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SHORT REPORT

Thrombotic thrombocytopenic purpura-like syndrome in the absence of schistocytes

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Summary. Thrombotic thrombocytopenic purpura is an uncommon disorder that if left untreated has a very high mortality. Schistocytes are generally considered essential for the diagnosis. A patient is presented with a thrombotic thrombocytopenic purpura-like syndrome in whom schistocytes were persistently absent and who responded to plasmapheresis.

Keywords: thrombotic thrombocytopenic purpura, platelets, schistocytes.

A 33-year-old female was admitted to our unit with a 3 h history of drowsiness, confusion, and pyrexia of 39·5°C. She was known to suffer from Darier's disease (keratosis follicularis) for which she had never received treatment. There was an ecchymosis (6 cm in diameter) on the left thigh. The haemoglobin concentration on admission was 5·0 g/dl, platelet count 24×10^9/l and white-cell count $16{\cdot}9 \times 10^9$/l with 87% neutrophils. The reticulocyte count was 29% and the blood picture showed marked polychromasia and occasional nucleated erythrocytes; schistocytes were persistently absent. Bone marrow aspirate revealed increased erythropoiesis and normal megakaryocytes with no foreign cells. Serum bilirubin was 40·2 μmol/l (reference range 0–17 μmol/l), whilst liver transaminases, serum B_{12} and ferritin were normal. Haemoglobinuria was present; Coombs and Ham's tests were negative. There had been no previous exposure to drugs or other chemicals.

The patient's level of consciousness continued to deteriorate; 5 h after admission she was deeply unconscious and not responding to any external stimuli (3 on the Glasgow scale). She had recurrent generalized tonic-clonic seizures which persisted after correction of the anaemia by transfusion. CT scan of the brain was normal; anti-nuclear (hep 2) and rheumatoid factors were negative. Renal function remained normal throughout her illness, with serum creatinine in the 50–60 μmol/l range. There was no evidence of consumptive coagulopathy at any stage: prothrombin time (INR), thromboplastin time, and serum fibrinogen were normal; fibrin degradation products were absent. Serum complement (C3 and C4) was normal.

Plasmapheresis with replacement using fresh frozen plasma was instituted; a single intravenous dose (250 mg) of methylprednisolone was given and the patient improved dramatically. She was fully conscious after the third plasmapheresis; return of haematological parameters to normal required eight sessions (2·5 litres replacement each). Erythrocyte G6P-DH level during remission was normal. There has been no recurrence after 30 months of follow-up, with reticulocyte counts, serum lactate dehydrogenase, and platelet counts remaining normal during this period. Antinuclear factor and Coombs test have remained negative.

Thrombotic thrombocytopenic purpura (TTP) is an uncommon disorder that if untreated has a very high mortality (Amorosi & Ultmann, 1966). As therapy is effective in most cases (Bell *et al*, 1991), early diagnosis and aggressive management is required. Diagnosis is easy when the classic pentad of fever, thrombocytopenia, microangiopathic (schistocytic) haemolytic anaemia, neurological manifestations, and renal failure is present.

However, cases in whom some of these features do not occur, or occur late, have become increasingly recognized (Murphy *et al*, 1992). It has been proposed that TTP should be redefined as a syndrome of thrombocytopenia and schistocytic haemolytic anaemia is absence of other possible causes of these abnormalities (Murphy *et al*, 1992; Rock *et al*, 1991).

We describe a case of TTP-like syndrome with the presence of thrombocytopenia, Coombs-negative intravascular haemolytic anaemia and neurological manifestations (loss of consciousness and fits). Schistocytes were persistently absent from the peripheral blood film. There was a dramatic response to plasmapheresis.

We suggest that the presence of schistocytes should not be considered essential for the diagnosis of TTP-related disorders. If there is a suggestive clinical picture, and other

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possible causes excluded, plasmapheresis should be seriously considered as a life-saving procedure.

The explanation for the absence of schistocytes in our case is unclear. It is possible that the condition was treated early in its course before the finding of schistocytes became evident. However, we feel that this is unlikely because of the features of established haemolysis at presentation (reticulocytosis, haemoglobinuria and active erythropoiesis on marrow cytology). A preceeding anaemia cannot be completely excluded; however, the complete and sustained response to plasmapheresis and negative investigation results make it unlikely that other causes of anaemia were overlooked.

There is evidence to suggest that immunological factors may be involved in the pathogenesis of TTP. There is elevation of various cytokines in the plasma (Wada *et al*, 1992); TTP responds to various immunomodulatory modalities such as plasmapheresis (Bell *et al*, 1991; Rock *et al*, 1991), glucocorticoids (Bell *et al*, 1991), and to intravenous immunoglobulin (Finn *et al*, 1987); and TTP is associated with autoimmune disorders such as systemic lupus erythematosus. It is possible that anaemia in TTP is, at least in part, due to an autoimmune process in spite of a negative Coombs test.

Another possible explanation could be that schistocytosis is not a sine-qua-non feature of microangiopathic haemolysis.

Our patient also suffered from Darier's disease (keratosis follicularis). This is a disorder characterized by the persistent eruption of multiple firm, crusted hyperkeratotic papules and inherited as an autosomal dominant trait with variable penetrance. Even though both Darier's disease and TTP are rare, we believe that their occurrence in the same patient is incidental.

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