Association Between Acute Myeloblastic Leukaemia and Sarcoidosis

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INTRODUCTION

Sarcoidosis is a systemic granulomatous disorder thought to be an exaggerated immune response to unknown antigens. It often presents with bilateral mediastinal lymphadenopathy and/or pulmonary infiltrates (1).

Sarcoidosis has been found in association with a variety of malignancies, including malignant myeloproliferative disorders (2). To date, only two cases of acute myeloblastic leukaemia (AML) preceding sarcoidosis have been reported; however, the relationship between the two disorders is still unclear (3, 4). Here, we describe a case diagnosed as mediastinal sarcoidosis which developed 17 years after AML.

CASE REPORT

A 32-year old Caucasian female was admitted to hospital, complaining of shortness of breath and left-sided chest pain for 9 hours.

Her medical history includes AML at age 15 years treated by post allergen-A BMT, asthma, seizure disorder, cerebral palsy, multiple left ankle surgeries complicated by deep venous thrombosis and pulmonary embolism for which she underwent inferior vena cava filter placement.

Physical examination found pleuritic pain and localized tenderness on the left side of the chest. A chest Computed Tomography (CT) scan demonstrated lymphadenopathy within the anterior tracheal nodal station, aorticopulmonary window and subcarinal nodal station (Fig 1). However, there was no evidence of pulmonary embolism or infiltrates. A complete blood count revealed a haemoglobin of 10.9 g/dL, haematocrit of 34.6%, WBC of 6300/µl and platelet count of 270000/µl without signs of leukaemia.

In view of the patient's history of leukaemia and the mediastinal lymphadenopathy, which was extensive, flexible bronchoscopic Transbronchial Needle Aspiration (TBNA) was performed. Anterior carinal and subcarinal lymph nodes were sampled using Wang 19-gauge histology and 21-gauge cytology needle. Both histologic and cytologic specimens were successfully obtained.

Examination of the TBNA histologic sections and cytologic smears showed epithelioid histiocytes forming granulomatous structures and aggregates of mature lymphocytes (Fig 2A, 2B). Neither necrosis nor mitoses were seen.

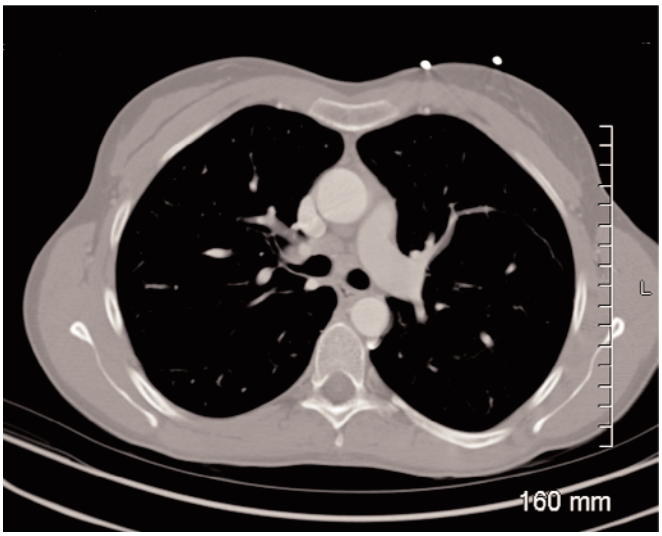

Fig. 1: Chest computed tomography scan (mediastinal window) showing mediastinal lymphadenopathy within the anterior tracheal and subcarinal nodal stations.

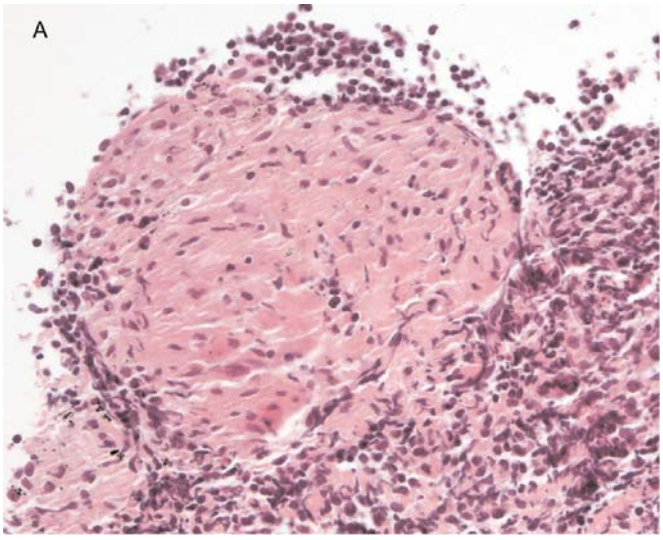

Fig. 2A: Histologic sections, haematoxylin and eosin x200 **(A)** and cytologic smears, papanicolaou x200.

