literature have failed to find a similar reported case. Therefore, we believe that this is the first report of a case of severe pectus excavatum causing chronic hypercapnic respiratory failure, pulmonary hypertension, and chronic cor pulmonale.

Surgical repair of the deformity provides cosmetic benefits, but the pathophysiologic benefits remain controversial. Although subjective improvement in exercise tolerance and dyspnea often are noted after surgery, pulmonary function improvement is infrequent and modest. Conversely, others have shown a reduction in pulmonary function after surgical repair. Moreover, it should be noted that all reported surgical series consist of patients with either normal or mildly impaired pulmonary function. Consequently, the appropriateness of surgical repair is debatable when a substantial improvement in lung function is the primary objective, as it is in our patient.

ACKNOWLEDGMENT: The authors thank Jenifer S. Khan for her assistance in editing the article.

REFERENCES
7 Fabricius J, Davidson HG, Hansen AT. Cardiac function in funnel chest. Dan Med Bull 1957; 4:251–257

Severe Immune Hemolytic Anemia in Disseminated Tuberculosis With Response to Antituberculosis Therapy*

Ping-Hung Kuo, MD; Pan-Chyr Yang, MD; Shoo-Shown Kuo, MD, FCCP; and Kwen-Tay Luh, MD, FCCP

Severe hemolytic anemia in patients with disseminated tuberculosis is exceedingly rare. We report an episode of Coombs’-positive hemolytic anemia in a previously healthy young man with miliary tuberculosis, resulting in a hemoglobin level of 3 g/dL and an undetectable haptoglobin level. The patient responded well to treatment with antituberculosis drugs, and the results of the direct Coombs’ test became negative without the need of blood transfusion or steroid therapy.


Key words: Coombs’ test; haptoglobin; immune hemolytic anemia; tuberculosis

Many reports have associated mycobacterial diseases with hematologic abnormalities. Minor degrees of anemia are commonly found in patients with disseminated tuberculosis, but hemolytic anemia is exceedingly rare. We describe an episode of severe immune hemolytic anemia due to miliary tuberculosis in a previously healthy young man.

CASE REPORT

A 26-year-old man presented to the emergency department of our hospital in January 1997 with a 2-week history of intermittent fever and exertional dyspnea. He also complained of malaise, fatigue, and weight loss of 4 kg over the preceding 3 weeks. There was no history of hematologic disorders or blood transfusions, and he was not receiving any drugs. The family history was noncontributory. On examination, the patient’s temperature was 38.4°C, the pulse was 100 beats/min, and the respirations were 28 breaths/min. The BP was 110/60 mm Hg. Several lymph nodes were palpated in the left neck and in both axillary regions. The patient’s chest radiograph showed a widened mediastinum and miliary lesions over both lung fields. A CT scan of the chest documented prominent mediastinal lymphadenopathy. Abdominal sonography revealed heterogeneous hepatic echogenicity but no splenomegaly. The results of laboratory investigations were as follows: hemoglobin level, 5.0 g/dL; hematocrit, 16.7%; mean corpuscular volume, 107 femtoliters; mean corpuscular hemoglobin concentration, 29.9 g hemoglobin per deciliter RBCs; total leukocyte count, 109/L (43% neutrophils; 3.0% lymphocytes; 10% monocytes); platelet count, 104/L (43% neutrophils; 3.0% lymphocytes; 10% monocytes; 2% myelocytes; and 41% band leukocytes); platelet count, 104/L (21.4%); albumin level, 3.8 g/dL; globulin level, 3.6 g/dL; total bilirubin level, 2.5 mg/dL (with a direct component of 0.6 mg/dL); aspartate aminotransferase

