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Familial Sarcoidosis: About Two Brothers and Prevalence Value in a Middle Eastern City

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ABSTRACT

Sarcoidosis is a systemic disease with no definite etiology, but a lot of potential precipitating factors. Familial sarcoidosis was mentioned in the literature long time ago and has been associated with different HLA phenotypes with a prevalence reaching values up to 4% and more; however, it was never studied in the Middle East. This article reports a case of sarcoidosis in two Lebanese brothers with the HLA phenotype related and estimates the prevalence of familial sarcoidosis in all cases of sarcoidosis treated by internists and pneumologists in a regional hospital where these brothers were treated. In our study, the HLA type (DRB) was similar to the familial polish cases and the familial prevalence of around 1.4 %, was much lower than that reported elsewhere.

Keywords: Sarcoidosis, familial, Lebanese, HLA DR B

"Running" title: Familial sarcoidosis in a Middle Eastern city

Introduction

Sarcoidosis is a multi-systemic disorder of unknown etiology. It affects adults between 20 and 40 years old. There are some evidences about the etiological role of genetic factors, infectious agents, environmental agents (titanium, metal dust, birds, molds, aerosolized plant,…) (1) and occupational exposures (education, agriculture, healthcare, firefighting, automobile manufacturer,…) (2), but the definite cause of sarcoidosis remains unknown (3).Despite evidence for a genetic component to sarcoidosis, to date, not a single gene has been identified as the "sarcoidosis gene". Variations in disease susceptibility, presentation, progression and prognosis have been associated with different HLA phenotypes (4). Several studies were conducted, but none has been conclusive (5). Presented results suggest that HLA-DRB alleles contribute to the susceptibility to sarcoidosis in the Polish population (5). In the Swedish population, there is an association of sarcoidosis with HLA B8 and HLA DR3 (6, 7). In the Italian population, sarcoidosis has been associated with HLA B8. HLA B35 was found more frequently in patients with onset of symptoms before 36 years old. B12 and DR4 may have a protective function against the disease (8).Sarcoidosis frequently presents with bilateral hilar adenopathy and pulmonary infiltration and often with ocular and skin

lesions. Diagnosis is established when supported by histologic evidence of non-caseating epitheloid cell granulomas .Chest x-rays and CT-scanner are usually used to diagnose and to determine the stage of the disease. Familial cases have been reported since 1920s (3). Results of studies for the frequency of familial sarcoidosis reveal that it's a rare disease. It is reported 3 to 3.5 times more frequently in African American patients (9). Frequency of familial sarcoidosis, when all races are considered, is 2.4% (10). Prevalence of familial sarcoidosis in Finland is of 3.6-4.7% and in Hokkaido of 2.9-4.3% (11).Family members of affected patients should be screened for the disease because of high prevalence in siblings (2.4%) (12).The real frequency of familial sarcoidosis is probably underestimated because of the big number of latent forms (13).

Case Description

We are reporting a case of two brothers R.Z. and F.Z.

R.Z is 32 years old, and was hospitalized in July 2009 for shortness of breath and fatigue. A chest x-ray done before the hospitalization showed a bilateral hilar enlargement.

A CT scanner of the chest was done: In the mediastinum, we notice the presence of multiple adenopathies in different compartments with nodes reaching a dimension of 2 cm. These mediastinal adenopathies were accompanied by hilar bilateral adenopathies reaching 2 cm on the left and 3 cm on the right, with sub-carinal adenopathies of 2.5 cm. In the pulmonary parenchyma, there were no nodes or masses. There were no pleural effusions. The slices passing in the abdomen do not show hepatic or adrenal lesions. Blood tests revealed: Angiotensine Converting Enzyme ACE=100.8 UI/ml (12-68) UI/ml; the rest of the hematological, biochemical and auto-immune results was normal. Mediastinoscopy was done for biopsy of the lymphnodes. The histological study showed chronic granulomatous non-necrotizing lymphadenitis with epithelioid and giant cells. The diagnosis of sarcoidosis was confirmed. No treatment was administered.

F.Z is an automobile mechanic, assisted by his brother R regularly during weekends, given that they share the same house in a rural zone surrounded by pine trees. F.Z is 35 years old and was hospitalized in 2008 for breathlessness, cough, weight loss and fever. The Chest x-ray showed mediastinal enlargement. The Chest CT scanner showed markedly enlarged lymphnodes in the mediastinum and hili. A 9 mm lymphnode has also been identified in the lower right jugular chain. No supraclavicular or axillary enlarged lymphnodes were seen. Few parenchymal nodules were seen, the largest measuring 12 mm. Minimal peribronchial thickening and interstitial infiltrates were present in the left parahilar area. No pleural infusion was found. The Abdominal CT scanner showed enlarged lymphnodes around the head of the pancreas along the lesser curvature of the stomach and in the porta hepatic. His workup showed the following results: ACE=78 UI/ml; PCR for tuberculosis in bronchial fluid (-); γ Glutamyl Transpeptidase (γ GT): 131UI/l (8-61); Alkaline Phosphatase: 145 UI/l (40-129), Erythrocyte sedimentation rate (ESR): 32 mm (3-8); the rest of the blood tests was normal. Bronchoscopy with bronchial biopsy revealed epithelioid and giant cell non necrotizing granulomatous inflammation. He was diagnosed with sarcoidosis and was successfully treated by corticosteroids.

The HLA type for the patient R.Z., by the LABTYPE SSO Typing test (Luminex one Lambda Inc technology) , showed these

results: HLA A 01, A 29, B 18, B 51, DQB1 01, DQB1 05 , DRB1 11, DRB1 15 … The HLA Typing for F.Z. was not done because the patient immigrated to Canada during our study and our literature review.

Interrogatory and physical exam of the mother and the only sister of our studied brother are not suggestive of sarcoidosis. Chest X-Rays, liver tests and ACE levels were also normal. Father's patients is death

During 2009, the year of our study, 6 sporadic cases of sarcoidosis (4 males and 2 females), were diagnosed in the departments of Internal Medicine and Respiratory disease of our hospital, located in the north of the capital Beirut, which is a medical care reference for about 200,000 people living around it . The majority of cases (5/6) were pulmonary with mainly hilar and/or mediastinal adenopathies; one male patient had Löfgren syndrome.

Discussion

We reported the first case of familial sarcoidosis (in two brothers) in the Middle East. The disease was ranged as mild for the first brother (R.Z) and moderate for the second (F.Z) and its presentation was similar to that seen in non familial sarcoidosis. In fact, other authors concluded that there was no clinical difference between familial sarcoidosis and usual forms of the disease (13), only Löfgren syndrome stood out (14).In our case, the relationship is a brother to brother matter. Other studies reported equal distribution of like sex and non like sex pairs (12).Whereas, some studies showed dominating relationships between sister-brother and mother-child relationships (11). The HLA type of our patient (DRB 15) was similar to the familial polish study (5) Environment agents are probably incriminated in the pathogenesis of sarcoidosis in our patients. Pine trees and the type of work (auto mechanic) are prevailing in this case. We should emphasize on the fact that those were considered among etiological agents for the disease (4), even though none have been directly incriminated ever. Finally, in our study the familial prevalence is around 1.4 %, much lesser than the values of 2.4-4.7% or more reported elsewhere (10, 11, 12, 13). In order to be more conclusive, we'll have to include more familial sarcoidosis cases in the region and conduct genetical and environmental studies on them.

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