ACUTE MYELOFIBROSIS (MYELOSCLEROSIS) PRESENTING AS A CASE OF SEVERE THROMBOCYTOPENIC PURPURA

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SYNOPSIS

Acute myelofibrosis, a variant of classical myelofibrosis (agnogenic myeloid metaplasia) is an accelerated form of myeloproliferative disorder, characterized by the absence of splenomegaly, marrow hyperproliferation with fibrosis and a rapidly fatal clinical course. We present a young woman with this rare disorder who responded favourably to therapy with prednisolone and vincristine.

INTRODUCTION

Myelofibrosis classically is associated with the triad of hepatosplenomegaly, a leucoerythroblastic anemia with tear-drop shaped red blood cells and bone marrow fibrosis (1), (2). In recent years a variant of this classical entity has been described (3), (4), (5), (6). This variant, acute myelofibrosis (myelosclerosis), differs from the classical form in the absence of splenomegaly. It is characterized by hyperproliferation of all three marrow cell lines, associated with sufficient fibrosis to preclude marrow aspiration and a rapidly progressive and fatal clinical course.

CASE REPORT

A twenty-seven year old housewife was admitted to the University Department of Medicine, Singapore General Hospital on 11 May 1980 with multiple bruises and bleeding gums for four days. There was no antecedent illness and she had previously been healthy. There was no drug or marrow toxin exposure.

On examination she was afebrile and extremely pale. The extremities were covered with petechiae and multiple ecchymoses. The gums were bleeding and multiple hemorrhages were noted in both fundi. The liver, spleen and lymph nodes were not enlarged. The possible diagnoses considered included aplastic anemia, acute leukaemia and idiopathic thrombocytopenic purpura (ITP).

The hemoglobin was 3.6 gm/dl. The reticulocyte count was 5%. The total white cell count was 12,000/cu mm with a marked shift to the left (11% myelocytes and 3% metamyelocytes) but no blast cells were present. Thus the possibilities of aplastic anemia and acute leukaemia were excluded by the reticulocyte count and the white cell differential respectively. The platelet count was

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5,000/cu mm. The peripheral blood film revealed the presence of nucleated red blood cells (10 NRBC/100 WBC). The low platelet count was expected in view of the hemorrhagic manifestations. The leucoerythroblastic changes (presence of myelocytes, metamyelocytes and nucleated red blood cells) in the peripheral blood film are evidence against the diagnosis of ITP. Such intense leucoerythroblastic changes are classically encountered in marrow fibrosis or in marrow infiltration by metastatic carcinoma. Repeated attempts at bone marrow aspiration were "dry". The marrow biopsy revealed a hypercellular marrow with hyperproliferation of all three cell lines and the presence of fibrosis. Other investigations included a modestly elevated erythrocyte sedimentation rate (35 mm/hour) due to the severe anemia, negative lupus erythematosus (LE) cell preparations on three occasions, normal coagulation tests (Prothrombin time, Partial thromboplastin time and Thrombin time), negative direct Coomb's test, normal levels of serum folate (4.4 ug/l) and vitamin B_{12} (300 ng/l), an elevated leucocyte alkaline phosphatase (LAP) score (110 against the control of 50) and microscopic hematuria. Special investigations excluded the presence of a platelet antibody.

The gingival bleeding persisted till 22 May 1980 and microscopic hematuria till 10 June 1980. The patient received packed cell transfusions to correct her anemia, platelet concentrates (obtained from single donors placed on the cell separator), prednisolone (60 mg daily) and vincristine (2 mg i.v. weekly). The platelet count started to rise twenty-three days after commencement of prednisolone therapy. As the platelet count returned to normal, vincristine was discontinued and the dose of prednisolone was gradually reduced (Fig. 1). A repeat bone marrow aspiration at seven weeks was successful on first attempt. Both the marrow aspirate and repeat biopsy showed a hyperproliferative marrow but without the presence of fibrosis.

In the subsequent eleven months it became apparent that the patient was dependent on steroid therapy to maintain an optimal level of platelets.

DISCUSSION

Acute or malignant myelofibrosis was first described in 1963 by Lewis and Szur (3). It is a rare and rapidly fatal variant of the classical, more chronic entity namely, agnogenic myeloid metaplasia (myelofibrosis). Subsequent reports confirmed the aggressive clinical behaviour of this disorder and its unresponsiveness to antileukemic therapy (4), (5), (6). It is important to differentiate between the variant and the classical form as the median survival for classical myelofibrosis is five years (7) whereas that of the acute variant is several months (5).

Nabil et al (6) described 2 cases of acute myelofibrosis following cytotoxic chemotherapy. This association was not encountered by Fabich et al (4) and Bearman et al (5). Lubin (8) considers acute myelofibrosis as an acute myeloproliferative disorder with

FIGURE 1. THE PLATELET RESPONSE TO PREDNISOLONE AND VINCRISTINE IN A YOUNG WONAN WITH ACUTE MYELOFIBROSIS.

