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Sarcoid-Like Reaction in Breast Cancers: A Single Center Experience

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Abstract

Introduction: Sarcoidosis is a common, often multi systemic idiopathic chronic inflammatory disease diagnosed histologically by findings of epithelioid non caseating granulomas. While Fluorodeoxyglucose FDG-avid lymph nodes on Positron Emission Tomography (PET) scan in a patient with histologically confirmed malignancy should raise suspicion for nodal metastases, sarcoidosis is a known cause of benign Fluorodeoxyglucose FDG-avidity in cancer patients and must be ruled out to avoid unjustified treatment and potential toxicities.

Methods: A single-center retrospective study involving 46 female patients with breast cancer was conducted. Patients included in the study had been found to have new FDG-avid mediastinal and hilar lymphadenopathy on Positron Emission Tomography (PET) scan and had undergone Endobronchial ultrasound (EBUS) / Endoscopic ultrasound (EUS) with TBNA (Trans-Bronchial Needle Aspiration).

Results: Of the 46 patients in the study, 31 patients (67.4%) were found to have lymph node metastases, noncaseating granulomas consistent with sarcoid-like reactions were found in 3 patients (6.5%), and negative exam (neither sarcoid-like reactions nor nodal metastases) was found in 12 patients (26.10%).

Conclusion: Pathological examination of hyper metabolic nodes must be carried out in cancer patients with PET scan findings concerning for lymph node metastases to prevent misdiagnosis and overtreatment.

Keywords: Sarcoidosis; Breast cancer; Ultrasound; Fluorodeoxyglucose

Introduction

The association between granulomatous reactions and malignancies has been debated for decades. We know now that these associations are not coincidental. It is impossible to differentiate between metastases and granulomatous reactions based on clinical presentation and imaging alone. Despite advances in imaging techniques for malignancies, they have not demonstrated high enough sensitivity to replace tissue sampling [1].

Sarcoidosis is the most common granulomatous disease with suspected chronic inflammatory auto-immune origin commonly involving the lungs, lymph nodes, eyes, and skin [2]. Diagnosis requires histopathological evidence of epithelioid non-caseating granulomatous inflammation in one or more involved organs along with clinical and radiological features of the disease.

Here we present a retrospective observational study of 46 patients with breast cancer who had hypermetabolic mediastinal and hilar lymph nodes on imaging. Subsequent sampling revealed a mix of cancer recurrence, sarcoid-like reaction, and negative histopathology for either disease.

Case Study

This was a single-center retrospective study among patients with histologically confirmed breast cancer referred to the Department of Interventional Pulmonology at the Cancer Centre of America-Atlanta from January 1, 2013, to December 31, 2015, for EBUS TBNA after new findings of FDG-positive mediastinal or hilar nodes on follow-up PET scans. These patients subsequently underwent TBNA of these nodes. Patients with noncaseating epithelioid cell granulomas on the histological exam of biopsied nodes were the focus of this study.

Data extraction was from electronic medical records. All pathological specimens were reviewed at the institute and classified as positive (lymph node metastases), sarcoid (non-caseating granulomas), or negative (neither malignant nor sarcoid-like).

Results

Forty-six female patients with breast cancer and new findings of FDG-positive mediastinal and hilar nodes underwent endoscopic (bronchial) ultrasound (EBUS) trans bronchial needle aspiration (TBNA). There were no documented complications following biopsy.

Histological examination of biopsied specimens revealed lymph node metastases in 31 patients (67.4%), non-caseating granuloma consistent with sarcoidosis like reaction in 3 patients (6.5%), and negative exam in 12 patients (26.10%). Negative specimens were interpreted as reactive lymphadenopathy, benign lymphoid tissue, or infectious the latter in a single patient with gram-positive bacteria isolated in nodes.

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Histological examination of biopsied specimens	No. of patients (46)	Percentage
Lymph node metastases	31	67.4%
Noncaseating granulomas consistent with sarcoid-like reactions	3	6.5%
Negative exam (neither sarcoid-like reactions nor nodal metastases)	12	26.10%

Table 1: Histological examination of biopsied specimens.

The Sarcoid Like Reaction (SLR) was found in the mediastinum in only 1 patient and in the hilar region for 2 patients (Table 1).

All patients with lymph node findings consistent with sarcoidosis were asymptomatic and free of nodal metastases at the time of data collection for this study. All interventions were conducted by a team comprising of breast surgeons, medical oncologists, radiologists, and interventional pulmonologists.

