TUBERCULOUS SPLENOMEGALY WITH THE HYPERSPLENISM SYNDROME

A Case Report

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ALTHOUGH secondary involvement of the spleen in tuberculosis is quite common, the clinical picture of an enlarged tuberculous spleen with little or no tuberculosis elsewhere is rare. This syndrome is often referred to as "primary tuberculosis of the spleen," and was first recognized by Coley in 1846. The term "primary tuberculosis of the spleen" implied that the principal location of the disease was in the spleen which acted as a focus for the dissemination of the tubercle bacilli and was responsible for the hematologic effects. Englebreth-Holm in 1938 felt that that term was misleading, as tuberculosis of the spleen must always be secondary, and insisted it be called tuberculous splenomegaly, a term now agreed to by most writers.

Recently there has been such a case in the University of Virginia Hospital following streptomycin-treated miliary tuberculosis. Although there was apparent recovery from miliary tuberculosis, a very marked splenomegaly developed in association with leukopenia and anemia. Following splenectomy, definite clinical improvement occurred and the blood picture returned to normal. However, six weeks postoperatively, the patient developed a fulminating tuberculous meningitis and died.

CASE REPORT

An 18 year old white male was admitted to the University Hospital on February 8, 1948. Two months previously, he had first noticed a nonproductive cough associated with a dull pain in the left chest. Three weeks before admission, the chest pain became more severe and simultaneously the cough increased and became productive of small amounts of yellowish sputum. Weakness, malaise, fever, and severe night sweats developed, necessitating confinement to bed. The patient was seen in the Outpatient Department five days before admission and an x-ray of the chest showed only accentuation of the pulmonary markings. A shaking chill occurred two days later and hospitalization was advised. There was a 2.5 pound weight loss.

On admission, temperature was 100.5 F, pulse 110, respiration 24, and blood pressure 120/65. The patient was pale with flushed cheeks, undernourished, and showed evidence of recent weight loss. There was a generalized lymphadenopathy of small, nontender, discrete nodes. Examination of the chest revealed dullness to percussion in the left base posteriorly, slightly diminished breath sounds over the right lower chest, and a few small crepitant rales in both bases. The liver was just palpable and a firm spleen edge extended 7 cm. below the costal margin. A dorsal kyphosis and scoliosis to the left were also noted.

The admission blood counts are shown in table 1. A mild anemia and marked leukopenia were present. The differential smear showed an increased number of monocytes and a normal number of platelets. The urine and Wassermann were negative. A sternal marrow examination revealed an increase in immature granulocytes. Numerous sputum examinations and cultures revealed only the usual flora. Repeated blood
Cultures, stool examinations, and agglutinations for typhoid, tularemia, brucellosis, typhus, and Rocky Mountain spotted fever were negative. No abnormalities were found in the spinal fluid.

Chest roentgenograms on admission revealed multiple miliary opacities throughout the lungs, and their appearance over a five day period strongly suggested miliary tuberculosis. Abdominal x-ray films disclosed a mass in the left upper quadrant which was thought to be the spleen as well as evidence suggesting an enlarged liver.

Course: During the early period of hospitalization the temperature ranged between 100 F and 104 F and the patient's condition became more precarious daily. Penicillin was started empirically without effect.

During the second week, gastric washings were found to be positive for acid-fast bacilli on two occasions. A tuberculin skin test (1:1000) was negative, and histologic examination of a lymph node biopsy showed only chronic lymphadenitis. Repeat chest x-rays demonstrated further increase in the lung markings and a progression of the soft, generalized, miliary infiltration. The diagnosis of acute miliary tuberculosis was considered established, and streptomycin was begun in a dosage of 2 Gm. daily on the ninth day.

By the thirteenth hospital day, the fever began to exhibit a downward trend. Five days later chest films showed further spread of the generalized miliary opacities, but the typical progressive picture of miliary tuberculosis appeared altered and this was attributed to the use of streptomycin. Consequently the dose of this antibiotic was increased to 3 Gm. daily. He improved slowly, and by the thirty-seventh day he was afebrile. The dosage of streptomycin was then decreased to 2 Gm. daily. Chest x-rays at this time demonstrated a beginning diminution of the miliary process.

