3 × 4 cm was palpated in the right submandibular area. Baseline laboratory studies and chest roentgenograms were within normal limits. Serologic tests for histoplasmosis, coccidiodomycosis, and blastomycosis were negative.

At operation, the right submandibular gland appeared normal, but it was surrounded by enlarged nodes. A 5 × 4 × 4 cm mass was resected, and frozen sections of the nodes revealed caseating granulomas and giant cells. Fixed sections showed extensive granulomatous inflammation with rare acid-fast bacilli. Sections of the adjacent submandibular gland were normal.

Skin tests with mycobacterial antigens gave the following results: PPD-A (actinum), 7 mm of induration; PPD-B (nonchromogen), 9 mm; PPD-C (scotochromagen), 6 mm; PPD-Y (photochromagen), 0 mm; PPD-F (fortuitum), 4 mm; PPD-S (5 TU), 13 mm; and a repeat PPD-S (5 TU), 0 mm. The discrepancy in the latter two tests could not be explained. At six weeks, cultures of the nodes grew M. avium-intracellulare. The organism was resistant to isoniazid, kanamycin, ethambutol, and rifampin and sensitive only to high levels (10 μg/ml) of streptomycin and to paraaminosalicylic acid.

The patient was treated initially with 300 mg of isoniazid and 600 mg of rifampin daily, but therapy was stopped after three months. The patient remains well one year after surgery.

**DISCUSSION**

Lymphadenitis caused by atypical mycobacteria is now thought to be more common than tuberculous lymphadenitis. The large majority of patients have been children, aged one to five years, and we know of only one other report of lymphadenitis with atypical mycobacteria in an adult. In that report, the patient presented with a painful unilateral submandibular mass with fever. The diagnosis of infection with M. avium-intracellulare was established only after therapy with antibiotics had failed, and the mass was excised and examined. In children, the illness usually presents with asymptomatic, unilateral swelling, most often of the submandibular nodes, without evidence of pulmonary infection. The clinical features of the present case were similar to those in children. The diagnosis was made only with culture of the nodes. The skin tests had some value in raising a suspicion of atypical mycobacteria but were confusing because of cross-reactivity among the antigens. Because of this cross-reactivity and poor standardization, their use is not currently recommended. Surgical excision of affected lymph nodes alone, with or without antituberculosis therapy, has been successful. Persistent local infection may develop if excision of all affected nodes is not carried out, and it is recommended that if surgery is abbreviated or not feasible, then antituberculosis therapy should be considered.

**REFERENCES**


**Lymphomatoid Granulomatosis**

**Report of a Patient with Severe Anemia and Clubbing**

Rachakonda Prabhu, M.D.;
Herbert W. Berger, M.D., F.C.C.P.;
Antonio Subietas, M.D.; and Manoo Lee, M.D., F.C.C.P.

We report a 31-year-old man in whom initially localized lymphomatoid granulomatosis was diagnosed at left pneumonectomy. He had severe anemia which is rare and clubbing of the fingers and toes, a feature not previously described. Five months following surgery, disease spread to the right lung, and atypical lymphomatous transformation occurred in cervical and mediastinal lymph nodes, leading to a superior vena cava syndrome. Chemotherapy with cyclophosphamide and prednisone resulted in significant resolution initially, but ultimately, the patient had progressive axillary node enlargement and succumbed. Clinical and roentgenographic improvement and later deterioration following pneumonectomy and improvement with chemotherapy were mirrored by changes in degree of clubbing, leukocytosis, and elevation of erythrocyte sedimentation rate.

Lymphomatoid granulomatosis was described by Liebow et al. in 1972 as an angiocentric and angiodestructive lymphoreticular proliferative and granulomatous disease predominantly involving the lungs. The skin, central nervous system, and kidneys are also commonly involved, but lymph nodes, spleen, and bone marrow are usually spared. Since etiology, prevalence, and prognosis are unknown, and the number of cases is still small, individual case reports may add to our knowledge and understanding of this disease. Our 31-year-old patient had several features only rarely or not previously described: severe anemia, clubbing of the fingers and toes, and development of a superior vena cava syndrome following lymphomatous transformation.

