Haemorrhagic Thrombocythaemia Treated with Radioactive Phosphorus

In recent years a few scattered reports have appeared of a rare type of haemorrhagic disease first defined by Epstein and Goedel (1934) under the broadly descriptive name of "haemorrhagic thrombocythaemia." Fuller criteria for the diagnosis were laid down by Reid (1940)—namely, "a tendency to haemorrhage and thrombosis associated with arteriosclerosis, great increase in the number of circulating blood platelets, moderate leucocytosis, polychromasia, anisocytosis and poikilocytosis with or without anaemia, and a great increase in the number of megakaryocytes in the marrow."

The following case would appear to fit into this group and is, so far as we can ascertain, the first to be treated with radioactive phosphorus.

CASE REPORT

The patient, a single woman aged 54, had worked for nineteen years as a Post Office clerk. When first seen in April, 1952, she gave a five years' history of fatigue, listlessness, loss of weight, recurrent epistaxis, frontal headache with exacerbations of a migrainous type, and increasing dyspnoea on exertion; more recently there had been some oedema of the ankles.

During this period she had noticed recurring spontaneous bruising of the skin over the trunk and limbs. The bruises had occurred in crops, each appearing as a subcutaneous lump developing within a few hours and followed by a spreading ecchymosis. Recently the lesions had been more numerous and larger, the bruising affecting areas of several square inches. In addition there had been vaginal bleeding after two years' absence of such loss.

When first seen her general condition was fair; clinical anaemia, superficial glossitis, and mild koilonychia were present; and the spleen and liver were just palpable. There was no peripheral arteriosclerotic change of note but the fundi showed grade 1 changes and the blood pressure was 190/115. The heart was normal, there were no abnormalities in any other system and no skin lesions at this time. A blood count showed a chronic iron-deficiency anaemia (M.C.V., 73 cubic μ ; M.C.H.C., 24%; P.C.V., 36%; haemoglobin, 58%; R.B.C., 4,900,000; W.B.C., 10,800). The blood film showed marked hypochromia with anisocytosis and poikilocytosis; target cells were present. A fractional test meal showed a normal secretion of free acid. There was no history of dyspepsia; the barium meal revealed an irritable duodenal cap, but no ulcer was seen; and the tests for faecal occult blood were negative. Examination of the nasal mucosa revealed no source of bleeding.

A course of oral iron and stilboestrol (the latter given because it was thought some of her symptoms were menopausal) produced no symptomatic improvement. Further blood counts revealed that we were dealing with an unusual disturbance. There was a period of polycythaemia during which the striking feature was the number of circulating platelets in the blood, figures up to 2,400,000 being obtained. Her facies became rather plethoric and a series of local haemorrhagic lesions appeared in the skin of the upper and lower limbs. These appeared each within a matter of a few hours as a central pale nodule 1–2 cm. in diameter, with ecchymosis spreading into the surrounding skin over a wide area. The lesions resolved within about a fortnight.

There was now more obvious enlargement of the spleen, the lower edge being palpable two fingerbreadths below the left costal margin.

Sternal Marrow (August 23, 1952).—An extremely cellular marrow showed excessive activity in erythropoiesis and leucopoiesis. The most striking feature, however, was the proliferation of the abnormal forms of megakaryocytes, many of which had bizarre nuclear forms. An occasional megakaryoblast was seen. There was a relative increase in the number of promyelocytes, but not of myeloblasts. Erythropoiesis was normoblastic and erythroblasts were frequent.

A blood count prior to treatment showed R.B.C., 5,100,000; W.B.C., 9,500; platelets, 1,208,000; bleeding time, 2 minutes; clotting time, 3 minutes. On September 8 she was given 4.5 millicuries of ^{32}P intravenously without ill effect. There resulted a rapid fall in the peripheral platelet count, the figure after six weeks being normal. The white-cell count fell somewhat but the red-cell count was little affected. There was a definite reduction in the occurrence of the skin lesions, only a few small ones appearing on the lower limbs, and first the spleen and then the liver became impalpable. Her general condition improved and she complained less of fatigue.

Six months after the first treatment her platelet count showed a tendency to rise (haemoglobin, 103%; W.B.C., 11,000; platelets, 466,000; bleeding time, 1 minute; clotting time, 4 minutes), she did not feel so well, and was still having occasional skin haemorrhages. A second dose of ^{32}P (4 millicuries intravenously) was given on May 28, 1953. Again there was a symptomatic improvement and skin haemorrhages became very infrequent.

Sternal Marrow (December 14, 1953).—The marrow was of average cellularity. The hyperplasia observed in the previous marrow film was no longer present. The megakaryocytes showed no significant proliferation and no megakaryoblasts were seen. Erythropoiesis and leucopoiesis were normal.

A third dose of ^{32}P (5.1 millicuries intravenously) was given on March 18, 1954, for a further mild relapse. Since that time she has remained in reasonably good health with only occasional headache and fatigue. Skin ecchymoses appeared only rarely and were very small. She carried on work without difficulty. The most recent blood examination (November 5, 1954) showed a normal count: R.B.C., 4,210,000; haemoglobin, 96%; platelets, 280,000. She has been on iron therapy by mouth for several months.

COMMENT

Some 14 cases of haemorrhagic thrombocythaemia are described in the literature, but in four the pathological conditions suggested that they were of secondary origin. The remaining 10 had most of the features required by Reid in his definition of the condition. Of these, four showed a high red-cell count at some stage—for example, in the patient described by Mortensen (1948) a count of 9,800,000 was noted, whilst in three others (Uotila, 1938; Lebel, 1947; Rowlands and Vaizey, 1938) the count was over 7,000,000.

There would, however, seem to be some significant differences between this condition and polycythaemia vera. The development of a transient anaemia in the absence of haemorrhage, though not invariable, is in contrast to the findings in polycythaemia. Also haemorrhage is invariable in the type of case described, whilst Lawrence *et al.* (1953) found that only 14 out of 159 cases of polycythaemia vera gave a history of bleeding. This bleeding tendency could clearly be related to the excess of, or abnormality in, the platelets in the blood, which is a reflection of the abnormal changes in the marrow. Nevertheless it must be noted that platelet changes occur in polycythaemia, Dameshek and Henstell (1940) describing such a case with a platelet count of 6,000,000.

The exact status of haemorrhagic thrombocythaemia in the "myeloproliferative syndrome" must, we consider, remain in doubt, but its response to ^{32}P suggests to us that at least it is closely related to polycythaemia vera.

J. C. WOODROW, M.B., M.R.C.P.,
Medical Registrar, David Lewis Northern Hospital, Liverpool.

S. COPE, M.D., M.R.C.P.,
Senior Medical Registrar, Royal Southern Hospital, Liverpool.

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