Pyoderma gangrenosum associated with acute myeloproliferative disease (? erythroleukaemia)

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Summary

Pyoderma gangrenosum at the site of sternal marrow aspirate was observed in a patient with acute myeloproliferative disease characterized by a high peripheral blood basophilia. Lesions with a similar appearance were also seen on the palate. No other disease known to be associated with pyoderma gangrenosum could be demonstrated. A review of the literature suggests that myeloproliferative disease should now be recognized as occurring in association with pyoderma gangrenosum.

Introduction

Pyoderma gangrenosum is a rare skin disorder which typically takes the form of one or more plaques, each with an area of central necrosis delineated by a characteristic bluish-red border. Although most commonly reported (Domonkos, 1971) in association with ulcerative colitis and rheumatoid arthritis, pyoderma gangrenosum has also been noted in other clinical syndromes including acute and chronic myeloproliferative disease (Perry and Winkelmann, 1972; Shore, 1976; Cramers, 1976). The authors now describe a patient with an acute myeloproliferative disorder characterized by a pronounced and persistent peripheral blood basophilia and the occurrence of pyoderma gangrenosum initiated by sternal marrow puncture.

Case report

A previously healthy 53-year-old salesman gave a 12-month history of malaise, weight-loss, night sweats and recurrent respiratory tract infections. There was a family history of diabetes mellitus, his mother being a late-onset, insulin-dependent diabetic. Initial clinical examination revealed generalized pallor, hepatomegaly of 5 cm and a spleen just palpable at the costal margin.

The initial haemoglobin concentration was 10.1 g/dl, with a platelet count of $64 \times 10^9/l$, a white cell count of $12.4 \times 10^9/l$ (differential: 19% neutrophils, 20% lymphocytes, 10% monocytes, 19% eosinophils, 22% basophils, 4% myelocytes, 4% promyelocytes and 2% blast cells), a reticulocyte count of

6.5%, erythrocyte sedimentation rate of 15 mm/hour and additionally two nucleated red cells per 100 white cells were noted. The blood film showed basophilic stippling, neutrophil toxic granulation and pseudo-Pelgerization. The leucocyte alkaline phosphatase score was 19 (normal range 20-100). Sternal marrow aspirate, obtained with difficulty, showed megaloblastic erythropoiesis, an increase in promyelocytes and blast cells, numerous bizarre basophils, basophil precursors and ringed sideroblasts. Iliac crest trephine biopsy demonstrated hypercellularity with a prominence of blast cells and excess reticulin. The serum B_{12} was greater than 1000 ng/l (normal range 170-7000 ng/l) and the serum folate and Schilling test were normal.

Stools were repeatedly strongly positive to testing for faecal occult blood, but barium studies of the gastrointestinal tract were normal and no abnormality of haemostasis other than thrombocytopenia could be demonstrated. There was no evidence of haemolysis in that the direct and indirect antiglobulin tests were negative, there was no urinary haemosiderin, and the plasma haemoglobin, serum methaemalbumin and plasma haptoglobin were within normal limits.

Initial treatment was blood transfusion. In addition, in view of his symptoms and the presence of a strongly positive Mantoux test, a diagnosis of occult tuberculosis was considered and a trial of ethambutol and isoniazid begun. Although night sweats and malaise diminished, bacteriological confirmation of tuberculosis was never obtained despite culture of urine, sputum and marrow.

On follow-up, utilizing standard surgical techniques and thiomersal as a topical antiseptic, a repeat sternal marrow aspiration was attempted but was a dry tap. One week later a large, painful, red swelling developed in the skin at the site of aspiration. This lesion developed central necrosis and when the necrotic area was removed the ulcer had a cribriform base with a ragged bluish-red overhanging edge characteristic of pyoderma gangrenosum. This lesion slowly extended in size to

FIG. 1. This illustrates the initial lesion of pyoderma gangrenosum over the sternum, and lower left is the second lesion at early stage of development.

reach a diameter of 5 cm. Later a second painful swelling, identical in appearance to the first, developed near the first lesion (Fig. 1). Biopsy of this second area showed an infiltrate of lymphocytic cells in the epidermis and around the dermal blood vessels, while bacteriological studies revealed *Staphylococcus aureus* but no anaerobic organisms. The pyoderma gangrenosum responded rapidly to 60 mg prednisolone/day, but mild diabetes mellitus, controlled well by diet and chlorpropamide, developed.

