The sea-blue histiocyte syndrome with hepatic porphyria and infectious mononucleosis

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SYNOPSIS  The syndrome of sea-blue histiocyte, hepatic porphyria, and infectious mononucleosis occurring simultaneously in a young girl is described. The cytochemical staining character of the bone marrow histiocytes strongly suggested that the storage material was glycolipid. The possible relationship between the multiple disorders in the same patient is discussed.

Sawitsky, Hyman, and Hyman (1954) initially described two patients with splenomegaly and large number of peculiar histiocytes in the bone marrow and spleen containing cytoplasmic storage granules staining blue with Romanowsky’s stain. Since then more than a dozen cases, including siblings (Jones, Gilbert, Zugibe, and Thompson, 1970; Lake, Stephens, and Neville, 1970) have been reported. Silverstein, Ellefson, and Ahern (1970) used the term ‘sea-blue histiocyte syndrome’ for this condition. Furthermore, the coexistence of sea-blue histiocytes and some haematological disorders such as myelofibrosis (Marshall and Adams, 1958) and sickle-cell disease (Kattlove, Gaynor, Spivack, and Gottfried, 1970) have also been reported.

The present patient is the first reported case of sea-blue histiocyte syndrome associated with acute intermittent hepatic porphyria and infectious mononucleosis.

Case Report

A 17-year-old girl presented with a two-month history of acute intermittent colicky abdominal pain, nausea, occasional vomiting, and tiredness. She gave a vague history of sore throat. During the course of her illness she noticed that her urine became dark red. Her past history was non-contributory. There was no history suggestive of porphyria in other members of the family. Physical examination revealed no lymphadenopathy, no jaundice, and no abnormality of the skin. The tonsils and throat were slightly congested; the liver and spleen were just palpable. The rest of the physical examination did not show any abnormality.

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INVESTIGATIONS

Haemoglobin was 14·2 g/100 ml, WBC 11 200/mm³ (neutrophils 23%, lymphocytes 75%, and monocytes 2%). A blood film showed that almost all the lymphocytes were abnormal in morphology and typical of infectious mononucleosis. Platelets were 125 000/mm³. The ESR was 45 mm/one hour. The bleeding time, clotting time, and prothrombin time were all normal. A Paul-Bunnell test gave positive result with a 1 in 112 dilution after absorption with guinea-pig kidney antigen. Bone marrow aspiration stained with Giemsa’s stain showed normal cellular components with many large histiocytes containing blue granules in the cytoplasm (see Fig.). A cytochemical stain was strongly PAS positive and Sudan Black was moderately positive suggesting that the storage material in the cytoplasm was glycolipid.

Liver function tests showed bilirubin 0·8 mg/100

Fig. Bone marrow aspiration stained with Giemsa’s stain showing typical sea-blue histiocyte × 600.
ml, SGOT 54 mIU/ml, SGPT 62 mIU/ml, ICDH 16 mIU/ml. Alkaline phosphatase was 9 KA units; serum cholesterol 170 mg/100 ml, blood urea 38 mg%, serum albumin 5.3 g/100 ml. Serum immunoglobulin estimation showed IgG 2,000 mg/100 ml, IgA 175 mg/100 ml, IgM 236 mg/100 ml. Antinuclear factor not detected.

Urine showed an increase in bilirubin and urobilinogen and porphyrins but no mucopolysaccharide was detected. The full porphyrin analysis results (see Table) confirmed the diagnosis of acute intermittent hepatic porphyria.

<table>
<thead>
<tr>
<th>Porphyrin Analysis Results</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte coproporphyrin</td>
<td>&lt;4.2 µg/100 ml cells</td>
</tr>
<tr>
<td>Erythrocyte protoporphyrin</td>
<td>&lt;3.5 µg/100 ml cells</td>
</tr>
<tr>
<td>Faecal coproporphyrin</td>
<td>&lt;5.0 µg/g dry wt</td>
</tr>
<tr>
<td>Faecal protoporphyrin</td>
<td>&lt;11.3 µg/g dry wt</td>
</tr>
<tr>
<td>Urinary coproporphyrin</td>
<td>&lt;250 µg/l</td>
</tr>
<tr>
<td>Urinary uroporphyrin</td>
<td>&lt;41 µg/l</td>
</tr>
<tr>
<td>Urinary delta aminolaevulinic acid</td>
<td>&lt;5.5 mg/l</td>
</tr>
<tr>
<td>Urinary porphobilinogen</td>
<td>&lt;3.5 mg/l</td>
</tr>
</tbody>
</table>

Table  Porphyrin analysis in present case

Discussion

The essential features of this rare disorder are splenomegaly and the presence of large number of bright blue histiocytes in the bone marrow and spleen, although hepatomegaly and thrombocytopenia may be present. The cytochemical reaction on bone marrow smears in this patient and previous cases (Silverstein et al, 1970; Jones et al, 1970) suggested that the storage material in the cytoplasmic granules was glycolipid and/or phospholipid.

The aetiology of this lipid storage disease is unknown, but most of the reported cases were predominantly young females as is the subject of the present report. Some authors have suggested that it is a hereditary disorder (Jones et al, 1970; Ardeman and Lewis, 1972) but the disorder may be acquired and associated with other diseases (Marshall and Adams, 1958; Kattlove et al, 1970).

The present case is interesting in that the syndrome presented with hepatic porphyria, a metabolic disorder of dominant inheritance, and infectious mononucleosis at the same time. The exact relationship between the sea-blue histiocyte syndrome, porphyria, and infectious mononucleosis is not clear. It seems that the sea-blue histiocyte syndrome and the porphyria are two hereditary metabolic disorders present in this patient and the latter might have been precipitated by an attack of infectious mononucleosis. On the other hand the sea-blue histiocyte in the bone marrow may be an acquired abnormality coexisting with infectious mononucleosis similar to other haematological disorders. Mild hepatosplenomegaly and thrombocytopenia may well be due to infectious mononucleosis. However, thrombocytopenia has been documented in this syndrome previously, as in this present case, but it should be followed up to ascertain this. Further biochemical and genetic studies are required to elucidate the pathogenesis of this entity.

References


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