Urticaria Pigmentosa Complicated by Polycythemia Vera

Report of a Case

By JOSEPH H. DIAMOND and LUDWIG GROSS

UNTIL ABOUT 15 years ago an abnormal proliferation of tissue mast cells was observed only as a cutaneous manifestation. Described originally by Nettleship in 1869, this was named "urticaria pigmentosa" about 20 years later by Sangster. The natural course of this disease is highly variable, since the cutaneous manifestations represent only one stage of a systemic disease which may not only become generalized, but also initiate changes resulting from biochemical properties of the mast cells. This paper presents the second reported case of urticaria pigmentosa complicated by polycythemia vera in an adult.

CASE REPORT

A 62-year-old man entered the hospital because of sudden onset of painful swelling of right leg. Twenty-five years previously he had had acute glomerulonephritis. Seven years ago he developed a nonitching skin rash diagnosed by biopsy as urticaria pigmentosa. Five years ago a right inguinal herniotomy and the removal of an intradermal nevus of the neck had been done. At that time, the peripheral blood film was within normal limits. No history of other skin rashes or allergic disorders was obtained.

In the family history one sister had died of cancer, and one granddaughter developed urticaria pigmentosa soon after birth and still has it at age 5. On physical examination, numerous red-brown macules and slightly raised papules were found scattered on the trunk and extremities which, when scratched, produced an itching sensation and areas of erythematous halos. The liver and spleen were not enlarged. The right leg was cyanotic and cool distally from the knee and tender on deep palpation of the calf region.

The urine showed 2+ albumin and occasional granular casts/high power field in the sediment. WBC was 27,200/cu. mm. on admission, fluctuating between 16,000 and 26,000 on numerous occasions, with an average of 72 per cent neutrophils, relative lymphocytopenia, and definite monocytosis between 9 and 21 per cent. Hematocrit was 49 per cent; hemoglobin, 15.9 Gm.; platelets, 370,000/mm³; and reticulocyte count, 0.6 per cent. Bleeding, coagulation, and prothrombin times were normal. The differential bone marrow count from a marrow aspiration showed: normoblasts 10.8 per cent; lymphocytes 2.5 per cent; promyelocytes 1.5 per cent; myelocytes 19.5 per cent; metamyelocytes 11.8 per cent; nonsegmented granulocytes 26 per cent; segmented granulocytes 20.8 per cent; and unclassified cells 5.8 per cent. No mast cells were found in the bone marrow. The blood urea nitrogen was 10 mg. per cent/100 ml., and uric acid was 6 mg. per cent. Total protein was 6.6 Gm. with A:G ratio 1:8; serum electrophoresis revealed normal pattern.

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Fig. 1.—Oil immersion photomicrograph of biopsy of skin lesion showing mast cells with granules. (Original magnification ×1000)

SGOT 20 units; LDH 235 units; alkaline phosphatase 6.2 Bodansky units; and acid phosphatase 3 Bodansky units. Wasserman test result was negative. ECG was within normal limits. X-rays of chest, gallbladder, upper gastrointestinal tract, skeletal survey, and intravenous pyelogram, revealed no abnormalities. Barium enema showed diverticulitis of descending colon. Liver and spleen were of normal size on flat plate of the abdomen.

The patient was given parenteral heparin in a dosage of 75 mg. intravenously q. 6 hours for 10 days. There was gradual improvement but fatigue, poor appetite, loss of weight, and vague abdominal pains persisted.

Three months later peripheral blood was normal except for leukocytosis of 21,000—neutrophils 58 per cent, band 5 per cent, lymphocytes 35 per cent, monocytes 2 per cent. Platelets were increased and leukocyte alkaline phosphatase was 174.

Seven months later the hemoglobin was 21.7 Gm.; RBC 8,140,000; WBC 15,500—neutrophils 68 per cent, lymphocytes 12 per cent, monocytes 17 per cent, eosinophils 3 per cent. Hematocrit was 61 per cent; platelets 680,000/mm.³; and reticulocytes count 0.6 per cent. At this time the patient complained of extreme fatigue and vague abdominal pains. The physical examination was essentially unchanged, but there was a definite plethoric appearance to the skin. A diagnosis of polycythemia vera was made. He was treated with a total of 8 mc. of P³² intravenously; the first 2 injections were given one month apart, and the third was given 6 months later. This therapy resulted in disappearance of all symptoms during the next 4 months.

