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Response of thrombotic thrombocytopenic purpura to chlorpromazine

Thrombotic thrombocytopenic purpura is a rare disorder characterised by haemolytic anaemia, thrombocytopenia, neuropsychiatric disturbances, and hyaline arteriolar occlusions.[1] It was previously associated with high mortality,[2] but repeated plasma exchange has improved the prognosis.[3] We describe a patient in whom chlorpromazine appeared to produce complete and sustained remission of the disease.

Case report

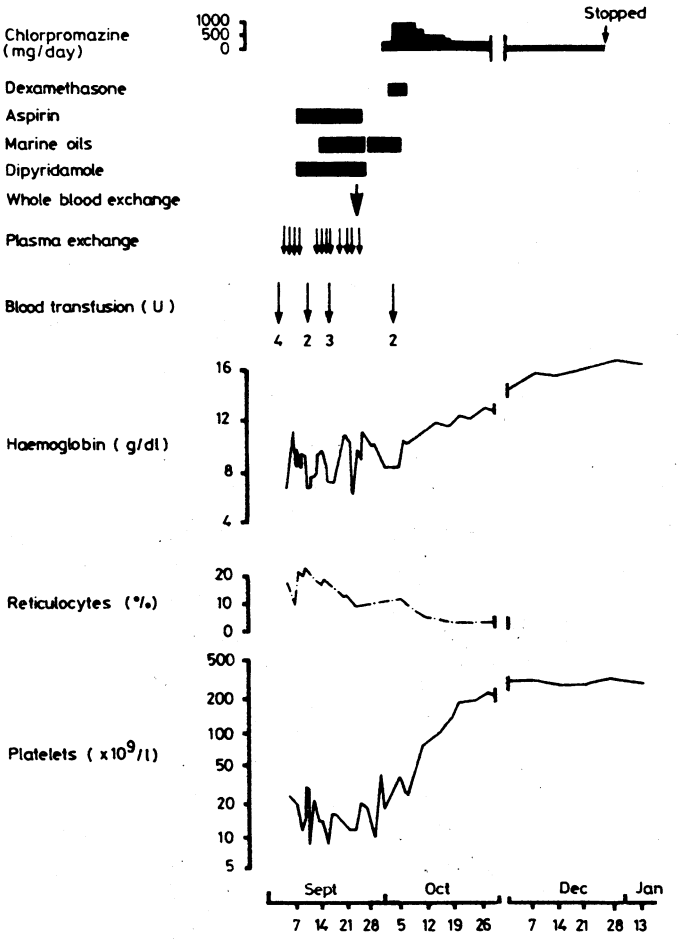
A 50-year-old industrial engineer had a two-month history of increasing lethargy, malaise, and anorexia and a two-week history of fever and painless haematuria. On admission to hospital he was confused and showed clinical anaemia, icterus, and a petechial rash. Haemoglobin concentration was 6·4 g/dl, platelet count 40×10^9/l, and reticulocyte count 5% (figure). A blood film showed polychromasia, anisopoikilocytosis, microspherocytosis, and red-cell fragmentation. Coagulation studies were mildly abnormal, with prothrombin time 17·5 s (control 15 s), activated partial thromboplastin time 48 s (control 35 s), and thrombin time 28 s (control 25 s) and the titre of fibrin and fibrinogen degradation products 1/16 (normal $\leq$1/8). A direct Coombs test and Ham's test yielded negative results. Free haemoglobin was present in the urine. Bone-marrow cytology showed hyperplasia of all circulating cell precursors. Blood cultures showed no growth. Thrombotic thrombocytopenic purpura was diagnosed.

He rapidly became comatose with severe cerebral irritation. Intensive treatment by repeated plasma exchange produced considerable but temporary benefit with normal conscious level and slight but transient improvement in circulating platelet concentrations. Intermittent red-cell transfusions were required for anaemia. Two grand mal seizures were treated by intravenous diazepam, and prophylactic phenytoin was given. No clinical or haematological improvement followed treatment with dexamethasone, marine oils (Maxepa; British Cod Liver Oils, Hull), low-dose aspirin, or dipyridamole.

Six weeks after admission he again became confused and showed amnesia, paranoia, sexual disinhibition, and visual and persecutory auditory hallucinations. An acute organic confusional state was diagnosed and high-dose (1 g daily) chlorpromazine prescribed, with rapid and permanent improvement in his mental state. Serial blood counts showed a sustained improvement in haemoglobin concentration and platelet counts and a reciprocal diminution of reticulocytosis. After two weeks' treatment with chlorpromazine the platelet count became normal ($>150 \times 10^9$/l) and after a further four weeks the haemoglobin concentration was greater than 14 g/dl. The chlorpromazine was gradually withdrawn and relapse did not occur.

Comment

The start of a course of chlorpromazine corresponded in our patient with the onset of eventual total remission of thrombotic thrombocytopenic purpura. We believe that this represents a true response of this unpredictable disease to the drug but recognise that it might have been fortuitous and due to a spontaneous remission. We had no opportunity for re-evaluating the effect of chlorpromazine as our patient remained in complete remission.



Time relation of changes in haematological variables to administration of oral chlorpromazine and other treatment.

The pharmacological properties of chlorpromazine lend weight to our argument that this was a true drug-related response of the disease. Chlorpromazine is a cell-membrane stabiliser that is antihaemolytic in vitro at concentrations that are found therapeutically,[4] and it also diminishes the haemolysis produced by shear stress at pressures similar to those found in arterioles.[5] The hyaline arteriolar lesions of thrombotic thrombocytopenic purpura[1] might represent the cause or effect of haemolysis at sites of high shear stress. Chlorpromazine may prevent haemolysis with its consequent liberation of adenosine diphosphate, which is a powerful platelet-aggregating agent.[5] This might be the underlying mechanism of the thrombocytopenia. We suggest that chlorpromazine should be evaluated as soon as possible in further cases of thrombotic thrombocytopenic purpura.

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