



Case report

Rare coexistence of sarcoidosis and lung adenocarcinoma



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A B S T R A C T

Keywords:

Sarcoidosis
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Case: An eighty year old African-American female was evaluated for cough, chest pain, asymptomatic anemia and 21 pound weight loss over a six month period. Computerized tomography (CT) revealed a spiculated 2.8 cm right upper lobe lung nodule, other smaller nodules and lymphadenopathy. Gallium scan revealed abnormal uptake of radiotracer in lacrimal, hilar and mediastinal glands. Broncho-alveolar lavage showed CD4/CD8 ratio of 2:1 with 15% lymphocytes. Biopsy of right upper lobe lesion and mediastinoscopic lymph node biopsy showed numerous matured uniform non-caseating granulomatous inflammation, however stains and culture for Acid fast bacilli (AFB)/fungal organisms were negative. Patient improved on oral steroids. Six months later she returned with worsening dyspnea and chest X-ray showed bilateral pleural effusions. Thoracentesis revealed Thyroid transcription factor 1 (TTF1) positive adenocarcinoma cells and Video assisted thoracic surgery (VATS) procedure revealed numerous pleural, pericardial, diaphragmatic metastasis. Biopsy also was positive for TTF1 adenocarcinoma and positive for Epidermal Growth Factor receptor (EGFR) mutation, however negative for Anaplastic Lymphoma Kinase (ALK). Talc pleurodesis was performed. She was treated with erlotinib while steroid was kept on hold. Initial tumor burden decreased but follow-up PET scan six months later showed progression of tumor with lymphadenopathy. After discussion with patient and family, patient opted for hospice care.

Discussion: Oncocentric theory postulates sarcoidosis as an immunological reaction to dispersal of tumor antigen. Sarcocentric theory postulates that cell-mediated immune abnormalities induced by sarcoidosis in CD4 and CD8 cells is involved in the onset of lung cancer. Thus considerable controversy exists regarding sarcoidosis and malignancy. In our case, TTF1 adenocarcinoma cells from thoracentesis suggest peripheral nodules in right upper lobe and lingula were likely metastatic, presenting as malignant pleural effusions. However if noncaseating granulomatous inflammation is expected as an immunological reaction to tumor antigen, it is very interesting to observe that initial tissue biopsy of primary right upper lobe mass and mediastinal lymph nodes showed matured uniform non-caseating granulomatous inflammation and no evidence of adenocarcinoma. This being said, it would be highly unlikely for sarcoidosis to progress to lung adenocarcinoma within six months. This adds further controversy to whether granulomatous inflammation is a precursor to future malignancy or whether this elderly African-American female was predisposed to develop granulomatous inflammation in presence of a tumor antigen. One can also speculate whether repeat tissue sampling from right upper lobe mass would have shown granulomatous inflammation or TTF1 adenocarcinoma.

Conclusion: While evidence is still lacking regarding association between sarcoidosis and lung adenocarcinoma, it is important for clinicians to exclude metastatic malignancy in patients exhibiting clinical and radiographic findings consistent with sarcoidosis.

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Case report

An eighty year old African-American female was evaluated for cough, chest pain, asymptomatic anemia and 21 pound weight loss over a six month period. Computerized tomography of chest,

abdomen and pelvis revealed a spiculated right upper lobe lung nodule measuring 2.8 cm (Fig. 1); 3 mm nodule in right upper lobe, 2 mm nodule in lingula, with mediastinal and hilar lymphadenopathy (Fig. 2); however no pelvic or abdominal lymphadenopathy was noted. Gallium scan showed abnormal uptake of radiotracer in lacrimal, hilar and mediastinal glands. Broncho-alveolar lavage (BAL) showed a CD4/CD8 ratio of 2:1 with 15% lymphocytes. Trans-bronchial biopsy of right upper lobe lesion and mediastinoscopic lymph node biopsy of levels II, III, IV, VII was done which revealed

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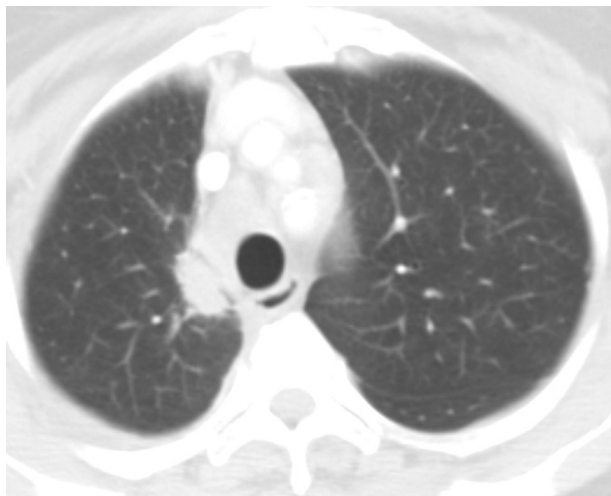


Fig. 1. Right upper lobe lung nodule.

