A 2 month old infant with Chediak-Higashi syndrome presenting in the accelerated phase

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(Key words: Chediak-Higashi syndrome, accelerated phase)

Introduction

Chediak-Higashi syndrome (CHS) is an autosomal recessive disorder due to *LYST/CHS1* gene mutation[1]. It is characterized by frequent bacterial infections, partial oculo-cutaneous albinism and abnormal large leucocyte granules[1]. It is also associated with clinical features involving the haematologic and neurologic systems[2]. In 85% cases, CHS enters an accelerated phase consisting of lympho-histiocytic infiltration of the liver, spleen, lymph nodes and bone marrow[3]. Once the accelerated phase has occurred, the disease is invariably fatal. There are only around 500 cases of CHS reported up to 2011[4]. According to the literature, onset of disease is from 2 months to 10 years[5]. However, the accelerated phase has only been reported in babies 9 months of age or more[6]. We report a 2 month old boy with CHS in the accelerated phase.

Case report

A 2 month old baby boy was brought to hospital with a history of fever for 5 days. He was the first child from a consanguineous marriage and was developmentally normal. There was no family history of CHS. He was febrile, weighed 4 kg, and had blonde hair and hypopigmentation of the skin all over the body. He had pallor with cervical lymphadenopathy. Cardiovascular and respiratory system examinations were normal. He had a distended abdomen with hepatomegaly (4cm) and splenomegaly (7cm). He had no focal neurological deficit.

Laboratory investigations showed leucopenia (3,100/cu mm), thrombocytopenia (24,000/cu mm) and anaemia (haemoglobin 7.4g/dl). Peripheral blood smear showed pancytopenia with lymphocytic inclusions. Child also had a high erythrocyte sedimentation rate (72mm in first hour), high serum ferritin levels (>2000 ng/ml), normal fibrinogen levels (231 mg/dl), and hypertriglyceridaemia (325 mg/dl). Bone marrow aspirate revealed large coarse azurophilic granules in the myeloid series and features of erythrophagocytosis in myeloid precursor cells (Figures 1 and 2).

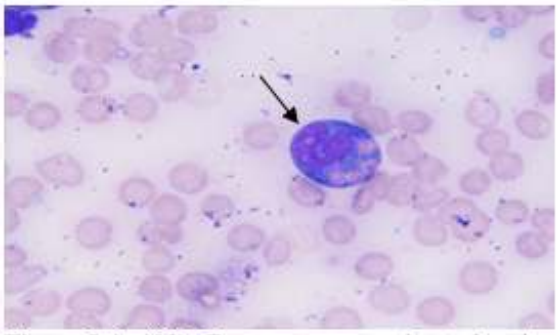

Figure 1 (x 400): ***Bone marrow aspirate showing azurophilic granules (shown by arrow)***

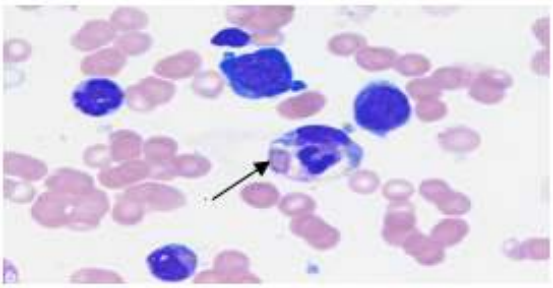

Figure 2 (x 400): ***Bone marrow aspirate showing erythrophagocytosis (shown by arrow)***

The patient fulfilled the diagnostic criteria for haemophagocytic lymphohistiocytosis (HLH) viz. fever, splenomegaly pancytopenia, high serum ferritin levels, hypertriglyceridaemia and haemophagocytosis in the bone marrow. Thus, the diagnosis of accelerated phase of CHS was made on the basis of clinical presentation (hypopigmentation, blond hair) and haematological findings (giant azurophilic granules in leucocytes). Blood and urine cultures were sterile. Chest X-ray was normal. Abdominal ultrasound revealed hepatosplenomegaly. Optical microscopy of the hair showed groups of pigment scattered along the

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length of the hair shafts, contrasting with the normal pattern of fine, diffuse pigmentation (Figures 3 and 4). The child was treated with ceftriaxone and vancomycin. He also received transfusions, including platelets and packed red blood cells for anaemia. Child expired on 5th day of hospitalisation.

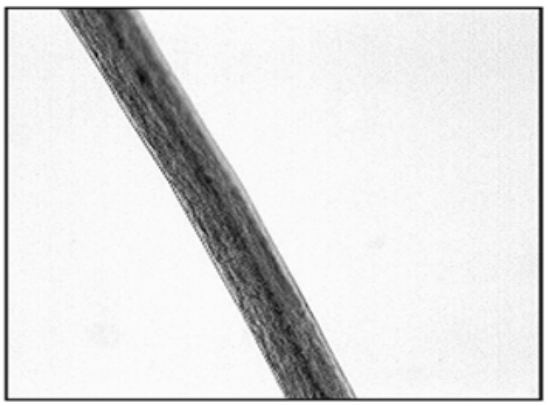

Figure 3: ***Microscopic examination of a normal hair shaft***

Figure 4 (x 400): ***Optical microscopic examination of the hair shaft showing larger melanin granules (shown by arrow)***

Discussion

CHS is a rare immunodeficiency disorder due to defective granulocyte function. Defective phagocyte, lymphocyte, and natural killer (NK) cell functions contribute to the enhanced susceptibility to infection[7]. The final stage of CHS is characterised by lymphohistiocytic cell infiltration in various organs[4]. *Staphylococcus aureus*, beta-haemolytic streptococci and pneumococci are the common pathogens causing recurrent infections such as pneumonia, otitis media, dermal and mucosal infections[8]. Mental retardation and neural deafness have also been reported[9]. Diagnosis of CHS can be confirmed by the presence of *LYST/CHS1* gene mutation[1]. The most important and hazardous complication of CHS is the acceleration phase, manifesting as fever, jaundice, hepato-splenomegaly and lymphadenopathy. The most effective treatment for CHS is allogenic haematopoietic stem cell transplantation (HSCT), but this therapy does not prevent the progressive neurological dysfunction frequently observed during long-term follow up[10].

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