*From the Departments of Internal Medicine (Drs. P.-H. Kuo and Yang) and Laboratory Medicine (Drs. S.-S. Kuo and Luh), National Taiwan University Hospital, Taipei, Taiwan. Received July 21, 2000; revision accepted November 16, 2000. Correspondence to: Kwen-Tay Luh, MD, FCCP, Department of Laboratory Medicine, National Taiwan University Hospital, No. 7, Chung-Shan South Rd, Taipei, Taiwan; e-mail: luhkt@ha.mc.nctu.edu.tw
level, 78 U/L; alanine aminotransferase level, 52 U/L; lactate dehydrogenase level, 1,309 U/dL; and haptoglobin level, below the detection limit of 5.8 mg/dL (normal level, 64 to 157 mg/dL). The serum levels of urea nitrogen, creatinine, and glucose-6-phosphate dehydrogenase were normal. The peripheral blood smear films for blood cells and parasites showed significant polychromasia and anisocytosis, with the presence of normoblasts but without plasmodia and microfilaria. The results of the direct Coombs’ test were positive. Osmotic fragility and hemoglobin electrophoresis were within normal limits. Serum protein electrophoresis showed polyclonal gammapathy. Serologic tests for antinuclear antibodies, cold hemagglutinin, as well as antibodies to Mycoplasma pneumoniae and HIV all were negative. Blood and sputum specimens for culture failed to show any notable growth. Bone marrow aspiration specimens showed erythroid hyperplasia. Granulomatous inflammation with caseous necrosis was identified in both the lymph node and bone marrow biopsy specimens, with numerous acid-fast bacilli present in the former. Antituberculosis therapy was instituted on January 26, 1997, including isoniazid (300 mg qd), rifampicin (600 mg qd), ethambutol (800 mg qd), and pyrazinamide (250 mg tid). The patient’s fever subsided 2 days after therapy was initiated, and there was a dramatic improvement in well-being and general health thereafter. The hemoglobin increased to 10 g/dL within 2 weeks of therapy, but the haptoglobin was still < 5.8 g/dL. He was discharged on February 15, 1997, and continued with regular follow-ups at the outpatient clinic. The Coombs’ test result became negative in April 1997. A culture from a lymph node specimen finally grew Mycobacterium tuberculosis. Antituberculosis therapy was maintained until January 1998 when the patient’s neck lymph nodes were determined to be almost impalpable. When he came back in May 1999, he was in excellent health and the results of all laboratory tests were normal (see Table 1 for the serial laboratory data in response to therapy).

**Discussion**

Possible mechanisms for the development of anemia in mycobacterial infection include nutritional deficiency, failure of iron utilization, malabsorption syndrome, marrow suppression, and shortened duration of RBC survival (hemolysis). Immune hemolytic anemia has been reported following a wide variety of infections, with the cornerstone of the diagnosis being a positive result of a direct Coombs’ test, which shows that the RBCs are agglutinated by an antiglobulin preparation. An early experimental study in Germany showed that the injection of tubercle bacilli or their products produced hemolytic anemia, pancytopenia, and myelofibrosis in small animals. In humans, the wide spread of tubercle bacilli may occasionally provoke a marked proliferation of reticuloendothelial tissues, resulting in varied and severe hematologic disorders through immune mechanisms. However, immune hemolytic anemia resulting in a hemoglobin level as low as 5 g/dL, as occurred in the case reported here, is exceedingly rare.

For infection-associated hemolytic anemia, immediate initiation of an appropriate antimicrobial therapy is of central importance and may be life-saving. The patient in our report was notable for a good recovery after antituberculosis chemotherapy, without the need of blood transfusion or steroid therapy. To our knowledge, only one similar patient who responded to antituberculosis therapy alone has been reported previously. In another report, one

---

**Table 1—Serial Laboratory Data in a 26-Year-Old Man With Disseminated Tuberculosis**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dL</td>
<td>5.0</td>
<td>5.2</td>
<td>8.9</td>
<td>10.2</td>
<td>12.7</td>
<td>14.6</td>
<td>16.3</td>
<td>16.6</td>
<td>16.6</td>
</tr>
<tr>
<td>RBC, 10^6/μL</td>
<td>1.55</td>
<td>1.49</td>
<td>2.51</td>
<td>2.95</td>
<td>3.46</td>
<td>4.98</td>
<td>5.31</td>
<td>5.35</td>
<td>5.34</td>
</tr>
<tr>
<td>Reticulocyte, %</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Haptoglobin, mg/dL</td>
<td>5.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>11.2</td>
<td>99.3</td>
<td>113</td>
<td>324</td>
<td>349</td>
</tr>
<tr>
<td>LDH, U/L</td>
<td>1,309</td>
<td>1,177</td>
<td>1,041</td>
<td>831</td>
<td>478</td>
<td>304</td>
<td>324</td>
<td>334</td>
<td>349</td>
</tr>
<tr>
<td>Bilirubin, mg/dL</td>
<td>2.5</td>
<td>0.6</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*LDH = lactate dehydrogenase. During the period from January 28, 1997, through January 3, 1998, the patient received antituberculosis therapy.*
patient with tuberculosis-related hemolytic anemia required prolonged steroid therapy to prevent the recurrence of hemolysis. Caution also should be exercised when selecting rifampicin or para-aminosalicylic acid for these patients, since both drugs are known to induce hemolytic anemia.2

The extremely low haptoglobin level in this patient was strong evidence of a severe intravascular hemolytic process, in which the rate of haptoglobin catabolism exceeded the rate of synthesis. A normal haptoglobin level, however, does not rule out active hemolysis, because it is an acute-phase reactant that may increase during a chronic illness. Another interesting feature of this patient is the delayed recovery of the haptoglobin level in comparison with the clinical symptoms and hemoglobin level, reflecting the persistence and severity of the underlying RBC destruction.

