



SHORT COMMUNICATION

Concurrent presentations of the sarcoidosis, tuberculosis and lymphoma in a single patient

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Summary A 56-year-old female patient, developing ALK-negative anaplastic T cell lymphoma 7 years after the diagnosis of sarcoidosis with clinical and histopathological features of tuberculosis has been presented. We herein present concurrent occurrence of the sarcoidosis, lymphoma and tuberculosis along with the confusing findings during the investigation for the establishing the diagnosis and management that represented a great challenge.

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Introduction

Sarcoidosis is a multisystem disease of unknown cause. A variety of infectious agents like mycobacteria have been suspected for the development of sarcoidosis.^{1,5} Commonly, the disease involves mediastinal lymph nodes and lungs but any other organ involvement may occur.^{1,2} Clinical presentation is variable, from asymptomatic to progressive lethal disease.¹ Pathological hallmark of the sarcoidosis is noncaseating granuloma; however, a rare necrotizing form has also been defined.² Sarcoidosis

is a diagnosis of exclusion and it might co-exist with other diseases,^{1,6} especially with tuberculosis,³ therefore establishing the diagnosis may be challenging in such cases. Association between sarcoidosis and malignancies particularly with lymphomas is still controversial.^{6–9} ALK-negative anaplastic T cell lymphoma is a high-grade lymphoma and concomitance with sarcoidosis has not been reported before.

Case report

A 56-year-old female patient with dyspnea, cough and fever was admitted to our clinic in February 2005. She had been found to have a mediastinal

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tumor during investigation for exertional dyspnea 7 years before and was operated for that. Mediastinal multiple lymphadenopathy was noted during the operation and the largest one, 5 × 6 cm in size, was excised. Histopathological examination yielded granulomatous lymphadenitis consistent with sarcoidosis. No medication was given after the diagnosis. She had been feeling well about 7 years until May 2004. After that time she began to suffer from exertional dyspnea and dry cough. Prednisolon 20 mg qd was prescribed. Despite regular medication use, her complaints progressed, cough turned to be productive and fever was added in the last month. She quit prednisolon 10 days prior to admission. On admission, her vital signs were stable except body temperature 38.7 °C. Physical examination revealed cervical, supraclavicular, axillary, inguinal lymphadenopathies, fine crackles on lower lung parts and a 5 cm of hepatomegaly. Pertinent routine laboratory investigation values were WBC $13.1 \times 10^3/\mu\text{L}$ with 20% eosinophils, Hb 11.3 g/dL, platelets $347 \times 10^3/\mu\text{L}$, ESR 17 mm/h, CRP 17 mg/dL, ALT 21 U/L, AST 38 U/L, GGT 87 U/L, ALP 234 U/L, total bilirubin 0.25 mg/dL, albumin 3.1 g/dL, LDH 408 U/L. Tuberculin skin test was anergic. Routine cultures and sputum examination for acid fast bacilli (AFB) and tuberculous PCR were negative, which were repeated for three times. Multiple mediastinal, hilar, portal, and intraabdominal lymphadenopathies and hepatomegaly were found at thoracoabdominal CT. There was no interstitial lung involvement on high-resolution thorax CT but a calcific milimetric nodule was found at left upper lobe. Liver biopsy exhibited intrahepatic cholangitis due to possible biliary outflow obstruction, with no signs of sarcoidosis or neoplastic infiltration. Bone marrow biopsy was normocellular. Excisional cervical lymph node biopsy revealed effacement of the lymph node architecture broadly by extensive fibrosis, hyalinization and granulomas containing multinucleated langhans-type giant cells. Minimally caseating necrosis and a few AFB were seen in a few areas. The tissue tuberculous PCR analysis was negative. However, because of AFB were seen, her clinical presentation was consistent with tuberculosis and tuberculosis is relatively prevalent in our region an empirical antituberculous therapy consisting of isoniazid, rifampin, pyrazinamide, ethambutol was instituted. After an 18 day-course of antituberculous treatment, no improvement was noted. Amikacin and moxifloxacin were added to her therapy for the possibility of resistant mycobacterial infection. One week later under that antimicrobial therapy, severe sepsis developed with new infiltrations on chest X-ray. Therefore meropenem

and vancomycin were employed and antituberculous therapy was discontinued. A second excisional lymph node biopsy from supraclavicular region was reported as ALK-negative anaplastic T cell lympho-

