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Sarcoid Like Reaction Following Adjuvant Chemotherapy of Breast Cancer

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Abstract

The development of noncaseating granulomas in patients who do not fulfill the criteria for systemic sarcoidosis is known as sarcoid-like reaction and has been described in association with many different types of solid-organ malignancy. In this report we describe a case in which a woman with breast cancer developed sarcoid-like reaction following chemotherapy.

Keywords: Sarcoidosis; Inflammatory disease; Intrathoracic; Malignancy

Introduction

Sarcoidosis is a systemic inflammatory disease of unknown etiology with an incidence that varies widely throughout the world. This variability may be due to differences in environmental exposures, surveillance methods, predisposing HLA alleles and other genetic factors.

The highest annual incidence of sarcoidosis has been observed in northern European countries. The adjusted annual incidence among black Americans is roughly three times that among white Americans [1]. Sarcoid granulomas can involve any organ, but in more than 90% of patients clinical sarcoidosis is manifest as intrathoracic lymph-node enlargement, pulmonary involvement, skin or ocular signs and symptoms, or some combination of these findings [1]. The link between cancer and sarcoidosis is controversial, but there is evidence to suggest that such relationship exists [2]. The development of noncaseating granulomas in patients who do not fulfill the criteria for systemic sarcoidosis is known as sarcoid-like reaction [3] and has been described in association with many different types of solid-organ malignancy [4]. Differentiating between sarcoidosis as an autonomous disease and sarcoid-like reactions requires considerable efforts. The use of FDG-PET in the management of malignancy is widely recognized and its use has been increasing in recent years. Sarcoid-like reaction is a well-known benign cause of FDG uptake in cancer patients and needs to be differentiated from active nodal metastatic disease [5]. In this report, we describe a case in which a woman with breast cancer developed sarcoid-like reaction following chemotherapy.

Clinical Presentation

A 54-year-old postmenopausal female diagnosed with right breast cancer after presenting with a right breast palpable mass and palpable axillary lymph nodes. Pre-surgical 18F-fluorodeoxyglucose-positron emission tomography computed tomography (FDG-PET/CT) scan only demonstrated uptake on the affected breast and axillary area. Patient underwent a right breast lumpectomy and axillary node dissection with the findings of a 1.0 cm invasive ductal carcinoma estrogen receptor positive (90% of tumor cells with nuclear positivity), progesterone receptor positive (60% of tumor cells with nuclear positivity), HER-2/neu negative, Ki-67 90%. Overall Nottingham Histologic Grade: Grade 2/3. One of 27 lymph nodes were involved by metastatic carcinoma, with extracapsular extension. The patient received adjuvant chemotherapy with doxorubicin plus cyclophosphamide every 2 weeks for 4 cycles (ddAC) followed by weekly paclitaxel 80 mg/m^2 for 12 weeks. Growth factors were given during ddAC. She received adjuvant Intensity-modulated radiation therapy (IMRT) to the right breast 5,500 cGY in 30 fractions over 43 elapsed days. After the completion of adjuvant radiation, adjuvant endocrine therapy was initiated with anastrozole 1 mg oral daily. Six months into adjuvant endocrine therapy the patient was found to have an elevated CA 15-3 level at 53 U/ml (reference range 0-25), suggesting non-symptomatic recurrence of disease. FDG-PET/CT scan demonstrated new (FDG) avid mediastinal and bilateral hilar adenopathy (Standardized Uptake Value (SUV) up to 6.3) with symmetric distribution and new FDG avid upper abdominal adenopathy (SUV up to 7.1), greater in the porta hepatis and portocaval region (Figure 1).

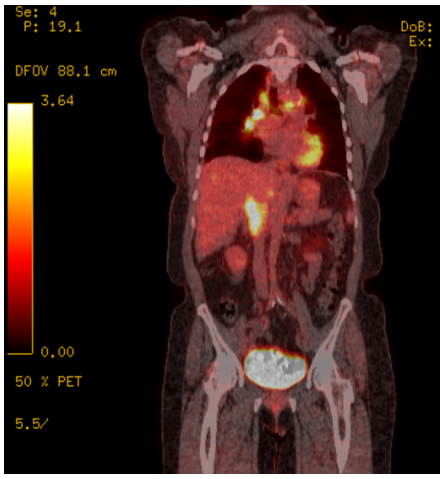

Figure 1: PET/CT scan demonstrating hypermetabolic mediastinal and porta-caval lymph nodes.

