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## Students' Corner

### **A Case of non-resolving Cough and Weight Loss**

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#### **Abstract**

Sarcoidosis is a chronic granulomatous multi-system disease with a clinical picture often mimicking tuberculosis. We present a case of a patient who presented with a clinical picture akin to both of these granulomatous disorders and was started on anti-tuberculous regimen despite the lack of any solid evidence pointing towards tuberculosis. As a result her clinical condition continued to deteriorate for months until finally a bronchoscopic biopsy established

her disease process as sarcoidosis. She was then started on systemic corticosteroid therapy for sarcoidosis and during the ensuing period has shown marked improvement in her clinical picture with near normalization of the biochemical and radiographic parameters of her pathology.

This case illustrates the need for vigilant interpretation of the clinical scenario in patients such as these where a misdiagnosis may lead to significant patient

distress as well as weighing down on the economic and health resources.

## Introduction

Sarcoidosis is a chronic systemic ailment prevalent all over the world. Despite its widespread global distribution, there is considerable underrecognition, particularly in the developing world. This holds particularly true for regions endemic to tuberculosis, where sarcoidosis is being overlooked as a possible diagnosis with increasing frequency, owing primarily to the similarities in the clinical and radiological manifestations of the two pathologies. This report presents a case of sarcoidosis which was continued on anti-tuberculous regimen for several months, leading to significant morbidity. Though not a rare scenario, this is one which demands our urgent attention in order to generate an insight for the better understanding of this critical issue.

## Case Report

A 50-year-old lady presented to pulmonary clinic with a six month history of productive cough and evening pyrexia. During this period she had lost around 33 pounds weight and noticed a gradual reduction in her exercise tolerance.

Her medical history was remarkable only for diabetes, under control on oral hypoglycaemics, and an exposure to pulmonary tuberculosis in the past.

On examination she appeared frail, though was vitally stable. Chest auscultation revealed normal vesicular breathing with no added sounds and equal bilateral air entry. Laboratory investigations were within normal limits apart from significantly elevated serum alkaline phosphatase and gamma glutamyl transferase, with values of 439 I.U./L and 514 I.U./L respectively. Sputum smear and culture both were negative for acid fast bacilli.

Chest X-ray revealed bilateral symmetrical hilar lymphadenopathy with mild interstitial thickening (Figure 1). CT scan of the chest confirmed the adenopathy and widespread miliary nodules (Figure 2).

In consideration of her clinical and radiographic findings and the endemicity of tuberculosis in the region she was started on four drug anti-tuberculosis therapy (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide). Anti-tuberculosis therapy was continued for nearly seven months. During this period there was cessation of her evening rise in temperature. Apart from that there was no noticeable improvement in her cough and she had lost another two pounds in weight. Serial chest X-rays revealed worsening of parenchymal infiltrates with no resolution of the hilar adenopathy.

With the continuing deterioration of her clinical and radiographic picture, a bronchoscopic biopsy was resorted

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Figure 1. Chest X-ray shows bilateral symmetrical hilar lymphadenopathy with basal interstitial thickening.

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Figure 2. CT scan shows bilateral hilar lymphadenopathy, causing obstructive sub-segmental atelectasis on the right. Tiny bilateral diffuse pulmonary nodules.

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Figure 3. Photomicrograph of bronchial biopsy showing non-caseating granulomas along with moderate chronic inflammation in sub-epithelial area. Note multi-nucleated giant cells. H&E stain (Magnification x 100).

to. Histopathology of the biopsy specimen showed multiple non-caseating granulomas composed of multinucleated

Figure 4. Photomicrograph of bronchial biopsy showing non-caseating granulomas along with moderate chronic inflammation in sub-epithelial area. Note multi-nucleated giant cells. The respiratory surface epithelium is unremarkable. H&E Stain (Magnification x 200).

giant cells containing calcifications, in the sub-epithelial fibrous tissue. Chronic granulomatous inflammation was confirmed (Figures 3 and 4) and special stains for acid fast bacilli, fungi and other micro-organisms were negative. Diagnosis of sarcoidosis was made and the patient was started on Prednisolone therapy with concurrent discontinuation of the anti-tuberculous regimen. She has continued her new treatment for nearly fifteen months now. During this time she has gained nearly 36 lbs in weight and complains no more of any respiratory or other symptoms. Her liver enzyme levels have returned to normal and a recent chest radiograph revealed almost complete resolution of the pulmonary infiltrates.