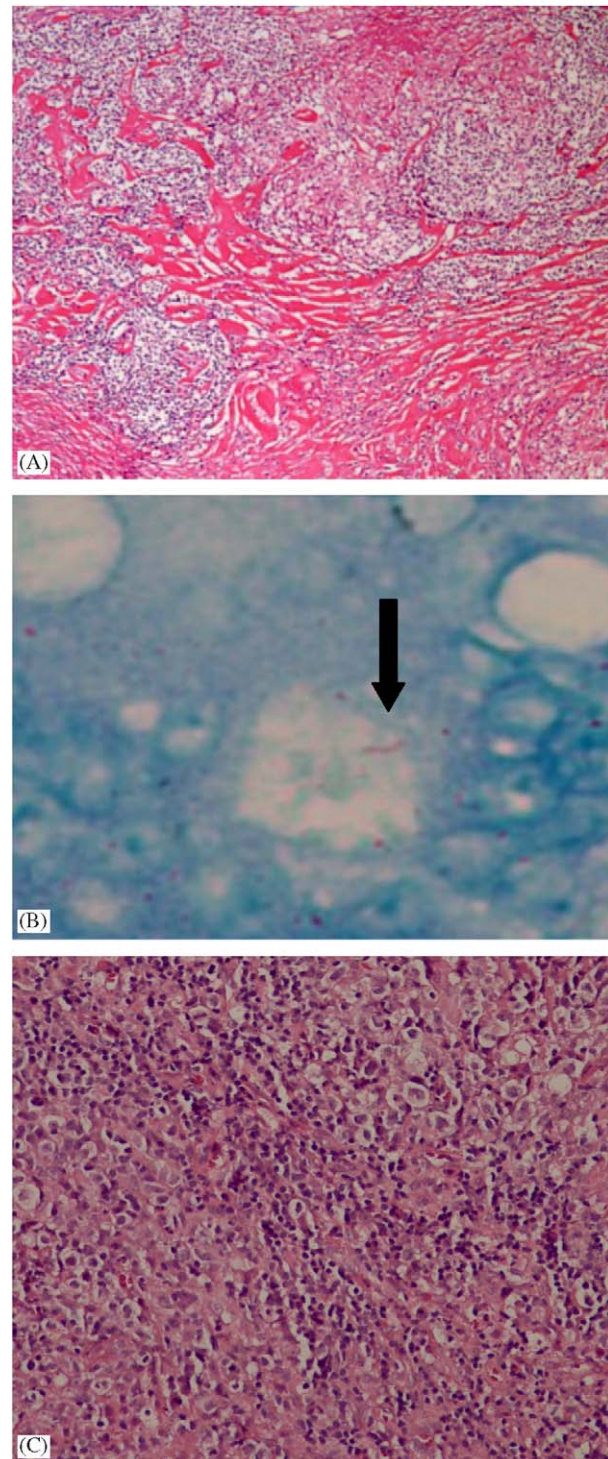


Figure 1 Histopathological images of patient's lymph nodes showing three distinct diagnoses: (A) typical sarcoid granulomas involving lymph node, (B) acid fast stained bacilli (arrow) and (C) lymphoma infiltration.

ma involvement (Fig. 1). She died due to acinetobacter sepsis soon after the diagnosis of lymphoma. Her tuberculous cultures of sputum, supraclavicular lymph node and bone marrow were found to be negative subsequently.

Discussion

Sarcoidosis is a clinico-pathologic diagnosis, pathological findings have value only in the presence of clinical findings.^{1,2} Since lymphoma and tuberculosis are common and their clinical features are quite similar to sarcoidosis, establishing the diagnosis can be challenging in some cases particularly for those without pulmonary involvement.

Although the etiology of sarcoidosis is still unknown, it is suggested to develop due to abnormal immune response to certain exogenous antigenic stimuli including mycobacteria.¹ Because some acid fast coccobacillary forms had been shown in tissue specimens of sarcoidosis patients, mycobacterium tuberculosis has been suspected to be involved in the pathogenesis of sarcoidosis.^{1,4,5} However causative role of tuberculosis in sarcoidosis is still controversial.¹ PCR is a sensitive and specific assay method for detecting mycobacterium tuberculosis DNA in tissue samples and was studied several times in sarcoidosis before, but results of these studies are inconclusive.^{1,4,5}

Lymphoma can be observed during the natural course of sarcoidosis which may be attributed to the chronic inflammation or underlying immunological disturbances.^{8,9} Increased risk of lymphoma was reported firstly by Brincker and Wilbek,⁷ and since that time several other cases about various types of lymphomas involving T- and B-cells had been reported to date and a sarcoidosis-lymphoma syndrome had been described.⁶⁻⁹ However, epidemiological reports on the increased risk of malignancy associated with sarcoidosis are still controversial.^{8,9} However, the presence of rapidly

progression of symptoms or any atypical clinical features should alert the physician for an additional pathology.¹

Conclusions

Lymphoma may develop during the course of the sarcoidosis and may not be easy to diagnose due to the overlapping clinical and histopathological features. In such cases, a lymph node biopsy may not be satisfactory and repeated biopsies may be necessary to establish the accurate diagnosis. We believe that this case is another evidence for the tuberculosis in the pathogenesis of sarcoidosis and the sarcoidosis-lymphoma relationship, which bringing them together.

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