ASSOCIATION OF ACQUIRED HEMOLYTIC ANEMIA WITH PERIARTERITIS NODOSA

Case Report

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ALTHOUGH the cause of periarteritis nodosa is still essentially unknown, there is considerable evidence to support the theory of Rich[1] that the disease is a manifestation of the anaphylactic type of hypersensitivity to various antigens. Acquired hemolytic anemia, in some cases, appears to be related to a hypersensitivity reaction with the production of auto-antibodies. It is somewhat surprising, therefore, that until very recently no report associating the two diseases has appeared in the medical literature.

Dameshek and Rosenthal[2] recently reported the association of periarteritis nodosa and acquired hemolytic anemia in 2 patients, both of whom showed remission with ACTH therapy. They also mentioned 4 cases of hemolytic anemia unaffected by splenectomy, in which a generalized and pronounced polyarteritis was found on postmortem examination.

The following case report represents another instance of associated hemolytic anemia and periarteritis nodosa. It is unique in that the acquired hemolytic anemia apparently subsided and was followed, 18 months later, by thrombocytopenic purpura and acute fulminating periarteritis nodosa.

Case Report

A married white woman, 26 years of age, was first seen on January 12, 1946 with a complaint of progressive weakness of 6 weeks' duration. It was obvious that she was severely anemic. Previously the patient had been in good health and worked steadily as a waitress. There was no history of excessive blood loss and no known exposure to hematopoietic toxins. The red blood cells numbered 700,000 per cu. mm; the hemoglobin was 3 Gm. The white blood cell count, differential, fragility studies, and platelet count were normal. The reticulocytes numbered less than one per cent. Bone marrow obtained by sternal aspiration was nondiagnostic. The icterus index was 20. The patient at this time was not hospitalized in our institution, but was seen in consultation by a member of our staff. The impression was "primary hemolytic anemia going into the aplastic stage." Multiple transfusions were administered.

From March 29, 1946 to November 4, 1947 the patient was seen at the Clinic at approximately 2 month intervals. Complete blood studies were done on each visit. There was a rather severe macrocytic anemia which gradually improved. The red blood cell count during this period rose from 1,880,000 per cu. mm. of blood to 3,080,000 with a rise in hemoglobin from 6.2 to 11 Gm. The volume index remained high, varying from 1.13 to 1.29. Intensive liver therapy caused no dramatic change. By March 1947 she felt well enough to resume her occupation despite a red blood cell count of 2,400,000

per cu. mm. and a hemoglobin level of 8 Gm. Because of her sense of well-being, the patient discontinued periodic check-ups after November 1947 and apparently remained in good health for more than a year and a half.

The patient next presented herself at the Clinic on July 5, 1949 complaining of black and blue spots on the feet and legs of one month's duration. During this period she had noted that she did not feel "up to par." Three weeks prior to admission she had suffered several bouts of cramping abdominal pain; one of the attacks was followed by the passage of several soft black stools. For one week she had experienced intermittent episodes of coldness, pallor, and numbness of the right index finger. Physical examination was essentially negative except for the presence of fading ecchymotic areas over both feet and legs.

Laboratory studies revealed no evidence of the previous anemia. The red blood cells numbered 4,460,000 per cu. mm.; hemoglobin 13 Gm.; blood cell volume 42 cc. per 100 cc. The volume index was 1.00, color index .90, and icterus index 4. The platelet count was 120,000, coagulation time (Lee and White) 8 minutes, bleeding time (Ivy) 7½ minutes, and prothrombin time 14 seconds (average normal value 14 seconds). Microscopic study of the bone marrow obtained by sternal aspiration was essentially normal except for the presence of an increased number of megakaryocytes and a decreased number of platelets. The white blood cell count was 8100 with a normal differential count. There were 3 per cent eosinophiles. The sedimentation rate was definitely elevated—1.88 mm. per minute. Serologic tests for syphilis, blood sugar level, gastric analysis, stool examination, chest x-ray and complete gastrointestinal series were negative.

