

# Unusual association of Hodgkin's disease and sarcoidosis

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## ABSTRACT

We report a 51-year-old patient who developed abdominal lymphadenopathy following Hodgkin's disease seven years after she was diagnosed as having sarcoidosis. The patient had been treated with steroids, methotrexate and azathioprine. After three cycles of chemotherapy for Hodgkin's disease, the patient again developed sarcoidosis in the mediastinal lymph nodes. A greater awareness of the co-existence of sarcoidosis and Hodgkin's disease could circumvent the diagnostic difficulties.

## INTRODUCTION

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas.<sup>1</sup> Although the aetiology of sarcoidosis is unknown, several features such as lymphocytopenia, an increase in T-helper (CD4+) lymphocytes, an increase in antigen expressing capacity and adhesion molecules on antigen presenting cells, and abnormal cytokine production suggest that there is a relationship between the host immune system and the pathogenesis of the disease.<sup>2</sup> The diagnosis can be established by the clinical presentation and by obtaining characteristic histology together with biochemical findings.<sup>1</sup> However, this is not an easy task because of insensitive and non-specific diagnostic tests, and overlap with other disorders. The latter especially concerns granulomas, which can be found in malignancy, including Hodgkin's disease, infections such as tuberculosis, and hypersensitivity to drugs. We describe a patient with Hodgkin's disease preceded

and followed by sarcoidosis to draw the attention to this unusual association and its diagnostic problems.

## CASE REPORT

A 43-year-old woman presented with enlarged supraclavicular lymph nodes, a skin lesion near the nose (lupus pernio) and persistent cholestatic liver enzyme disturbances. Histological examination of the lymph node and liver tissue showed multiple granulomas. Broncho-alveolar lavage findings and histological examination of the transbronchial biopsy of the lung were consistent with sarcoidosis. Two years later, the skin lesion of the nose bridge became larger, and treatment was started with methotrexate (MTX) for approximately three months, followed by prednisolone. Two years later, azathioprine was started, because the pulmonary condition and the liver abnormalities had deteriorated. Two years later, after treatment with MTX for three months (because of worsening of the liver abnormalities), the patient was seen with weight loss. Ultrasonography and computer tomography (CT) of the abdomen revealed lymph nodes and a large tumour (*figure 1*). At laparotomy, extensive retroperitoneal lymphadenopathy was found. Pathological examination of the lymph nodes revealed a Hodgkin's disease (stage III-b) of the nodular sclerotic subtype, of which the cells were CD15 and LMP-1 positive, and CD30, panB and panT negative. The large tumour contained benign myomas. At that time some granulomas (*figure 2*) and minor lymphadenopathy in the mediastinum and axillary lymph nodes (*figure 3*) were present. The patient was treated with mitoxine, vincristine,



**Figure 1**  
*CT scan of the abdomen showing lymph nodes and myoma of the uterus*



**Figure 2**  
*CT scan of the thorax with nodules*



**Figure 3**  
*CT scan of the thorax with axillary lymph node*

procarbazine, prednisolone, adriamycin, bleomycin and vinblastine. After three courses, evaluation took place. Mediastinal lymph nodes were shown to be present. Histological examination was consistent with sarcoidosis. To date (after six courses), no recurrent activity of the sarcoidosis or Hodgkin's disease has been detected.

## DISCUSSION

Sarcoid-like granulomas can be found in infectious diseases, neoplastic diseases including Hodgkin's disease, hypersensitivity to drugs, and other conditions.<sup>1</sup> Therefore, a non-specific local sarcoid-like reaction should be ruled out before the diagnosis of multisystem sarcoidosis is made. Even when a diagnosis is made, another granuloma-containing disorder can appear or co-exist, as illustrated by the present case.

The association of sarcoidosis with malignancy, in particular lymphoma<sup>3-10</sup> and lung cancer,<sup>11</sup> has been reported before. The existence of a sarcoidosis lymphoma syndrome was suggested,<sup>3</sup> in which the sarcoidosis precedes the lymphoma. This concept was disputed in the literature,<sup>12,13</sup> whereas others have confirmed the association.<sup>14</sup> Including our case, 27 cases with co-existing sarcoidosis and Hodgkin's disease have been published thus far. Both sexes are equally represented; mean age of sarcoidosis at onset was 41 years. In the majority of the cases, the Hodgkin's disease was preceded by sarcoidosis except for three cases. The mean interval from sarcoidosis to Hodgkin's disease is 76 months. In our case, Hodgkin's disease was found 84 months after diagnosing sarcoidosis. The disturbed host immune system in sarcoidosis may have predisposed to the lymphoma. Moreover, immunosuppressive treatment<sup>15,16</sup> could have contributed.<sup>17,18</sup> By virtue of its immunosuppressive properties, MTX could be carcinogenic or could facilitate infection with pro-carcinogenic viruses such as the Epstein-Barr virus. Remission of malignancies after withdrawal of MTX suggests that there is at least an association between MTX and the development of lymphomas. However, the duration of treatment with MTX was too short and the cumulative dose too low to induce adverse effects in our patient.

Reich *et al.*<sup>19</sup> suggested that sarcoidosis is a systemic cell-mediated immune reaction to tumour antigens. This could explain the development of sarcoidosis in mediastinal lymph nodes during treatment for Hodgkin's disease in our patient. Five other reports of sarcoidosis following chemotherapy for Hodgkin's disease have appeared.<sup>3,8,10</sup> In these reports, the Hodgkin's disease was not preceded by sarcoidosis, in contrast to our patient. Whether this sarcoidosis or sarcoid-like reaction is induced by chemotherapy for Hodgkin's disease remains conjectural.

In conclusion, our patient has some characteristics that have

not been reported before in one patient: an uncommon presentation of the sarcoidosis, the development of Hodgkin's disease after immune suppressive treatment of sarcoidosis, and a flare-up of sarcoidosis in the mediastinum during treatment for Hodgkin's disease. Because of potential confusion in the differential diagnosis of granulomas, clinicians should be aware of the co-existence of sarcoidosis and Hodgkin's disease.

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