*From the Pulmonary Section, Department of Medicine, and the Department of Pathology, Mount Sinai Services-City Hospital Center at Elmhurst, and the Mount Sinai School of Medicine of the City University of New York, NY.
†Assistant in Medicine.
‡Professor of Clinical Medicine.
§Assistant Professor of Clinical Pathology.
‖Instructor in Medicine.

**LYMPHOMATOID GRANULOMATOSIS 883**

**CHEST, 78: 6, DECEMBER, 1980**

**Reprint requests:** Dr. Prabhu, Mt. Sinai Services, 79-01 Broadway, Elmhurst, New York 11373
CASE REPORT

A 31-year-old white man was admitted to Mount Sinai Services-City Hospital Center at Elmhurst in May 1978. He had been seen by a private medical doctor for fever of 38.3 to 38.8°C, cough, and expectoration of two weeks' duration in March 1978. Chest x-ray film in March revealed lingular consolidation and cavitation. Sputum culture grew Klebsiella pneumoniae. He was treated with cephalaxin without improvement. In May 1978, he also complained of weight loss, anorexia, and night sweats. He was mentally retarded from birth. Past history was remarkable for cervical lymphadenopathy at age nine with a supposedly normal biopsy.

On physical examination, temperature was 38.8°C, respiratory rate 20 per minute, and pulse rate, 100 beats per minute. Several pea-sized lymph nodes were palpable in the neck. Examination of the chest revealed splitting of the left hemithorax with dullness on percussion and occasional rales. Marked clubbing of fingers and toes was present. There were no skin lesions or neurologic signs other than mental deficiency, hepatomegaly, or splenomegaly. His hematocrit value was 21 percent; white blood cell count, 22,900/cu mm with 78 percent neutrophils, and erythrocyte sedimentation rate, 150 mm/hour. Hematologic investigation revealed microcytic, hypochronic anemia with a nondiagnostic bone marrow aspiration. Sputum examination showed numerous polymorphonuclear leukocytes with mixed flora on culture. Blood and urine cultures for routine organisms and sputum cultures for tubercle bacilli and fungi were negative. Arterial blood gas studies showed a pH of 7.46, PaO₂ of 99 mm Hg, and PaCO₂ of 36 mm Hg. Intermediate and second strength tuberculin skin tests were negative. Gamma globulin was 2.1 gm/100 ml. Chest x-ray film showed a “Swiss cheese” appearance of the lingula and left lower lobe from destruction by multiple cavities. The right lung was normal. There was no mediastinal lymphadenopathy (Fig 1). Intravenous administration of clindamycin and gentamicin was begun for presumed suppurative pneumonia. Cough, expectoration of whitish sputum, fever, and roentgenographic changes persisted. Bronchoscopy revealed no endobronchial lesions and culture of bronchial washings grew mixed flora.

When he failed to improve after six weeks of intensive antibiotic therapy, left pneumonectomy was performed on July 14, 1978. At surgery, the left lung was highly noncompliant and contained multiple cavities. Pathologic examination of lung and pleura revealed numerous confluent, sharply outlined nodular lesions measuring from one to several centimeters in diameter. Histologically, the lesions consisted of angiocentric, angiodestructive pleomorphic lymphomatoid infiltrates displaying areas of necrosis and polymorphonuclear infiltration. In addition to mature lymphocytes and plasma cells, there were occasional mononucleated or multinucleated atypical lymphoreticular cells resembling histiocytes. No inclusion bodies were found (Fig 2). Pathologic diagnosis was lymphomatoid granulomatosis. Mediastinal and peribronchial lymph nodes were not enlarged and were normal microscopically.