The diagnosis at this time was mild idiopathic thrombocytopenic purpura.

Three weeks later, on July 27, 1949 the patient was admitted to the hospital because of intermittent fever which had been present for 2 weeks. She also complained of diffuse, transitory joint and muscle aching, 2 or 3 loose bowel movements daily, and increasing weakness. There had been a loss of 10 pounds in weight during the past 2 months. The temperature on admission was 101.3 F., the pulse 108 beats per minute, the blood pressure 135/75 mm. Hg. Physical examination revealed no abnormal findings except for a palpable and movable right kidney. Complete blood studies again were essentially normal except for a platelet count of 80,000 per cu. mm. and 7 per cent eosinophiles. Repeated blood and urine cultures were sterile. During the 10 days of hospitalization the evening temperature was consistently elevated to about 102 F. A trial of aureomycin therapy resulted in no improvement.

During the next few months after discharge from the hospital the patient's general condition improved, the fever gradually disappeared, and there was a weight gain of 5 pounds. In October 1949 the cramping abdominal pains returned and sudden exacerbation of the pain on October 5 resulted in rehospitalization. At this time the blood pressure was 155/90 mm. Hg. It was noted that the temporal arteries were tortuous, thickened and dilated. No definite nodules were present and the arteries were neither painful nor tender although pulsations in them were bothersome. Urinalysis on this occasion revealed a trace of albumin and numerous red blood cells in the centrifuged specimen. The total white blood cell count was not elevated but the differential count revealed 5 per cent eosinophiles.

A biopsy specimen of the thickened right temporal artery was obtained. Pathologic report by Dr. John B. Hazard noted the following: "Longitudinal section of the artery reveals areas of intimal thickening with foci of infiltration by polymorphonuclear leukocytes and areas of fibrinoid necrosis. Cross sections of the artery show the same type

of intimal thickening, fibrinoid necrosis, and occasional polymorphonuclear leukocytes. Diagnosis: Arteritis, acute. So-called periarteritis nodosa." (Figs. 1 and 2).

During the next few weeks the condition of the patient rapidly deteriorated. The blood pressure increased to a level of 180/120 mm. Hg., the pulse rate became more rapid—120 to 140 beats per minute, and a moderate fever of 100 F. to 101 F. persisted. Cardiac auscultation revealed protodiastolic gallop rhythm; cardiac enlargement was demonstrated by x-ray examination. Renal failure became evident and on November 2 the blood urea was 144 mg. per 100 cc.; creatinine 3.0 and plasma CO_2 24.5 vols. per cent. Terminally there was complete arterial occlusion of the right leg with incipient gangrene of the foot. There was severe cyanosis and coldness of the terminal phalanges of all fingers, and toes of the left foot. The patient died on November 4, 1949, 5 months after onset of the final illness. Permission for postmortem examination was refused.

