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Thrombocytopenic Purpura Associated with Tuberculous Lymphadenitis

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THAT purpura may be associated with tuberculosis in its fatal and non-fatal forms[1] has been recognized for many years. Although it is known that various types of blood dyscrasias may occur with miliary tuberculosis, relatively few cases of thrombocytopenia associated with tuberculosis can be found in the medical literature.

In 1952 Ellman and Johnson,[2] in an extensive review of the literature, described only 77 cases of purpura associated with tuberculosis: of these, 31 were of the thrombocytopenic variety, of which 10 were associated with tuberculous splenitis, 11 with pulmonary tuberculosis, two with abdominal tuberculosis, and one case each with cervical lymphadenitis, tuberculous septicemia, and following an intradermal test with old tuberculin.

By 1956 only three further cases of thrombocytopenic purpura associated with tuberculosis had been reported.[3] To the time of preparation of this manuscript, the authors have been able to find reports of approximately 90 cases of purpura associated with tuberculosis. The association of purpura and tuberculous lymphadenitis appears particularly uncommon and the only previous case report describing the association of thrombocytopenic purpura with tuberculous lymphadenopathy was that of de la Vega *et al.*[4] in 1939. The patient described below presented with tuberculous lymphadenitis and severe thrombocytopenic purpura and may thus represent the second case reported with such an association.

F.M., a 27-year-old unmarried Greek woman, was admitted to the Royal Victoria Hospital, Montreal, on March 7, 1961, complaining of fatigue of five months' duration, a swelling in the neck for one month, and purpura for one day.

She had been well until five months before admission, when she noted the onset of weakness, fatigue and lethargy. During this period she had lost 12 lb. in weight. One month before admission she noted the appearance of a swelling in the neck following a mild upper respiratory tract infection for which she received no medication. On the day before admission the patient noticed a bruise on her lower abdomen, followed several hours later by a profuse petechial eruption. There was bleeding from the gums but no gross hemoptysis, hematemesis, epistaxis, melena or hematuria. The patient was admitted to hospital with a tentative diagnosis of idiopathic thrombocytopenic purpura. Further history revealed that the patient worked as a machine operator in a dress factory. She denied contact with noxious fumes or chemicals, and had not taken any medication during the previous several months. She denied previous severe illnesses.

Physical examination revealed a well-developed, well-nourished, apprehensive woman. Blood pressure, pulse and admission temperature were normal. There was generalized purpura with marked oozing of blood from the gums. A diffuse swelling was noted in the left side of the neck, consisting of several mobile, non-tender, firm lymph nodes, 1-3 cm. in diameter. A few small nodes were found in the axillary and submandibular areas. The spleen and liver were not palpable and the remainder of the physical examination was within normal limits.

LABORATORY DATA

Urinalysis revealed a specific gravity of 1.025, protein 3+, and marked microhematuria.

Hematology: Her hemoglobin was 11.6 g. %; packed cell volume 35%; and mean corpuscular hemoglobin concentration 33%. Platelets were scanty on the smear, and the direct platelet count was 8000 per c.mm. The total leukocyte count was 5500 per c.mm. with a normal differential count.

Biochemistry: The non-protein nitrogen (NPN) was 29 mg. %; alkaline phosphatase 6.2 King-Armstrong units; serum bilirubin 0.4 mg. %; and uric acid 4.7 mg. %. A Paul-Bunnell test was negative. Serum electrophoresis revealed increased gamma globulin. A search for L.E. cells was negative.

Radiographic examination of the chest and abdomen was normal. There was no evidence radiologically of splenomegaly.

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Canad. Med. Ass. J.
Feb. 1, 1964, vol. 90

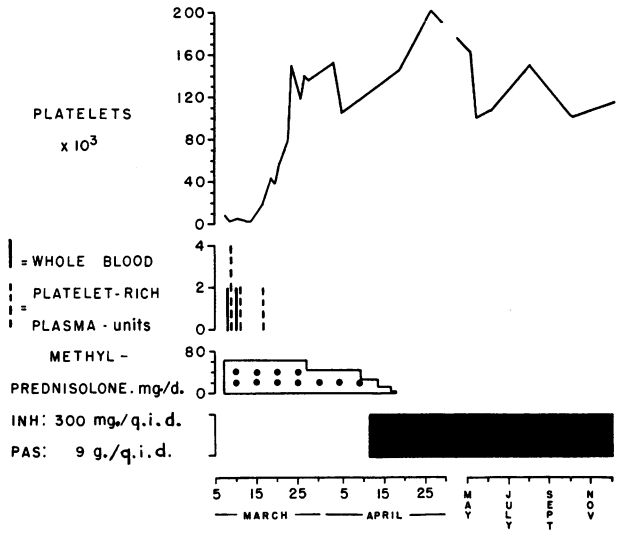

Fig. 1.—Effect of therapy on thrombocytopenia.