Following surgery, the patient felt better, his fever disappeared, and he gained weight. Clubbing of fingers and toes decreased. His anemia improved (hematocrit value, 36 percent), white blood cell count returned to normal, and erythrocyte sedimentation rate fell to 25 mm/hour. He was readmitted in November 1978 with a left pleurocutaneous fistula which was treated by open drainage and marsupialization. In December 1978, he complained of high fever, cough, mucoid expectoration, and anorexia. Cervical and subclavicular lymph nodes were markedly enlarged compared to earlier admissions with three of them measuring greater than 5 cm in diameter. Finger clubbing was more prominent. Conjunctival plethora, venous prominence of the upper limbs, and distension of jugular veins were noted. Examination of the right lung revealed decreased breath sounds with occasional rales. His hematocrit value was 34 percent, erythrocyte sedimentation rate, 100 mm/hour, and white blood cell count, 22,000/cu mm with 78 percent polymorphonuclear leukocytes. Chest x-ray film showed a 7-cm cavity in the right lower lobe with pericavitary infiltrates and nodules. Considerable right-sided mediastinal lymphadenopathy was now present (Fig 3). An excised cervical lymph node measuring 3 × 2 cm showed a generally effaced architecture, although in some areas, rare lymph follicles were still identifiable. The stroma displayed frequent arborizing blood vessels exhibiting fibrin thrombosis associated with patchy areas of liquefactive necrosis and severe polymorphonuclear infiltration. The cellular elements consisted of mature lymphocytes and plasma

Figure 1. Chest x-ray film May 31, 1978, showing lingula and left lower lobe consolidation and cavitation.

Figure 2. Atypical lymphoreticular infiltrate with mature lymphocytes and occasional polymorphonuclear leukocytes (original magnification × 400).
Lymphomatoid granulomatosis is a distinct entity with unique clinical and pathologic features. It is usually seen in middle age, and most patients present with pulmonary symptoms and a clinical diagnosis of pneumonia as in our patient. Neurologic symptoms, arthralgias, myalgias, skin rash, and gastrointestinal symptoms are sometimes present.

To our knowledge, clubbing in association with this disease has not been described previously. Clubbing, as well as leukocytosis and erythrocyte sedimentation rate elevation, decreased following surgery, worsened with progression of his disease, and then improved after initiation of chemotherapy. While most patients have a normal or only slightly decreased hematocrit value, our patient had marked microcytic, hypochromic anemia, a finding described only twice previously. The hematocrit level improved after left pneumonectomy, and the patient remained only mildly anemic until his death.

Unilateral pulmonary involvement, as noted in our patient, initially is seen in only 21 percent of cases of lymphomatoid granulomatosis, and in 15 percent of those the other lung is eventually involved. Common roentgenographic findings in this disease include bilateral cavities and nodules often mistaken for metastatic tumors. Diffuse fluffy alveolar and reticulonodular infiltrates are sometimes present. Hilar adenopathy is seen in only 2 percent of patients. We believe that right lung involvement in our patient was secondary to lymphomatoid granulomatosis since it resembled the original abnormality in the left lung. It is interesting to speculate whether progression of disease could have been prevented by starting chemotherapy immediately after pneumonectomy. Twelve percent of patients with lymphomatoid granulomatosis develop malignant lymphoma some time during their course, with diagnosis during life in only 33 percent of these cases. Our patient developed marked cervical and mediastinal adenopathy with superior vena cava syndrome five months after pneumonectomy. Superior vena cava syndrome has not been previously reported and was due to lymphomatous enlargement of lymph nodes. Lymph node histologic findings were remarkable for the presence of intranuclear inclusions. This suggested a viral infection of either coincidental or etiologic significance. Further observations are required in this respect.

Mortality of lymphomatoid granulomatosis is high; only 25 percent of patients have recovered with or without treatment. Treatment modalities have included corticosteroids, cyclophosphamide, azathioprine, combinations of nitrogen mustard, vincristine, procarbazine, and chlorambucil, and radiotherapy. No particular mode of therapy has been consistently effective. Our patient responded to chemotherapy satisfactorily with clinical and partial radiologic improvement initially, but finally died with progressive lymphomatous lymph node enlargement and resistance to chemotherapy.

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