matured uniform non-caseating granulomatous inflammation (Fig. 3). Stains and culture for AFB and fungal organisms on biopsy were negative. Because of weight loss and cough patient was started on oral steroids and symptoms markedly improved. However she returned six months later with worsening shortness of breath. Chest X-ray at the time showed bilateral pleural effusions. Thoracentesis was performed which showed Thyroid transcription factor-1 (TTF1) positive adenocarcinoma cells. Video assisted thoracic surgery was performed for staging and revealed numerous pleural, pericardial and diaphragmatic metastasis. Biopsy also was positive for TTF1 positive adenocarcinoma cells (Fig. 4). Epidermal Growth factor mutation (EGFR) mutation was positive and Anaplastic Lymphoma kinase (ALK) mutation was negative. There was no evidence of thyroid cancer. Talc pleurodesis was performed for symptomatic relief of pleural effusions. She was treated with erlotinib and steroid was kept on hold. Initial tumor burden decreased but follow-up PET scan after six months of therapy showed progression of right upper lobe mass and new upper abdominal and right supraclavicular lymphadenopathy. After discussion with patient and family, patient declined to undergo repeat tissue sampling and decided to stop chemotherapy, therefore hospice care was initiated.

Discussion

Epidemiological studies and linkage analysis have provided evidence that sarcoidosis and malignancy may be etiologically



Fig. 2. Mediastinal lymphadenopathy with right upper lobe lesion.

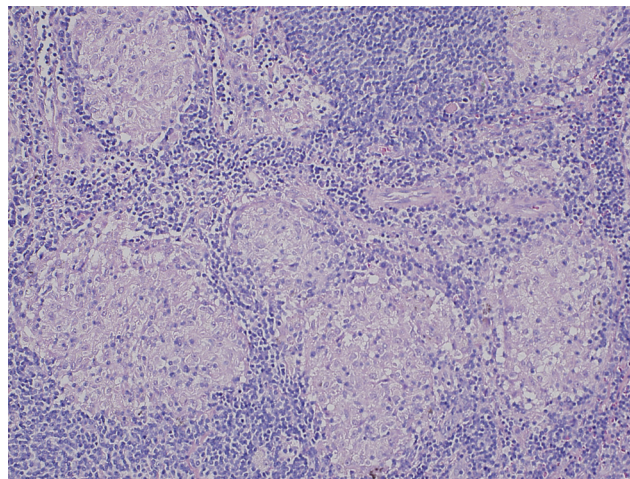


Fig. 3. Mediastinoscopic lymph node biopsy revealing non-caseating granulomatous inflammation.

related in at least 25% of cases in which both are present [1]. The link between sarcoidosis and lung cancer has been controversial ever since 1973 when Brincker and Wilbek proposed that the disease sarcoidosis can induce the development of solid neoplasms by an unknown mechanism [2]. It has been postulated that lung cancer originates in fibrous tissue found with sarcoidosis [3]. Another theory postulates that cell-mediated immune abnormalities induced by sarcoidosis is involved in the onset of lung cancer [3]. Therealso exists an oncocentric theory that postulates sarcoidosis as an immunological reaction to dispersal of tumor antigens [4]. This concept originates from observations of variety of solid and lympho-hematogenous malignancies eliciting systemic granulomatous response that is indistinguishable from sarcoidosis [4,5]. Thus considerable controversy exists regarding association between sarcoidosis and malignancy raising the question of causality. In our case, initial tissue biopsy of primary right upper lobe mass along with mediastinal lymph nodes showed matured uniform non-caseating granulomatous inflammation with no evidence of adenocarcinoma. However repeat thoracentesis done six months later showed TTF1 positive adenocarcinoma cells suggesting peripheral nodules in right upper lobe and lingula were likely metastatic. If non-caseating granulomatous inflammation is

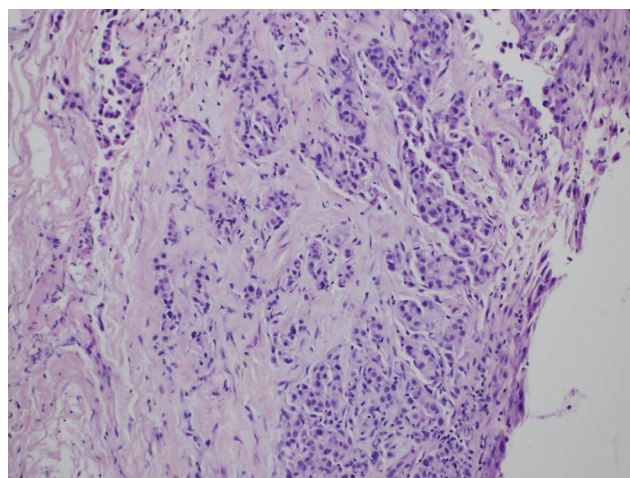


Fig. 4. Pleural biopsy with Video assisted thoracic surgery revealing non-small cell adenocarcinoma of lung.

expected as an immunological reaction to tumor antigen, it is very interesting to observe that initial biopsy was negative for malignancy. This being said, it would be highly unlikely for sarcoidosis to progress to lung adenocarcinoma within six months. This adds further controversy to whether granulomatous inflammation is a precursor to future malignancy or whether this elderly African-American female was predisposed to develop granulomatous inflammation in presence of a tumor antigen, making it impossible to determine a cause vs effect relation. Further clinical studies are warranted to determine if any association does exist, however currently the two are managed as if they exist separately.

Conclusion

While evidence is still lacking regarding association between sarcoidosis and lung adenocarcinoma, it is important for clinicians

to exclude metastatic malignancy in patients exhibiting clinical and radiographic findings consistent with sarcoidosis.

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