In summary, disseminated tuberculosis should be listed among the etiologies of infection-associated hemolytic anemia. Physicians should start rapid empiric antituberculous therapy without hesitation in the appropriate clinical setting.

REFERENCES
2 Cameron SJ. Tuberculosis and the blood: a special relationship? Tubercle 1974; 55:35–72
3 Siribaddana SH, Wijesundera A. Autoimmune haemolytic anaemia responding to anti-tuberculous treatment. Trop Doct 1997; 27:243–244

Ticlopidine-Induced Interstitial Pulmonary Disease*

A Case Report

Christophe F. Persoz, MD; Fedra Cornella, MD; Pierre Kaeser, MD, and Thierry Rochat, MD

We report a case of interstitial pulmonary disease that occurred together with lymphocytic colitis during treatment with ticlopidine. The drug was prescribed for transient ischemic cerebrovascular accidents. Ticlopidine treatment was stopped, and a prolonged course of prednisone was necessary to treat the pulmonary and intestinal symptoms. So far, few cases of pulmonary side effects caused by ticlopidine have been reported. This case is unique in that interstitial lung disease evolved in parallel with colitis and caused severe hypoxemia. Special care should be taken when pulmonary symptoms appear in association with ticlopidine treatment.

(CHEST 2001; 119:1963–1965)

Key words: collagenous colitis; eosinophilic pneumonia; interstitial pulmonary disease; lymphocytic colitis; ticlopidine

Abbreviations: BOOP = bronchiolitis obliterans and organizing pneumonia; TIA = transient ischemic accident

Ticlopidine is an inhibitor of platelet activation. It inhibits the adenosine diphosphate receptors of the platelet and thus prevents partial platelet attachment. Many randomized studies with ticlopidine have shown a reduction of stenosis in stents after percutaneous transluminal coronary angioplasty. Its usefulness is also proven in cerebrovascular ischemic diseases. A few side effects are well known, such as neutropenia (2.4% of treated cases; of these, 0.8% are severe), thrombocytopenia, cholestatic hepatitis (rare), thrombocytic thrombocytopenic purpura (very uncommon) and, more frequently, GI symptoms (nausea and vomiting in up to 40%). Sometimes, chronic diarrhea is associated with microscopic lymphocytic colitis.1–4 To our knowledge, no interstitial pulmonary disease has been described with ticlopidine treatment in association with diarrhea. We report herein the case of a new onset of diarrhea, followed by dyspnea and dry cough, in an old woman treated with ticlopidine for cerebrovascular transient ischemic accident (TIA).

Case Report

A 79-year-old woman was treated since November 22, 1998, with aspirin and ticlopidine for recurrent TIA. No clear etiology was found for the TIA. Ticlopidine was added to the treatment because of repetitive neurologic symptoms with aspirin alone. At that time, the patient did not have any respiratory or digestive symptoms. On January 14, 1999, she was admitted to our hospital for diarrhea and progressive dyspnea. Diarrhea appeared 10 days after the introduction of ticlopidine. At the time of hospital admission, the patient had 8 to 10 watery stools per day with no blood and no abdominal pain. She had no significant weight loss and was in good general condition with no fever. Physical examination was normal, including chest and abdomen. Aspirin and ticlopidine were stopped immediately, and oxygen supplementation was administered for dyspnea. Results of bacteriologic studies of the stool, searching for the presence of blood and fat, as well as parasites, and Clostridium difficile toxin were all negative. Results of a lactose tolerance test and gastroscope were normal. Thyroid, liver, and pancreatic function test results as well as serum electrolytes were also normal. CBC count showed no eosinophilia (31 g/L). Results of antinuclear antibodies, rheumatoid factor, antineutrophil cytoplasmic antibodies, and complement C3 and C4 were all normal. A colonoscopy was performed with biopsies, showing lymphocytic colitis associated with mini-