On further investigation at this time the following results were negative or within the normal range: urea and electrolytes, liver function tests, calcium, phosphate, uric acid, serum proteins, protein electrophoresis, immunoglobulins, cryoglobulins, serum viscosity, anti-nuclear factor, LE cell preparation, rheumatoid arthritis latex test, ASO titre, VDRL flocculation test, TPHA test, prothrombin time ratio, PTTK, fibrinogen, fibrin degradation products ethanol gelation test, prothrombin consumption index, serum lysozyme, neutrophil function tests, skin antibody immunofluorescence tests and CH_{50} and C_4 levels, while the C_3 level was slightly elevated at 2.74 g/l (normal range 0.85–2.54 g/l).

The patient appeared to improve subjectively on the treatment previously outlined with an increase in his sense of well-being and reduction in night

sweats. His steroid dosage was gradually reduced to 10 mg/day, but he then developed two necrotic areas in the palate closely resembling the pyoderma gangrenosum present on his chest (Fig. 2). No significant bacterial infection could be demonstrated in these lesions.

He became more anaemic, requiring further blood transfusions which eventually totalled 34 units in the 4 months after presentation, and severely thrombocytopenic (platelet count $12 \times 10^9/\text{l}$), resulting in purpura and recurrent epistaxes. His total white blood count remained within normal limits, but the basophil count fluctuated markedly, reaching more than 40% of the total white cell count on several occasions. Myeloid precursors were invariably present in the peripheral blood count, but the blast cell count never exceeded 5%.

A trial of oxymetholone produced no clinical improvement or reduction in transfusion requirement, and eventually the patient died 4 months following his initial presentation. A post-mortem failed to reveal any known association of pyoderma gangrenosum. The marrow showed intense erythroid hyperplasia, normoblastic in type and negative to periodic acid-Schiff staining, with reduction in all other cell lines. Whilst no firm diagnosis could be reached the overall appearances were considered to be consistent with erythroleukaemia.

FIG. 2. This illustrates two large ulcerated areas on palate resembling pyoderma gangrenosum.

Discussion

Pyoderma gangrenosum has been reported in association with ulcerative colitis, rheumatoid arthritis, regional ileitis, dermatitis herpetiformis, hypogammaglobulinaemia, paraproteinaemia and myeloma (Domonkos, 1971). Other associations include active chronic hepatitis (Byrne, Hewitt and Summerly, 1976), immunosuppression (Haim *et al.*, 1973) and disseminated intravascular coagulation (Staughton and Copeman, 1976). Alterations of cellular immunity have also been noted (Shore, 1976). Pyoderma gangrenosum has occurred in a case of acute lymphoblastic leukaemia maintained in remission by prednisolone, methotrexate and 6-mercaptopurine, whilst non-specific leukaemia has occurred following 6-mercaptopurine, for pre-existing pyoderma gangrenosum (Shore, 1976).

There have been a number of reports in the literature of this rare skin condition occurring in association with myeloproliferative diseases, including acute myeloblastic leukaemia, myelofibrosis, chronic myeloid leukaemia, polycythaemia rubra vera and acute myelomonocytic leukaemia (Perry and Winkelmann, 1972; Shore, 1976; Cramers, 1976). Few of these reports, however, were fully documented and the authors were fortunate in being able to investigate their patient extensively. Nevertheless, no definitive haematological diagnosis was possible but the initial marrow findings together with the abnormal peripheral blood, the rapid progression of the disease and the post-mortem findings suggest

that the disorder could be classified within the myeloproliferative spectrum as defined by Gunz and Baikie (1974), and was acute in type. A peculiar feature was the persistent peripheral blood basophilia. Whether the pyoderma gangrenosum and the basophilia were causally related is open to speculation.

Finally, accepting the fact that there is no satisfactory means of causally linking the skin lesions and the underlying haematological disorder, the nature of the pyoderma gangrenosum in this case was unusual in two respects. The primary lesion developed on the site of a recent sternal marrow puncture suggesting that direct trauma by some unknown means precipitated the epidermal necrosis. Secondly, the patient had lesions resembling pyoderma gangrenosum on the palate, a site of involvement which has rarely, if ever, been implicated.

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