Endo-bronchial ultrasound guided transbronchial fine needle aspiration (EBUS-TBNA) of mediastinal lymph nodes demonstrated non-caseating granulomas (Figure 2).

Discussion

The patient was diagnosed to have sarcoid-like reaction following

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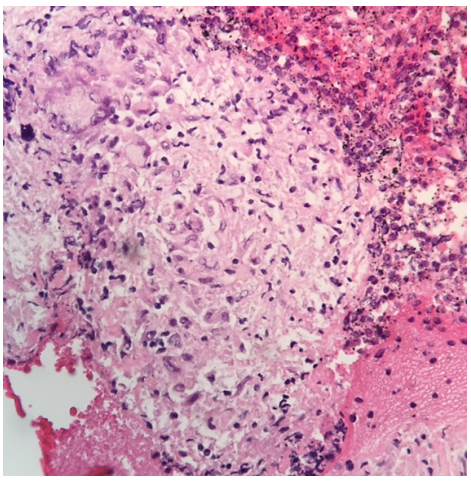

Figure 2: Non-caseating granulomas on hematoxylin and eosin staining of EBUS-TBNA biopsy from mediastinal lymph nodes.

adjuvant therapy for breast cancer. The pathology report described non-caseating granulomas. In the absence of hypermetabolic lymphadenopathy seen on the initial staging FDG-PET/CT scan, the diagnoses of sarcoid-like reaction was made. In general, sarcoid-like reactions can occur in a number of conditions other than malignancies, including tuberculosis, and fungal infections. On this reported case, the stains for fungal or mycobacterial infections were negative.

Sarcoid reactions occur most commonly in the lymph nodes draining a malignant tumor, but they have also been observed in the organ of tumor origin and distant tissues. The mechanism of a tumor-associated sarcoid reaction in regional nodes has not been elucidated, although some authors have suggested that the relationship between a malignant tumor and a sarcoid reaction is a reaction of host resistance to the tumor, or a reaction to metabolic disintegration substances released from tumor cells [6]. Reported cases of sarcoidosis have been associated with increased levels of CA 15-3 [7], consistent with the misleading elevation of this biomarker in this case.

In a comprehensive literature review identifying 104 patients diagnosed with breast cancer and sarcoidosis, about one-third of patients presented with sarcoidosis before cancer and one-third had a regional sarcoid-like reaction to the cancer. In 22% the cancer presented first, and in 10% both diseases occurred within less than one year of each other [8].

Some therapeutic agents have been found to induce a sarcoid-like reaction [9]. Our patient received adriamycin, which has been associated with sarcoid-like reactions following chemotherapy for Hodgkin's disease [10].

FDG-PET/CT is useful for the detection of lymph node metastasis, but can produce false-positive results in cases of sarcoidosis or other inflammatory diseases [11]. Sarcoidosis affected tissues demonstrate a non-specific ability to avidly accumulate FDG with a sensitivity for identification of sites of involvement of 80% to 100% [12]. With the increasing use of FDG PET/CT in the imaging of cancer patients, the potential for false negatives is increasing.

The prevalence of sarcoid-like reaction on FDG PET/CT examinations undertaken for staging and restaging of cancer patients ranges from 0.6% to 1.1% depending on the criteria used for the diagnosis of sarcoid-like reaction (pathologic or based on imaging). FDG uptake in sarcoid-like reaction most often appears as mediastinal and symmetric hilar node activity [12].

Retrospective studies have shown that sarcoid-like reaction is seen more commonly in restaging FDG PET/CT in patients with suspected recurrence than in those undergoing FDG PET/CT for tumor staging. This observation suggests that this phenomenon may be related to an anti-neoplastic immune phenomenon that represents a host defense mechanism against the spread of tumor cells. This theory is supported by the finding that sarcoid-like reactions are associated with a better prognosis in patients with gastric cancer and Hodgkin's lymphoma [13].

The ability to non-invasively differentiate sarcoid-like reaction from recurrent malignancy using FDG PET/CT patterns of disease and semi-quantification of the SUV max would be of potential clinical benefit, but there is not enough data. A large, prospective study could clarify whether non-invasive characterization using FDG PET/CT can be accurate enough to preclude the need for histological clarification.

Conclusion

Breast cancer is rarely associated with sarcoidosis or sarcoidosis-like reaction, but this possibility should be considered when follow-up FDG-PET/CT demonstrates rapid development of metastatic disease to lymph nodes, following adjuvant systemic therapy.

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