Limitations of the study include small sample size and loss of vital patient characteristics including age at diagnosis of breast cancer and age at diagnosis of sarcoid reaction. The information was lost during data collection.

Discussion

Sarcoidosis is a multiorgan disease with varying presentations; these variations have been attributed to different degrees of genetic predisposition and environmental exposures [3]. The classical non-caseating granulomas of sarcoidosis can involve any organ system; however, intrathoracic and pulmonary manifestations are the most common findings.

Sarcoidosis and sarcoid-reaction are different spectrums of the same disease. While sarcoidosis is often a multisystemic disease, sarcoid-reaction or sarcoid-like reaction is defined by the presence of epithelioid noncaseating granulomas in patients without systemic manifestations of sarcoidosis [1,3-5]. Both have been shown to co-exist with or mimic malignancies resulting in diagnostic and therapeutic difficulties. Prognostic implications differ, however, as pre-existing systemic sarcoidosis has been associated with increased risk of developing malignancy and potentiating metastases by creating dysfunctional immune regulatory pathways [3,6-10]. This causal relationship has been extensively described with noted syndromes including sarcoidosis-lymphoma and sarcoidosis-malignancy. On the other hand, sarcoid-reactions are a positive prognostic factor in some malignancies – such as Hodgkin's lymphoma and gastric carcinoma and have been noted in some studies to decrease nodal metastases [8,10-12]. Sarcoid-reactions are mostly tumor-related, often noted during diagnosis or staging of malignancies, and mostly occur in the organ of tumor involvement or in the lymph nodes draining that malignancy. They have been described as an antitumor response to tumor antigens.

Sarcoid-like or sarcoid reactions and breast cancers are separate disease entities with overlapping features like pulmonary symptoms and imaging findings of axillary and intra thoracic lymphadenopathy and pulmonary nodules. There have been multiple case reports of breast cancers presenting as sarcoidosis and vice versa [13-24]. This is the third case series, to our knowledge, on sarcoid-like reactions in patients with breast cancer. Our case series is the largest and also the first to detail the incidence of intra-thoracic sarcoid reactions in patients with breast cancer. The first case series by Martella et al. [11] published in 2011 included 8 breast cancer patients: 6 patients who were found to have sarcoid reactions within the thorax and 2 patients had sarcoid reactions in the axilla. In the second study from Israel by Chen, et al. [24] 5 patients with both sarcoidosis and breast cancer were enrolled in the study. In the two case series as in ours, patients with breast cancers and sarcoidosis/sarcoid-reactions had no oncological relapse during a period of follow-up.

Another case series that closely mirrors the index study was a retrospective study by Ravaglia et al. [3] published in the European Respiratory Journal in 2013, of 48 patients who underwent endoscopic ultrasound and transbronchial needle aspiration for new FDG-avid hilar and mediastinal lymph nodes. These 48 patients, however, had different types of malignancies, not just breast cancer. Of the 45 patients whose procedures were diagnostic, sarcoidosis/sarcoid-reaction was found in 12 (26.7%), nodal metastases in 13 (28.9%), and hyperplastic nonspecific lymphadenopathy in 20 (44.4%) patients. Eleven of 12 cases with noncaseating granulomas were sarcoid-like reactions, as they had no systemic manifestation; 1 patient required steroids for asthenia.

The incidence of the sarcoid reaction was 6.5% in our study, which is higher than 4.4% in patients with carcinomas as noted by Brincker et al. [5] and lower than 26.7% as noted by Ravaglia et al. Despite the similarities in methodology between our study and that of Ravaglia et al., the marked difference in the percentage of sarcoid reactions can be attributed to the inclusion in that study of patients with different malignancies. For instance, lung cancer patients were included in the study and thus, the intra-thoracic lymph nodes sarcoid-reaction found is likely loco regional antitumor response to the lung malignancy, as opposed to breast cancer patients where this antigenic response will more likely be seen in the axillary lymph nodes.

Our case study is moderately sized compared to previous similar studies and demonstrates the incidence of sarcoid-reactions exclusively in breast cancer patients. Further larger-scale studies are needed before concluding the above findings.

Conclusion

F-FDG PET/CT imaging has gained widespread acceptance in the initial staging of tumors and the diagnosis of distant metastases and recurrence. Granulomatous reactions, active infections, and flare phenomena are some known causes of benign FDG-avidity and thus, must be taken into consideration when interpreting imaging results. And while symmetrical, hilar FDG-uptake with low standardized uptake value (SUV<3) has been associated with benign lesions the F-FDG PET scan is not sensitive or specific enough to preclude tissue sampling.