One year later the blood picture was normal except for relative monocytosis. The skin eruption remained unchanged and another biopsy of skin was consistent with urticaria pigmentosa (Fig. 1). A skeletal survey was normal.

Four months later the patient showed progressive increase in red and white cells again; however, the platelet count remained about 400,000/mm.³, and he had persistent monocytosis. A 24-hour urine collection for 5-hydroxyindole acetic acid was 13.5 mg. (upper limit of normal 11 mg.). Serum histamine level of blood was normal. Blood volume determined with labeled human albumin was 88 ml./Kg., with normal plasma volume. Clinically, the patient was asymptomatic.
URTICARIA PIGMENTOSA

DISCUSSION

Initially systemic mast cell disease and later a neoplastic disorder complicated by erythrocytosis were suspected. About 10 months later the picture of polycythemia vera was evident.

Review of a large series of cases of mast cell disorders and urticaria pigmentosa reveals that this disease is associated with a variable degree of anemia, leukocytosis, leukopenia, eosinophilia, thrombocytopenia, thrombocytosis and rarely with hemorrhagic tendencies. Also, well-documented cases of mastocytosis characterized by systemic hyperplasia of mast cells with infiltration of various organs—particularly the reticuloendothelial system, acute forms of mast cell leukemia, and a case of urticaria pigmentosa complicated by monocytic leukemia—have been reported. In the latter group the finding of large numbers of mast cells in the bone marrow was the early indication of systemic mast cell disease. In the only reported case of urticaria pigmentosa and polycythemia vera a scattered accumulation of mast cells in the bone marrow was demonstrated with Unna Pappenheim staining; otherwise the differential bone marrow count was normal with the exception of increased myelocytes (32.5 per cent).

It is also of interest and suggestive of a genetically transmitted factor that the granddaughter of the above patient was born with urticaria pigmentosa. Three cases suggestive of a genetic relationship have been reported.

The use of radioactive phosphorus appeared to have had no effect upon the multiplication of the mast cells in the skin; its effects on the polycythemia vera were well defined. In addition, it is to be noted that the functional properties of an increased mast cell proliferation—the production of heparin, 5-hydroxytryptamine, and histamine—were lacking in this case.

Until the etiology of urticaria pigmentosa and polycythemia vera are better understood, it is impossible to state definitely whether the association of these conditions is independent or concurrent. However, since the mastocytosis syndrome resembles the myeloproliferative disorders, and in view of the fact that this is the second reported case, this association may be more than a chance observation. The unitarian concept of the myeloproliferative disorders advocated by Dameshek permits the following speculative conjectures: The protean pathologic complications of a disease which usually starts as mast cell infiltration of the skin, and later involves other blood-forming cells by stimulation or depression of particular hematic cells, suggests a possible underlying specific stimulus which affects the multipotential reticulum cells. The active response may initially cause multiplication of mast cells and later proliferation of the entire erythroid series, leading to polycythemia vera.

SUMMARY

The coexistence of polycythemia vera with urticaria pigmentosa in a 62-year-old man is reported apparently for the second time. Review of literature indicates that mast cell disorder, manifested initially only in skin changes, may
involves many systems. The possible mechanism responsible for the occurrence of the two disorders in the same individual is discussed. Administration of radioactive phosphorus had no effect on the mast cell infiltration of the skin, but resulted in a temporary suppression of erythropoiesis.

**SUMMARIO IN INTERLINGUA**

Es reportate un caso—apparentemente le secunde in le litteratura—del coexistentia de polycythemia ver con urticaria pigmentose. Le patiente in question es un masculo de 62 annos de etate. Un revista del litteratura indica que un disordine mastocytic initialmente manifeste solo in anormalitates cutanea pote de facto afficer multe differente systemas. Es commentate le mechanismo possibilemente responsabile pro le occurrentia del duo disordes in le misme individuo. Le administration de phosphoro radioactive habeva nulle effecto super le infiltration cutanea per mastocytos sed resultava in un suppression temporari del erythropoiese.

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