Throughout the rest of his hospital stay he remained afebrile, and gained 14 pounds with notable symptomatic improvement. However, the spleen remained enlarged and repeated blood studies showed a persistent leukopenia and anemia (Table I). Another tuberculin skin test was done and was found positive in the 1:10,000 dilution. Further chest roentgenograms taken on the sixty-second hospital day revealed no evidence of tuberculosis. On April 14, 1948 after 66 days of hospitalization he was discharged in an asymptomatic state to a tuberculosis sanatorium for further care. He had received a total of 107 grams of streptomycin.

While in the sanatorium, although streptomycin was not continued, he was afebrile, and gained 22 pounds in the next three months. Fever recurred in July and a downhill course ensued with the loss of 18 pounds in the next two months. Frequent examinations of the spleen showed progressive enlargement. Associated with this was an increase in the leukopenia and anemia. (Table I)

When readmitted to the University Hospital on September 27, 1948, for further studies, the patient...
appeared chronically ill and had a temperature of 100 F. A smooth, slightly tender spleen could be palpated extending almost to the pubic symphysis and well across the midline of the abdomen. Blood studies again revealed an anemia, marked leukopenia, and granulocytopenia (table 1). The sternal bone marrow was hyperplastic. Bleeding time, clotting time, clot retraction, and tourniquet tests were normal. Liver function studies were normal. Urine and stool examinations were again negative. Roentgenograms of the skull, spine, hands, pelvis, and femora were negative. During this hospitalization of six days his temperature ranged from normal to 102 F. A diagnosis of tuberculous splenomegaly was made on the basis of the history of miliary tuberculosis, fever, splenic enlargement, and the findings in the blood.

Splenectomy was advised. After receiving 1500 cc. of whole blood he was discharged to the sanatorium for further streptomycin therapy before surgery.

He remained in the sanatorium twenty-four days and during the latter twenty-one he was afebrile. However, he continued to lose weight and the splenic enlargement increased.

On October 26, 1948 he was readmitted to the University Hospital for splenectomy. Physical examination and the laboratory findings were as before. On the following day a laparotomy was performed and a very large spleen was found, filling the entire left side of the abdomen and displacing the viscera to the right. The inferior pole of the spleen extended below the sacral promontory and the capsule was extensively adherent to the surrounding structures. The liver was slightly enlarged but appeared normal. The spleen (fig. 1) was removed without difficulty and was found to weigh 3363 grams. It was smooth with a purplish grey color and had a fairly soft consistency.
On histologic examination the architecture was almost entirely replaced by tubercles with a few areas of caseation. Tubercle bacilli were demonstrated in the spleen by acid-fast stains. The hilar lymph nodes were also involved with tubercles. Emulsified spleen injected into guinea pig resulted in the development of typical caseous tuberculous lesions and acid-fast organisms were demonstrated in the tissues.

Within twenty-four hours after the operation there was a striking increase in the white cell and platelet counts (table 1). The patient's postoperative course was uneventful except for a moderate fever. Streptomycin was continued and penicillin was added for prophylactic purposes. He was discharged to the sanatorium on the ninth hospital day for further treatment.

For the first six weeks in the sanatorium he was asymptomatic, afebrile, and gained weight. Streptomycin was discontinued at the end of four weeks. The hematologic studies remained normal and follow-up chest x-rays showed no evidence of miliary tuberculosis. However, during the seventh week he began to run a fever and developed a stiff neck. Spinal fluid studies confirmed the clinical impression of tuberculous meningitis. Despite the resumption of streptomycin intramuscularly and intrathecally, he went rapidly downhill and died within a week.

Autopsy: Postmortem examination revealed a healed primary tuberculous lesion at the periphery of the left lower lobe of the lung; and miliary tuberculosis of the lungs, liver, lymph nodes, and meninges. These lesions were evident grossly and microscopically, and tubercle bacilli were present in smears taken from the meninges. In the cortex of the left temporal lobe there was a 5 mm. area of caseation with overlying meningeal adherence. This was probably the direct source of the meningeal infection. Death was undoubtedly due to tuberculous meningitis.

Discussion

The miliary tuberculosis in this case at first responded dramatically to streptomycin therapy. Despite the use of this drug, the spleen, which previously had been moderately enlarged, gradually increased in size until it occupied most of the abdomen. Along with this was the development of a marked leukopenia and anemia. Three months after streptomycin was discontinued, fever returned asso-
cated with a progressive loss of weight. A diagnosis of tuberculous splenomegaly was made and the antibiotic therapy resumed. His temperature fell to normal but he continued to lose weight and "go downhill." Consequently, a splenectomy was done with the prompt reversion of the blood picture to normal and notable improvement of the patient for six weeks. However, during the seventh postoperative week he developed a fulminating tuberculous meningitis and succumbed a few days later.

