CONCOMITANT INFECTIOUS MONONUCLEOSIS AND HEMOLYTIC ICTERUS

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This communication describes a case of hemolytic anemia occurring in the course of infectious mononucleosis. A careful review of the literature reveals no precisely similar case.

Dameshek reported an instance of hemolytic anemia in a patient with infectious mononucleosis who had been given sulfadiazine. The patient had cold hemagglutinins in his serum. Our case differs from that of Dameshek in that sulfonamide preparations had not been given, there was no preceding infection, and tests of the serum for cold agglutinins were negative. Ellis, Wollenman and Stetson described a case of acute hemolytic anemia in an illness resembling infectious mononucleosis. Their patient was unlike ours in that tests of the serum showed auto-hemagglutinins and hemolysins together with a positive Donath-Landsteiner reaction.

Case Report

A 22-year-old, white, single male was admitted to the Beth-El Hospital on September 30, 1946. He had been well until five weeks before his admission, when he noticed weakness, fatigue, and a "rust-colored" urine. Jaundice and fever appeared in the fourth week of illness. He was hospitalized following a fainting spell. As a child, he had experienced attacks of weakness followed by fainting spells. He underwent an appendectomy in 1943. Repeated bouts of furunculosis were successfully treated with penicillin while he was in Germany in 1945. No history referable to malaria or other hospital diseases was elicited.

On his admission the patient was slightly asthenic, with icteric skin and sclerae. The pharynx was injected, and small discrete lymph nodes were scattered throughout the neck. The spleen was palpable 4 cm. below the costal margin. Rectal temperature was 103 F. No other significant findings were noted.

Laboratory examinations on the morning following his admission were: hemoglobin, 4.3 grams (28 per cent); red blood corpuscles, 1.4 million, and 8,800 leukocytes per cu. mm. The differential count showed 70 per cent lymphocytes, 18 per cent segmented neutrophiles and 2 per cent staff neutrophiles. A few atypical lymphocytes characteristic of infectious mononucleosis were seen. About 25 per cent of the red blood corpuscles were spherocytic. A marked anisocytosis was present. Reticulocytes numbered 7 per cent. Five normoblasts per 100 W.B.C. were found on the blood smear. Platelets numbered 390,000 per cu. mm. Bleeding time, coagulation time, clot retraction time and prothrombin time were normal.

A sternal marrow aspiration revealed a granulocytic-erythrocytic ratio of 0:0. Megakaryocytes were normal in number, and the granulocytic elements were made up of 35 per cent myelocytes, 35 per cent segmented neutrophiles, 10 per cent metamyelocytes and 20 per cent staff neutrophiles.

The heterophile agglutination test was positive in a dilution of 1:512. The red blood corpuscle fragility test with hypotonic saline solutions showed initial hemolysis at 0.48 per cent, and complete hemolysis at 0.42 per cent. (With normal blood, hemolysis usually begins in the tube containing 0.44 or 0.42 per cent salt solution and is complete in the tube containing 0.34 per cent salt solution.) The urine was strongly positive for urobilinogen. Bile, hemosiderin and hemoglobin were absent from the urine.

Blood chemical examinations showed an icterus index of 15, a delayed van den Bergh reaction and a serum protein of 7.1 grams per cent. The albumin was 3.9 Gm. per cent and the globulin was 3.2 Gm. per cent. Serum total cholesterol was 100 mg. per cent and the cholesterol esters were 115 mg. per cent. The urea nitrogen, sugar and chlorides were normal. The cephalin flocculation test was 3 plus.

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The Kline test was negative. Blood cultures showed no organisms. Repeated fecal examinations failed to reveal any parasites or ova. No malarial parasites were found in the bone marrow and peripheral blood specimens. The patient was Rh positive and group 'O'. Agglutination tests for brucellosis, typhoid, paratyphoid A and B, and typhus fever were negative.

Roentgenologic examinations of long bones and chest were normal. The basal metabolic rate was plus 18. Fragility tests done on the blood of the patient's relatives were within normal limits and no cytologic abnormalities were found.

The patient was given 3500 cc. of blood during the first week of hospitalization. The hemoglobin rose to 5.5 Gm. (36 per cent) with a red blood cell count of 1.9 million. The other hematologic and biochemical examinations were relatively unchanged. The urinary urobilinogen reached a titer of 1:100.