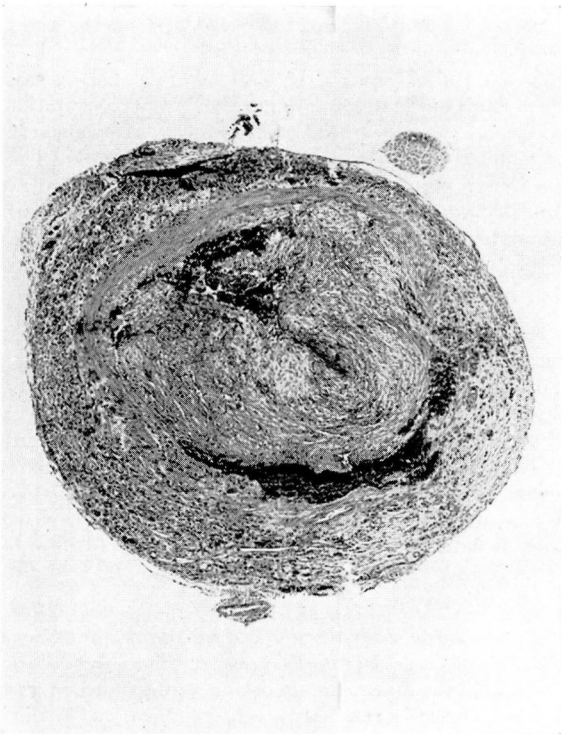

FIG. 1. Cross section temporal artery showing intimal thickening, medial necrosis with fibrinoid degeneration and hemorrhage, and polymorphonuclear infiltration (H. and E. x 50).

Comment

It should be emphasized that the anemia was extreme; the initial blood count being 700,000 red blood cells per cu. mm. with a hemoglobin of 3 Gm. Gradual improvement took place over a period of 1 year, at which time the patient considered herself to be in good health for an interval of 18 months.

The terminal illness was accompanied by purpura at the onset, but eventually showed all the cardinal clinical features of periarteritis nodosa and was proved by biopsy.

While the development of periarteritis nodosa after recovery from severe acquired hemolytic anemia could have been coincidental, it appears more likely that some underlying immunologic derangement might have been responsible. Dameshek has speculated that, in his patients in whom the diseases occurred concurrently, the administration of some medication such as penicillin, given in several courses, might result in hypersensitivity with the development (a) of the vascular allergy, periarteritis nodosa and (b) of an immunohemolytic mechanism, acquired hemolytic anemia. In our patient no such

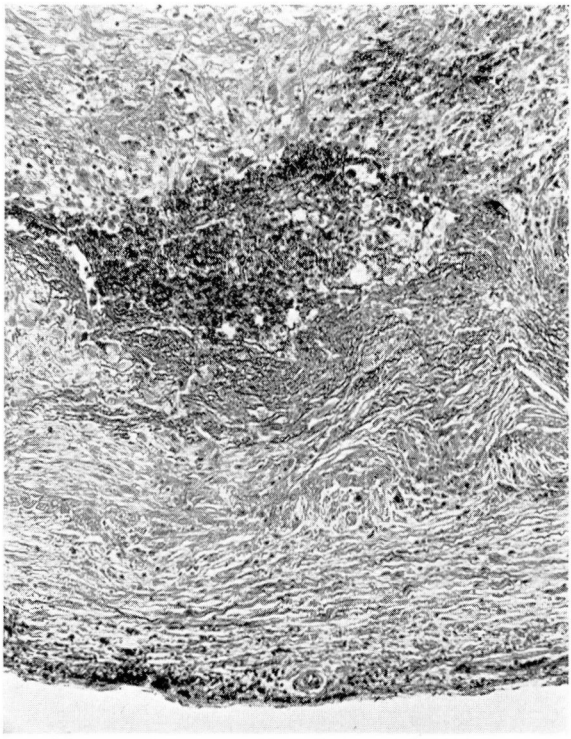

FIG. 2. Longitudinal section of temporal artery (H. and E. x 100).

definite relationship was evident. It is noteworthy that thrombocytopenic purpura occurred with the periarteritis nodosa rather than an exacerbation of the previous hemolytic anemia, as one might have expected.

Summary

Another instance of the association of acquired hemolytic anemia and periarteritis nodosa has been presented. In this case fatal periarteritis nodosa occurred 18 months after complete remission of the hemolytic anemia and was associated with thrombocytopenic purpura.

References

1. Rich, A. R.: Role of hypersensitivity in periarteritis nodosa. Bull. John Hopkins Hosp. **71**:123 (Sept.) 1942.
2. Dameshek, W. and Rosenthal, M. C.: Treatment of acquired hemolytic anemia with note on relationship of periarteritis nodosa to hemolytic anemia. M. Clin. North America p. 1423-1440 (Sept.) 1951.