Although Winternitz in 1911 felt that the blood picture in "primary tuberculosis of the spleen" was not constant, of the 51 cases that he collected, 42 per cent had an anemia, and 23 per cent had polycythemia. In this series only 19 had white cell counts and 27 per cent of these had a leukopenia of 5,000 or less. He also noted purpura in 2 cases. In the twenty years following this classic exposition, isolated reports appeared noting the association of this disease with leukopenia, anemia, thrombocytopenia, and purpura. In 1931, Price and Jardine described 4 cases resembling Banti's syndrome which were diagnosed at operation or by autopsy as "primary tuberculosis of the spleen." Englebreth-Holm in 1938 after reviewing the literature and studying 4 cases of splenomegaly following miliary tuberculosis, observed its frequent association with anemia, leukopenia, and other evidences of bone marrow inhibition. He concluded that tuberculous splenomegaly caused inhibition of the emission or the maturation of the blood cells in the bone marrow. In 1941, Weiner and Carter reviewed the previously reported cases of thrombocytopenia and purpura associated with tuberculous splenomegaly and added another. The entire subject of the hemopoietic effect of this splenic disorder was reviewed briefly in 1942 by Brown, Mason, and Lucia and again by Dietz in 1946. To date less than 100 cases have been published. The occurrence in this type of splenic tuberculosis of leukopenia, anemia, and thrombocytopenia, singly or together, fits well into Dameshek's recent theory of "selective" and "total" types of hypersplenism. Dameshek postulated that the development of the one or more cytopenias in hypersplenism is due to abnormal or excessive splenic activity causing bone marrow inhibition. It is also consistent with Doan and Wright's concept of excessive destruction of blood cells by an abnormal spleen.

The diagnosis of tuberculous splenomegaly is difficult and usually is made at the operating table or on postmortem examination. It is found most commonly in the 20 to 40 age group and the diagnosis depends on such features as a history of previous tuberculosis or exposure, splenomegaly, evidences of tuberculosis in other organs, moderate fever, evidences of bone marrow inhibition, and a downhill course. Occasionally calcium deposits can be demonstrated in the spleen by x-ray and splenic puncture with culture for the tubercle bacillus is considered of diagnostic value by some, for the organisms are quite plentiful in this organ. This type of splenomegaly should be differentiated from Banti's syndrome, leukemia, lymphosarcoma, Hodgkin's disease, cirrhosis of the liver with splenomegaly, malaria, certain parasitic infections, thrombosis of the splenic vein, agnogenic myeloid metaplasia of the spleen, Felty's syndrome, and others.

Splenectomy, by unanimous agreement, is the treatment for this disorder, for
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The outcome without it is generally considered to be invariably fatal. The object is the elimination of the focus of dissemination of tubercule bacilli by hematogenous spread, to remove the inhibiting effect on the bone marrow, and to relieve the discomfort caused by the splenic enlargement. In some instances the patients may not survive because of tuberculosis in other organs. With the addition of streptomycin the prognosis should be improved. The use of streptomycin in this case did not eliminate the need for surgery.

The pathology of these spleens is quite interesting. The majority are usually huge, weighing from 1000 to 3000 grams. The spleen in this case weighed 3,363 grams and is one of the largest reported. On macroscopic examination tuberculosis may or may not be seen, while caseation or abscess formation is extremely rare. The histopathologic appearance is that of a very cellular pulp with numerous partly confluent miliary tubercles with little or no necrosis and only a few small malpighian bodies. The splenomegaly is secondary to proliferation of the reticulum cells of the pulp and to the presence of tuberculous foci.

Had the correct diagnosis been made earlier in the case reported and had splenectomy been done within the first or second month after the notable response to streptomycin, the outcome might have been different. The spleen by remaining in situ with its infection could have acted as the focus for reinfection and establishment of other foci after the organism had become resistant to streptomycin.

SUMMARY

A case of tuberculous splenomegaly with leukopenia and anemia following miliary tuberculosis has been presented. Splenectomy was required after streptomycin failed to control the cytopenias, progressive emaciation, and splenic infection. However, following what appeared to be six weeks of marked improvement, the patient developed a fulminating tuberculous meningitis and died.

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