References

1. Aurelio C, Takashi S, Mark B, Barbara R, David M, et al. (2016) Sarcoid like reaction following adjuvant chemotherapy of breast cancer. Oncology and Cancer Case Reports 2: 3 .
2. Spiekermann C, Kuhlencord M, Huss S, Rudack C, Weiss D, et al. (2017) Coexistence of sarcoidosis and metastatic lesions: A diagnostic and therapeutic dilemma. Oncol Lett 14: 7643-7652.
3. Ravaglia C, Gurioli C, Casoni GL (2013) Sarcoid-like lesion is a frequent benign cause of lymphadenopathy in neoplastic patients. Eur Respir J 41: 754-755.

4. Brincker H (1986) Sarcoid reactions in malignant tumours. Cancer Treat Rev 13: 147-156.

5. Brincker H, Wilbek E (1974) The incidence of malignant tumours in patients with respiratory sarcoidosis. Br J Cancer 29: 247-251.

6. Grados A, Ebbo M, Bernit E (2015) Sarcoidosis occurring after solid cancer: A nonfortuitous association: report of 12 cases and review of the literature. Medicine (Baltimore) 94: e928.

7. Cohen PR, Kurzrock R (2007) Sarcoidosis and malignancy. Clin Dermatol 25: 326-333.

8. Ji J, Shu X, Li X, Sundquist K, Sundquist J et al. (2009) Cancer risk in hospitalized sarcoidosis patients: A follow-up study in Sweden. Ann Oncol 20: 1121-1126.10.

9. Wirk B (2010) Sarcoid reactions after chemotherapy for Hodgkin's lymphoma. Clin Med Insights Case Rep 3:21-25.

10. Steinfort DP, Irving LB (2009) Sarcoidal reactions in regional lymph nodes of patients with non-small cell lung cancer: Incidence and implications for minimally invasive staging with endo bronchial ultrasound. Lung Cancer 66: 305-308.

11. Martella S, Lohsiriwat V, Barbalho DM (2012) Sarcoid-like reaction in breast cancer: A long-term follow-up series of eight patients. Surg Today 42:259-263.

12. Urschel JD, Loewen GM, Sarpel SC (1997) Metastatic breast cancer masquerading as sarcoidosis. Am J Med Sci 314: 124-125.

13. Tolaney SM, Colson YL, Gill RR (2007) Sarcoidosis mimicking metastatic breast cancer. Clin Breast Cancer 7: 804-810.

14. Chen W, Miller R, Hebbe K, Guron G (2004) Sarcoidosis and breast carcinoma : Three case reports and a review. Journal of Clinical Oncology 22: 867.

15. Tareila AM, Aswad BI, Ward RC, Hillstrom MM (2018) Bilateral breast sarcoidosis mimicking synchronous primary breast cancer. R I Med J 101: 39-40.

16. Bush E, Lamonica D, O'Connor T (2011) Sarcoidosis mimicking metastatic breast cancer. Breast J 17: 533-535.

17. Braza DW, Nelson PA (2014) Vertebral sarcoidosis masquerading as breast metastasis. Am J Phys Med Rehabil 93: 274.

18. Donaldson BA, Polynice A, Oluwole S (1995) Sarcoidosis of the breast: Case report and chart review. Am Surg 61: 778-780.

19. Dragoumis DM, Tsiftsoglou AP, Assimaki AS (2008) Pulmonary sarcoidosis simulating metastatic breast cancer. J Cancer Res Ther 4: 134-136.

20. Akhtari M, Quesada JR, Schwartz MR, Chiang SB, Teh BS,et al (2014). Sarcoidosis presenting as metastatic lymphadenopathy in breast cancer. Clin Breast Cancer 14: e107-110.

21. Zivin S, David O, Lu Y (2014) Sarcoidosis mimicking metastatic breast cancer on FDG PET/CT. Intern Med 53:2 555-2556.

22. Gallimore AP, George CD, Lampert IA (1990) Subcutaneous sarcoidosis mimicking carcinoma of the breast. Postgrad Med J 66: 677-678.

23. Shin HC, Choe JW, Ryu HS (2014) Sarcoidosis mimicking metastatic breast cancer in Korean woman with breast cancer. Breast J 20: 198-199.

24. Chen J, Carter R, Maoz D, Tobar A, Sharon E, et al. (2015) Breast cancer and sarcoidosis: Case series and review of the literature. Breast Care (Basel) 10: 137-140.