## Discussion

Sarcoidosis is a chronic inflammatory systemic disorder of unknown etiology. It is characterized by the formation of non-caseating granulomas in the diseased tissues, intrathoracic in 90% of the cases. Reported from all over the world its frequency is influenced by race, gender, age and the sophistication of regional medical care and screening programs, with genetic predisposition and infective agent being other probable factors.

The clinical picture is variable among races and includes constitutional symptoms as fever, fatigue, weight loss, anorexia, cough and dyspnea. Hepatomegaly, splenomegaly and lymphadenopathy are also seen. Common hematological derangements include anemia, lymphopenia and raised ESR, while hypercalcemia and hypergammaglobulinemia are also recorded. Usual immunological findings encountered are depression of cutaneous delayed-type hypersensitivity and an increased T helper cell type response at disease sites. Signs of B cell hyperactivity may also be seen along with circulating immune complexes.

In 90% to 95% of the patients there is an abnormality in chest radiographs at some point of time during the course of their illness<sup>1</sup>, commonly lymphadenopathy.<sup>2</sup> Classical radiological presentation is symmetric bilateral hilar adenopathy with paratracheal adenopathy and the characteristic bronchopulmonary adenopathy. Parenchymal involvement is seen in a little less than half of the cases at the time of presentation.<sup>1</sup> Alveolar sarcoidosis is characterized by consolidative features (air-space opacities) frequently accompanied by nodal involvement, as in this case.

Amongst imaging modalities, HRCT (High Resolution Computed Tomography) is now the globally preferred technique. CT scanning is superior to the chest X-ray for studying both the adenopathy and the parenchymal involvement. It also aids in the differential diagnosis of sarcoidosis and other granulomatous disorders, especially tuberculosis, and helps in following up for the detection of any complications, like fibrosis.<sup>3</sup> Nevertheless, chest X-ray is still considered to be the most informative technique in elucidating the disease activity.<sup>4</sup>

The elevated alkaline phosphatase and gamma glutamyl transferase levels in our patient suggest probable liver involvement by sarcoidosis. Incidence of hepatic involvement amongst systemic manifestation of sarcoidosis is 66%.<sup>5</sup> The liver enzyme values have been known to normalize after appropriate therapy.<sup>6</sup>

Despite these advancements, there is still a global underrecognition of the cases of sarcoidosis. This is owing to the variable disease presentation, lack of consistent case definition, lack of specific investigations and a dearth of systemic epidemiological research in this direction. The 'great masquerader' should always be kept in mind in scenarios such as this one and others where the regional endemicity and atypical clinical and radiological features may point elsewhere. This is of particular relevance for the developing world where tuberculosis is considered to be endemic in a number of nations. The diagnosis of sarcoidosis should be made on carefully evaluated clinical and/or radiological findings, histological evidence of noncaseating granulomas and exclusion of other diseases capable of producing a similar histological or clinical picture.

Even though cytotoxic agents have proven to be of value in selected patients, corticosteroids are the drugs of choice for the management of sarcoidosis.<sup>7</sup> Although there does exist controversy amongst the indications for the medical therapy of sarcoidosis, standard therapy for symptomatic, progressive disease consists of corticosteroids.<sup>8</sup> Prednisone is perhaps the most commonly used agent. Other drugs have been used and found to be useful in various clinical scenarios. Lung transplantation has been found to be successful in end-stage disease with first year survival

useful in various clinical scenarios. Lung transplantation has been found to be successful in end-stage disease with first year survival rates comparable to other forms of diffuse lung diseases.<sup>9</sup>

The clinical course of sarcoidosis is variable. Most persons with sarcoidosis have spontaneous remission of their disease, although between 10% and 30% may be afflicted with chronic or progressive disease.<sup>10</sup> The health related quality of life is globally diminished. Mortality is usually owing to pulmonary and cardiac complications.

In conclusion our patient is a typical case in which sarcoidosis was initially overlooked as a possible diagnosis and anti-tuberculosis therapy initiated despite the absence of solid evidence towards tuberculosis. This is a common practice in many territories endemic for tuberculosis and has contributed towards increasing the burden of disease in many developing regions of the world. This highlights again the need for careful evaluation of the clinical and radiologic evidence in all typical and atypical presentation patterns of sarcoidosis.

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