Two weeks after admission, additional laboratory examinations were done: tests for cold agglutinins, for paroxysmal hemoglobinuria by Mackenzie's modification of the Donath-Landsteiner test, and for Marchiafava's disease by the Ham and Horack procedure were all uniformly negative. The heterophile agglutination test was positive in a dilution of 1:256. The Davidsohn exclusion test confirmed the diagnosis of infectious mononucleosis.

The clinical course during the ten weeks of hospitalization was uneventful. The temperature returned to normal on the twelfth day, after reaching a peak of 104 F. forty-eight hours after admission. The lymphadenopathy persisted. The spleen became barely palpable. A slight icteric tint to the skin was still perceptible on discharge.

Laboratory examinations carried out during the last week of hospitalization showed a hemoglobin of 9 grams (58 per cent) with a red blood cell count of 2.8 million. Leukocytes were 7000 per cu mm. of which 53 per cent were segmented neutrophiles, 4 per cent eosinophiles, 42 per cent lymphocytes and 2 per cent monocytes. No atypical lymphocytes were seen. A few macrocytes and an occasional spherocyte were seen on the stained blood smear. Reticulocytes were 3 per cent, and the platelets numbered 380,000 cu. mm. Sternal marrow showed a granulocytic-erythrocytic ratio of 60:40. Granulocytic series showed 20 per cent neutrophilic myelocytes, 10 per cent eosinophilic myelocytes, 12 per cent metamyelocytes, 15 per cent staff neutrophiles and 5 per cent eosinophiles. The icterus index was 17. Quantitative serum bilirubin was 0.8 mgs. per cent. The heterophile agglutination test was negative. The red blood cell fragility test had returned to normal. Initial hemolysis began at 0.44 per cent and was completed at 0.34 per cent. The urinary urobilinogen was positive in a dilution of 1:100.

There was nothing in the patient's history prior to the onset of the infectious mononucleosis to indicate a pre-existing hemolytic disease. The subject was not seen until eighteen months after discharge. He looked well, had no icterus, and the spleen was not palpable. Laboratory examinations at this time were: hemoglobin, 15.4 grams (100 per cent) red blood corpuscles, 4.6 million, and 6,000 leukocytes per cu. mm. The differential count showed 51 per cent segmented neutrophiles, 10 per cent staff neutrophiles, 33 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophiles. No pathologic cells were seen. Reticulocytes numbered 1.5 per cent, platelets 450,000/cu. mm. Bleeding and coagulation time were normal. The heterophile agglutination test was negative. The red blood corpuscle fragility test with hypotonic salt solution showed initial hemolysis at 0.44 per cent, and complete hemolysis at 0.34 per cent. Blood chemical examinations showed an icterus index of 4.3 units, a negative cephalin-cholesterol flocculation test and a zinc turbidity test of 6.2 units. Bile, hemoglobin and hemosiderin were absent from the urine. The urinary urobilinogen was within normal limits.

**COMMENT**

Following the report of the laboratory findings, it became apparent that the patient had hemolytic anemia and infectious mononucleosis concomitantly. The diagnosis of infectious mononucleosis was supported by the lymphocytosis with atypical lymphoid cells, the positive heterophile agglutination test, the lymphadenopathy and the splenomegaly. However the unusual findings were the presence of jaundice, anemia, an increased red blood cell fragility to hypotonic salt, spherocytosis, increased urinary urobilinogen and an erythroblastic marrow; i.e., the findings characteristic of hemolytic anemia. The occurrence of infectious mono-
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Infectious mononucleosis with jaundice has been previously described. Infectious hepatitis might be considered as a possible diagnosis but cases of infectious hepatitis almost invariably show an increased resistance to hypotonic saline. Paroxysmal nocturnal hemoglobinuria was ruled out by a negative Ham acid test. Reed and Helwig reported 300 cases of infectious mononucleosis of which 3 presented severe anemia, but the anemia was associated with a marked reduction of the white blood cells and platelets. The authors considered this pancytopenia to be part of the infectious mononucleosis.

Summary

Hemolytic anemia concomitant with infectious mononucleosis, was observed in a 22-year-old white male whose history indicates no pre-existing hemolytic disease. Recovery occurred spontaneously.

References

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