Special stains and culture results for acid-fast bacilli and fungi were negative. On the basis of clinical, radiological and pathologic findings, a diagnosis of sarcoidosis was made. A clinical follow-up was arranged.

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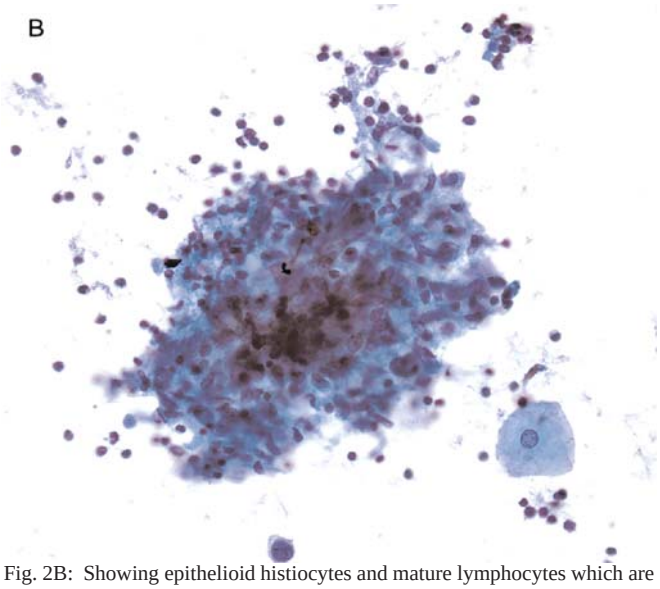

Fig. 2B: Showing epithelioid histiocytes and mature lymphocytes which are forming granulomas.

DISCUSSION

Acute myeloblastic leukaemia has been previously reported in association with sarcoidosis in case reports. In several cases reports, sarcoidosis is recognized prior to or at the same time as the diagnosis of AML (5–8). Linkage between the leukaemia and sarcoidosis was suggested in these previous reports by pronounced T cell dysfunction which appears in sarcoidosis. In this case report, we present the occurrence of AML preceding the diagnosis of sarcoidosis. There are only two reported cases in the literature with diagnosis of AML preceeding the diagnosis of sarcoidosis similar to the present case. Pagona *et al* (3) reported pulmonary sarcoidosis in a patient with a diagnosis of AML present 11 months before the diagnosis of sarcoidosis. Isoda *et al* (4) described AML followed four years later by cutaneous sarcoid. This case is of interest not only because it adds a third case of AML preceding sarcoidosis, but also because of the 17-year time interval between the two diagnoses. In this regard, this case raises the question of an AML-sarcoidosis association: Is it causal or coincidental?

Reich reports that the AML-sarcoidosis association is strong, consistent and specific, considering the rarity of AML (2). However, the nature of the relationship between AML and sarcoidosis remains speculative. Some studies demonstrate the strong induction of antileukaemic immune responses to tumour-associated antigens and a high incidence of circulating immune complexes in AML patients (9–10). Reich suggests that if the presence of granulomatous inflammation within tumours or tumour-draining lymph nodes represents an immunologic response to a large variety of insoluble antigens, multisystem granulomatous inflammation may occur in instances in which the tumour antigens were widespread, such as leukaemia (2).

Acute myeloblastic leukaemia patients are usually under close medical supervision which should help to make a timely diagnosis of sarcoidosis. The paucity of reported cases in the literature may be explained by the generally poor outcome of AML or other individuals may not have had symptomatic sarcoidosis.

The possibility of transmission of sarcoidosis by BMT and donor-acquired sarcoidosis has been suggested (11, 12). A transmissible agent, perhaps of infectious origin, was proposed as a cause of sarcoidosis. In our case, BMT was performed 17 years ago, following the diagnosis of AML. Despite the long latent period after BMT, donor-acquired sarcoidosis still remains a possible aetiology.

In this case, the diagnosis of sarcoidosis was made based on findings of granulomas from mediastinal lymph nodes by TBNA. Wang *et al* (13) reported that flexible bronchoscopic TBNA may be a valuable tool in the diagnostic evaluation of patients with suspected sarcoidosis. TBNA may preclude the need for surgical biopsy. On the other hand, the presence of granulomas in a lymph node biopsy specimen is not specific to sarcoidosis. Sarcoid-like granulomas can be found in infections or malignancies. Therefore, the diagnosis of sarcoidosis must be based on compatible clinical, radiological and pathologic features. In this case, cultures of the biopsy specimens were negative and routine laboratory evaluation failed to disclose other causes for granulomatous disease. However, it may be still either over or under-diagnosed in the setting of haematologic malignancy depending on no readily ascertainable markers for sarcoidosis.

In conclusion, we report a case of sarcoidosis that developed 17 years after a history of AML and BMT. Although there is no significant association with AML and sarcoidosis in the published compendia dealing with either entity, to collect all cases of sarcoidosis associated with AML in a series might help resolve the pathogenesis and uncover the realities about an AML-sarcoidosis relationship, whether it is causal or coincidental?

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