Thrombocytopenic purpura as the sole manifestation of a recurrence of Hodgkin's disease

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SYNOPSIS A man with apparently quiescent Hodgkin's disease presented with acute severe isolated thrombocytopenic purpura. Splenectomy revealed macroscopic involvement with Hodgkin's tissue and cured the thrombocytopenia.

In the absence of marrow involvement by disease, or depression by drugs, the platelet count in Hodgkin's disease, if disturbed, has generally been found to be increased (Hoster, Dratman, Craver, and Rolnick, 1948). Indeed, a raised platelet count may be a useful indicator of the disease activity, particularly in the absence of any external evidence of the disease process (Barry, Laroche, and Del, 1966). Thrombocytopenia, however, without any other depression of haematopoietic elements is distinctly rare, and it may thus be of some interest to detail a case of apparent idiopathic thrombocytopenic purpura which proved the only herald of a relapse of Hodgkin's disease.

Case Report

R.C., a 23-year-old Orcadian male, presented in September 1968 with six weeks' asthenia and anorexia. He had noticed for six months a progressively enlarging, painless mass in the right axilla. There was no pyrexia, nor other lymphadenopathy, and a chest radiograph was normal. The haemoglobin was 12.7 g/100 ml, WBC 5800/cmm, platelets 299 000/cmm. Biopsy of the lump showed it to be matted lymph nodes. The axilla was partly cleared and five lymph nodes weighing 80 g were removed. Histologically, the lymph nodes were completely replaced with a mixed cellular infiltrate of eosinophils, plasma cells, and many Reed Sternberg cells; fibrosis was scanty. There was invasion of the capsule of two nodes. The diagnosis was Hodgkin's disease of mixed cellularity. He was treated with radiotherapy, receiving 3000 R central dose to the right axilla over two weeks.

He returned to his employment as a lorry driver, well and free of evidence of disease. One year later, a 1.5 cm mobile, soft lymph node was noted in the

right supraclavicular region, but was not thought of significance. In August 1970, some two years after initial presentation, there was sudden enlargement of the right supraclavicular nodes, associated with a soft indefinite swelling infraclavicularly. A chest radiograph was again normal. Cobalt telotherapy (3000 R in a fortnight) cleared the swellings and he remained well without lymphadenopathy.

In October 1971 he presented with one day's haematuria, petechiae over the shoulders, arms, and inside the mouth. For 10 days previously, he had received ampicillin for a slightly sore throat, which was almost certainly due to petechiae of the buccal mucosa and tongue. In the previous fortnight he had noted slight itch but had suffered no chills, night sweats nor weight loss. Up to one month before admission he had been exposed to petrol and refrigeration plant fumes. Examination revealed no abnormality but the petechiae and a few tiny nodes in both cervical and axillary regions.

Haemoglobin was 13.6 g/100 ml, white count 6000/cmm, platelets 3000/cmm, bleeding time (Duke's method) 30 minutes. Serum electrolytes, bilirubin, alkaline phosphatase, protein electrophoresis, and liver function tests were all within normal limits. Blood group was O Rhesus positive, a direct antiglobulin test was negative and no cold autoagglutinins were detected. Platelet and leucocytes agglutinins were absent, indirect antiglobulin consumption and complement-fixation tests for incomplete platelet antibodies were all negative. The leucocyte alkaline phosphatase score was low normal, and the antinuclear factor was negative. A chest radiograph, and radiographs of thoracic and lumbar spine and pelvis were all normal.

