accompanied by increased alveolar permeability, reduced lung compliance and surfactant alterations. In this case, these changes occurred initially in the right lung, leading to volume loss on the right with compensatory hyperinflation of the left lung. With additional time both lungs were involved, although clearing of the left lung lagged behind the right with treatment.

This case also represented the first documented occurrence of \textit{P carinii} at our institution in five years since the widespread use of trimethoprim-sulfa methoxazole prophylaxis for most pediatric leukemia patients. Use of intensive chemotherapy as primary treatment for children less than three years of age with brain tumors is a relatively new and promising therapy and this case demonstrates that these patients are at risk for \textit{P carinii} pneumonia and should also receive prophylaxis with TMP-SMZ. 

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Myocardial Sarcoidosis Unresponsive to Steroids

Treatment with Cyclophosphamide

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Sarcoidosis affecting the pleura, pericardium, and myocardium is described in a patient who demonstrated continued disease activity while on therapy with high-dose steroids. Cyclophosphamide was found to be highly effective in suppressing her disease over a period of six years.

Corticosteroids are the mainstay in the treatment of chronic sarcoidosis. Only recently have immune-altering medications been used, usually in patients who have been shown to have disease unresponsive to steroid therapy. The following case exemplifies this unusual aspect of sarcoidosis.

CASE REPORT

A 37-year-old black woman presented in January, 1979 with shortness of breath and bilateral hilar lymphadenopathy. Sarcoidosis was diagnosed by mediastinoscopy and biopsy. Prednisone was prescribed, but she discontinued its use after two months due to Cushingoid side effects. In August, 1979, she presented with a massive left pleural effusion. An exhaustive workup revealed only sarcoidosis. Prednisone was started at 30 mg per day. The pleural effusion initially resolved but gradually recurred. After eight months of steroid treatment consisting of at least 30 mg/day, a massive left and small right pleural effusion were seen on the chest x-ray film. Cardiomegaly was also seen and an echocardiogram demonstrated gross pericardial effusion. Therapy with high-dose prednisone (60-100 mg/day) was associated with an immediate reduction in the pleural and pericardial effusions. These findings later recurred and by August, 1980, the physical examination revealed anasarca.

Throughout her course, all biochemical and immunologic parameters for sarcoidosis were either negative or normal. These tests included serum and urine for calcium, urine for hydroxyproline, SACE, immunoglobulin and complement levels, and tests for circulating immune complexes. The PPD result was negative and an anergy battery was positive. All studies of other organ systems were equally unrewarding, with the exception of a gallium scan which showed diffuse uptake in the region of the pulmonary hila and a thallium scan of the heart which was consistent with cardiomyopathy.

A 24-hour Holter monitor revealed one PVC in a 24-hour period. Pericardioectomy was performed due to the features of constrictive pericarditis which was unresponsive to conventional therapy. At surgery, the myocardium was noted to be almost completely covered with white tubers believed to be involvement with sarcoidosis (Fig I). The pericardial tissue revealed granulomatous inflammation consistent with sarcoidosis. She was discharged home in an improved condition on therapy with 40 mg of prednisone per day.

The left pleural effusion never disappeared completely, and by April, 1981, it had achieved massive proportions which again caused dyspnea. Prednisone therapy was gradually increased, and despite doses up to 100 mg per day, the effusion persisted. Cyclophosphamide therapy was empirically started in June, 1981 at a dose of 25 mg/day.

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Myocardial Sarcoidosis (Stephen L. Demeter)
mg bid. There was rapid diminution in her dyspnea and fatigue and a sense of well-being returned. Prednisone therapy was gradually tapered and subsequently discontinued. The gallium scan reverted to negative and has remained so. Over the years, attempts were made to reduce the dose of cyclophosphamide to 25 mg per day. On each attempt, her sarcoidosis again became active either clinically (pleuritic chest pain), electrocardiographically (arrhythmias), or radiographically (chest nodules which were biopsied and showed non-caseating granulomas). She is now maintained on 50 mg per day.

**DISCUSSION**

This patient displayed several unusual features of sarcoidosis, namely: the large, bilateral pleural effusions, myocardial and pericardial involvement, lack of systemic "markers" for the disease process, and lack of response to steroids. It is estimated that approximately 1 percent of patients with sarcoidosis have pleural involvement. The presence of either bilateral or massive pleural effusions are usually the subjects of case reports.

Sarcoidosis may affect any area of the heart—pericardium, myocardium, or endocardium. Of these, the myocardium is most frequently involved. The exact incidence of cardiac involvement, however, is difficult to ascertain. Autopsy series suggest an incidence between 20 and 30 percent, although these figures are probably quite high for all patients with sarcoidosis. Pericardial involvement, by contrast, is unusual. Only 31 cases of pericardial granulomas (usually diagnosed at necropsy) were identified by 1979. The frequency of small pericardial effusions (which may be due to disease affecting the pericardium or the epicardium) appears to be subject to the diligence of the search. Nineteen percent of 48 consecutive sarcoidosis patients in a series by Kinney et al had small pericardial effusions diagnosed by echocardiography. Thus, it is unclear how often and to what extent sarcoidosis may affect the heart.

Corticosteroid medications are the usual mainstay of treatment for sarcoidosis. Cytotoxic medications have been used only rarely (mainly because steroids are almost uniformly effective, although an exact incidence could not be found in a literature search). Kataria used chlorambucil therapy in ten patients with sarcoidosis, either alone or in combination with steroids; eight improved. All ten were placed on therapy with this agent after a lack of medical response to steroids or contraindications to their use. Similarly, Israel et al used chlorambucil in eight patients not responding to corticosteroid therapy, with a beneficial response in four.

Two recent reviews of sarcoidosis mentioned reports of patients being treated with immunosuppressive medications including methotrexate, azathioprine, chlorambucil, and (investigationally) cyclosporin A. The total number of patients was less than 100 and, except for limited use in patients with dermal sarcoidosis, these medications are reserved for use in patients who have critical organ involvement and who have failed a course treatment with steroids. Benefit was seen in the majority of patients. Chronic sarcoidosis has been likened to an immunologic disorder and, superficially, immune-altering drugs would be expected to be efficacious. However, Kinney et al could find no precise mechanism(s) for the beneficial results.

The lack of response to corticosteroid therapy in my patient with bilateral pleural and pericardial effusions prompted both the pericardectomy and the use of cyclophosphamide. The lack of any systemic markers for her disease has proved distressing since her disease activity can only be assessed by the appearance of pleural effusion or by the changes on the thallium and gallium scans. These objective indices, however, have shown marked improvement and there has been a complete subjective response. Equally distressing is the inability to reduce the drug dosage to less than 50 mg per day. Thus, cyclophosphamide may prove beneficial to the patient with sarcoidosis. Caution must be used in patient selection since there exists concern that cyclophosphamide, even in low doses, may have neoplastic potential.

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