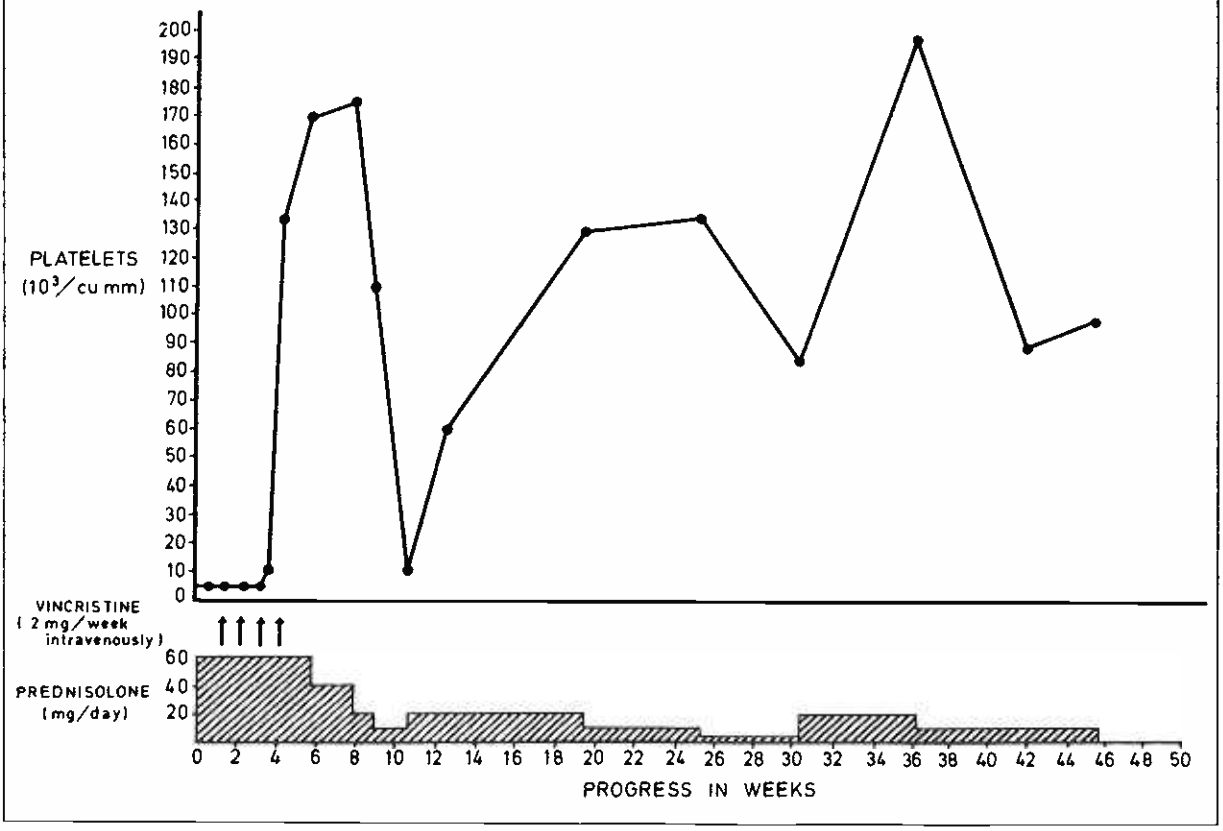

Figure 1. The platelet response to prednisolone and vincristine in a young woman with acute myelofibrosis

mixed features of myeloid metaplasia and acute myelogenous leukemia. It has been suggested (9) that myelofibrosis is due to a disordered proliferation of marrow stem cell caused by an abnormal stimulus which is also responsible for the fibrosis.

The therapy of acute myelofibrosis is uniformly unsuccessful. Prednisolone alone or in combination with antileukemic agents (vincristine and cytosine arabinoside) failed to achieve a control of the disease. Patients all died within nine months of the diagnosis from either septicemia or pneumonia (5).

Our patient fulfilled the criteria for the diagnosis of acute myelofibrosis. She is unusual, however, in two significant aspects. Firstly her response to prednisolone and vincristine has been remarkably favourable. At eleven months from the diagnosis, she remains free of bleeding and infectious complications. Secondly the marrow fibrosis disappeared following prednisolone and vincristine therapy. None of the reported cases in the literature had a repeat bone marrow examination presumably because there was no indication for repeating it as the fibrotic component was regarded as irreversible. Despite the disappearance of the fibrosis, the marrow was not normal and the patient requires ongoing prednisolone treatment. However at 10 mg daily she manifests few adverse side effects of prednisolone therapy apart from cushingoid changes.

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