He was treated with immediate corticosteroid therapy; hydrocortisone 100 mg intravenously and then prednisolone 60 mg orally daily. There was no haematological improvement and eight days later he

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suffered epistaxis and a significant bleed into his right elbow; ACTH, 40 units im daily, was added but with no improvement, and after a week, azathioprine 175 mg daily was introduced and the steroids slightly reduced to prednisolone 40 mg daily and ACTH 40 units im on alternate days. Sternal marrow aspiration immediately before the introduction of the azathioprine showed a highly cellular marrow with normoblastic and moderately hyperplastic erythropoiesis and normal white cell precursors. Megakaryocytes were markedly hyperplastic, many granular, some promegakaryocytes, and none producing platelets. There was no evidence of Hodgkin's disease in the marrow. Three days after commencing azathioprine he suffered an epistaxis and had four days of melaena requiring 4 units of red cell concentrate. With failure to obtain any significant haematological improvement after 30 days' steroids and 16 days' azathioprine and with increasing problems with oropharyngeal moniliasis and follicular pustular acne, splenectomy was recommended and performed under cover of platelet concentrate transfusions in late November 1971.

At laparotomy a slightly enlarged and macroscopically normal spleen was found weighing 195 g. Two fleshy white lymph nodes, 2 cm in diameter, were noted at the splenic hilum. No paraaortic nodes were found. Liver biopsy was undertaken. Haemorrhage was not a troublesome feature of the operation.

The spleen was studded with 1 cm white nodules throughout the red pulp. Histologically, the nodules were made up of Hodgkin's tissue of very similar appearance to the initial lymph node biopsies, with a very mixed cellular infiltrate. One of the splenic lymph nodes was completely replaced by Hodgkin's tissue, the other partly replaced. The liver biopsy was entirely normal.

The postoperative course was uneventful and within five days of splenectomy the platelet count had risen to 700 000/cmm. He has subsequently remained well apart from a superficial thrombophlebitis of the left arm postoperatively. He is currently being treated with cyclical courses of quadruple chemotherapy: mustine, vinblastine, procarbazine and prednisolone. There is no detectable lymphadenopathy, the chest radiograph remains normal and his ESR is only 6 mm/hour (Westergen). The platelet count varies between 200 000/cmm and 400 000/cmm.

Discussion

Splenectomy in this patient was not undertaken in search of Hodgkin's tissue but was performed as a life-saving procedure when steroids, ACTH,

and immunosuppressive therapy had produced no remission of the thrombocytopenia. It is becoming widely appreciated, however, that the certain detection of Hodgkin's infiltration of the spleen or upper abdominal lymph nodes clinically or radiologically is not possible (Rosenberg, 1971). Nevertheless the abdominal involvement in this man was not surprising, for there was previous clinical involvement of supraclavicular nodes in histologically proven 'mixed cellularity' Hodgkin's disease, features known to predispose to subdiaphragmatic extension of the disease (Peters, 1971). Also, the radiation dosage and fields were smaller than the standard radiotherapy techniques now employed (Kaplan, 1966).

While autoimmune thrombocytopenic purpura is readily recognized as complicating the course of chronic lymphatic leukaemia (Ebbe, Wittels, and Dameshek, 1962) and lymphomas (Harrington, Minnich, and Arimura, 1956), isolated thrombocytopenia of this type is a distinct rarity in Hodgkin's disease. Only 10 cases have been reported and these as brief mentions in surgical series (Perlman and Fox, 1941; Williams, Andrews, and Zanes, 1951; Reinhard and Loeb, 1955; Rousselot, Rella, and Rottino, 1962). The only fully described case of thrombocytopenic purpura in Hodgkin's disease (Gledhill and Shillitoe, 1952) seems to belong to the group of cases associated with gross splenomegaly and pancytopenia, recently reviewed by Lowenbraun, Ramsey, and Serpick, 1971). This paucity of cases of isolated thrombocytopenic purpura in Hodgkin's disease is presumably a reflection of the much less common tendency to antibody formation in this disorder than in the lymphoproliferative diseases. Perhaps there is a difference in balance between cellular immunity to platelets and the serum factor which blocks delayed-type hypersensitivity (Clancy, 1972) in the two groups of diseases. In this case no antiplatelet antibodies were detected *in vitro* but the platelet count recovered after splenectomy in the manner of a true 'idiopathic' thrombocytopenic purpura and there has been no recurrence of the thrombocytopenia.

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