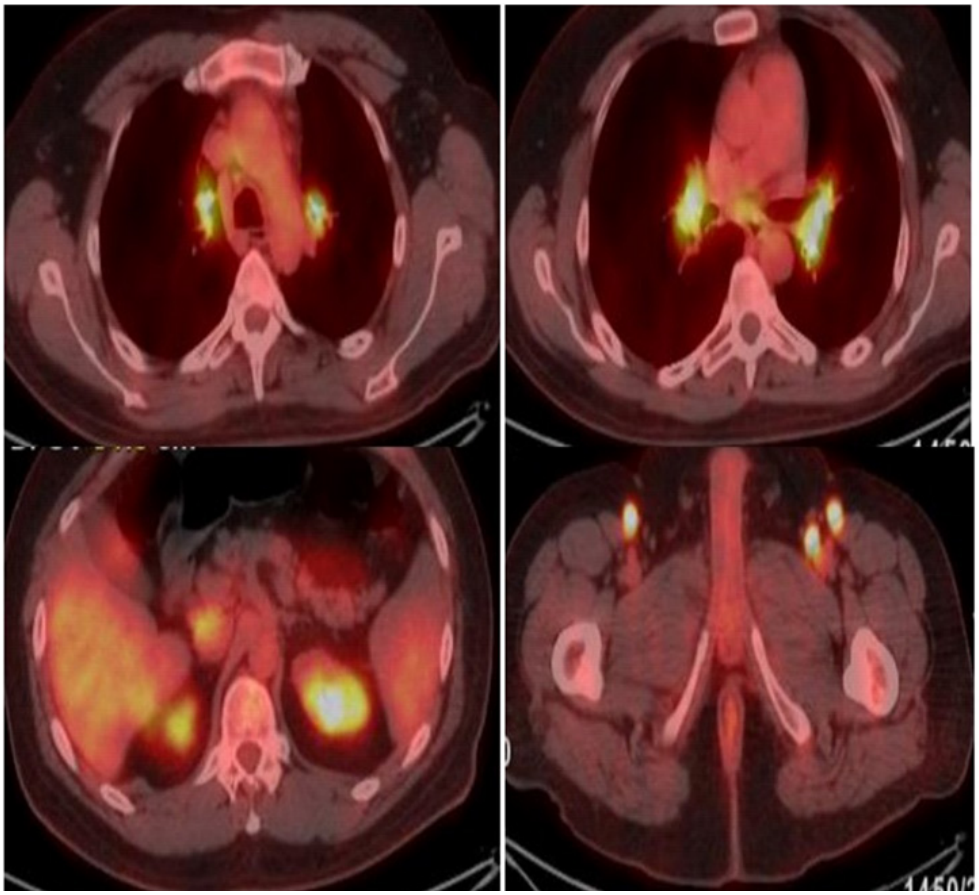

Figure 5: Case 2 Thorax CT Sections.

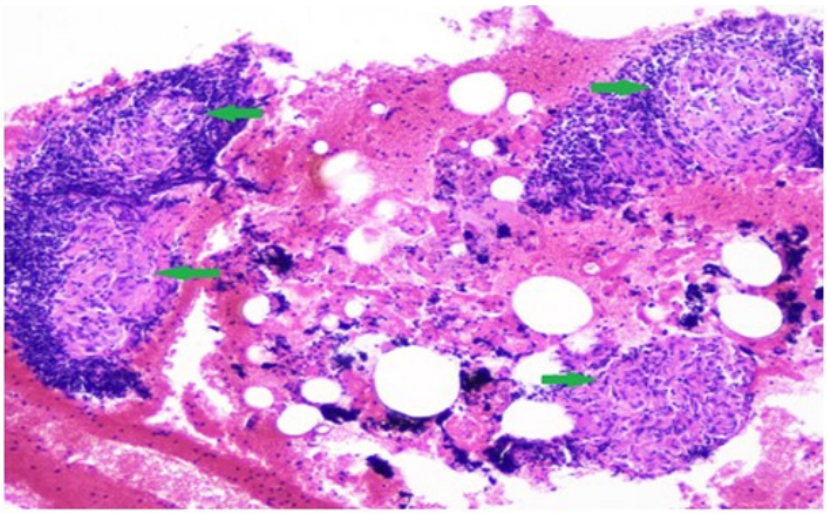

Figure 6: Case 2 PET-CT Sections.

4. Discussion

In summary, sarcoidosis or sarcoid-like reactions can emerge in FDG-avid lymph nodes at various times following the completion of cancer treatments. Maintaining a high level of clinical suspicion and conducting thorough multidisciplinary follow-ups are essential to initiate the correct therapy promptly.

A retrospective analysis of FDG-PET/CT scans conducted between January 2009 and December 2011 reviewed oncology patients who underwent more than two such scans. Among these, cases exhibiting symmetrical increases in FDG uptake within hilar or mediastinal lymph nodes and later diagnosed exclusively with sarcoidosis or sarcoid reactions-were identified. Out of 376 patients, four met these criteria. Elevated FDG uptake with SUV max values reaching up to 17.7 was noted not only in hilar and mediastinal nodes but also in abdominal, pelvic, and inguinal lymph nodes, as well as in the spleen and lung tissue. These findings appeared between nine months and six years after anticancer therapy. Notably, one patient received additional chemotherapy due to suspicion of tumor recurrence [8]. This research highlights the possible association between sarcoidosis or sarcoid reactions and malignancy, underlining the critical role of careful patient monitoring and accurate differential diagnosis.

Consequently, clinicians should always include sarcoidosis or sarcoid-like reactions in the differential diagnosis when encountering FDG-avid lesions in patients following antineoplastic therapy.

5. Conclusion

Sarcoidosis and sarcoid-like reactions can mimic cancer recurrence or metastasis, especially when FDG-avid lymph nodes are seen on PET-CT in cancer survivors. Differentiating between metastatic disease and granulomatous inflammation is crucial, as misinterpretation may lead to unnecessary or inappropriate treatments. Histopathological confirmation through biopsy remains essential to establish a diagnosis of sarcoidosis and exclude malignancy. Sarcoidosis may involve multiple organ systems and manifest long after the completion of cancer treatment, highlighting the need for long-term vigilance. Multidisciplinary evaluation and close follow-up are key to managing patients with suspected sarcoidosis in the post-oncologic setting.

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