Examination of bone marrow aspirate revealed numerous megakaryocytes with basophilic cytoplasm and no platelet budding. The myeloid: erythroid ratio was normal, as were erythropoiesis and myelopoiesis. There was a slight increase in the number of plasma cells and plasmacytoid lymphocytes. The appearance of the bone marrow thus was compatible with idiopathic thrombocytopenic purpura.

COURSE IN HOSPITAL

The patient was treated with infusions of fresh blood and platelet-rich plasma, and with large amounts (64 mg. per day) of methylprednisolone, in divided doses. Three weeks after institution of therapy the platelet count had risen to 43,000 per c.mm. and the dose of methylprednisolone was reduced to 48 mg. per day (Fig. 1). The number of platelets continued to rise. Because of the persistent lymphadenopathy, biopsy was performed and microscopic examination revealed granulomatous infiltration consistent with a diagnosis of tuberculosis. Therapy was commenced with isoniazid and para-aminosalicylic acid, and the dosage of steroids was gradually reduced. At the time of discharge the platelet count varied between 100,000 and 200,000 per c.mm. The patient was followed up in the outpatient department and remained well.

Antituberculous therapy was discontinued on March 6, 1962. The patient remained well until June 1962, when she noted slight swelling of the left side of her neck. She was readmitted to hospital, and biopsy of the enlarged lymph nodes revealed active tuberculosis with acid-fast bacilli present. Antituberculosis therapy was reinstituted. The platelet count remained normal during this admission despite the fact that she received no steroid therapy. A repeat bone marrow aspirate was entirely normal.

DISCUSSION

Although an etiological relationship between tuberculous lymphadenitis and the idiopathic thrombocytopenic purpura cannot be firmly established in the patient described above, such a relationship is probable. The onset of the severe life-threatening thrombocytopenia during the early months of symptomatic lymphadenitis suggests that some relationship may have existed between the tuberculosis and the thrombocytopenic purpura.

The possible mechanisms by which the systemic tuberculosis may induce thrombocytopenic purpura include:

1. Drug-induced thrombocytopenia related to the administration of certain antituberculous agents.
2. The precipitation of latent idiopathic thrombocytopenic purpura by the tuberculous infection.
3. Tuberculous splenitis with a "hypersplenic" syndrome.
4. Generalized reticuloendothelial hyperplasia with hypersequestration of the platelets or the elaboration of anti-platelet antibodies.
5. Bone marrow replacement by granulomata and fibrosis.

In addition to these, anaphylactoid purpura has been described in response to old tuberculin.[5, 6]

In the patient described above, splenomegaly was not found on clinical examination. This does not exclude splenic tuberculosis, since Akkermann and Teodorovich[7] studied five patients with pulmonary tuberculosis and thrombocytopenic purpura in whom the spleen was not palpable. Two patients were subjected to splenectomy because of the severity of the clinical symptoms. Following operation the platelet count returned dramatically to normal levels, and on microscopic section, tuberculous granulomata were found in the spleen.

The observation that at least 60% of cases of miliary tuberculosis show splenic tuberculosis indicates that if the tuberculous adenitis was secondary to a transient miliary form at some previous time, the patient described here may well have had splenic tuberculosis.[8] It is doubtful that the presence or absence of granulomata in the spleen ever will be determined if this patient does not come to operation. It is of interest that in the relapse of the tuberculous lymphadenitis which occurred one year after the initial illness, thrombocytopenia did not reappear. The reason for this may be that while the antituberculous therapy eradicated the infectious foci in the spleen, it did not accomplish this effectively in the cervical lymph nodes, perhaps because of the previous local surgery which had interfered with the effective blood supply to this area.

SUMMARY

A case of tuberculous lymphadenitis associated with severe thrombocytopenic purpura is described and the possible interrelationship of the two conditions is discussed.

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