Idiopathic Atypical Hemolytic Uremic Syndrome (aHUS) with Trilineage Myelodysplasia

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Abstract Atypical hemolytic uremic syndrome (HUS) is a heterogeneous group of disorders, with an unexplained pathogenesis. We report here with an interesting case of a 6 years old male child presenting with atypical feature of HUS and bone marrow trilineage myelodysplasia.

Keywords Hemolytic uremic syndrome · Trilineage myelodysplasia

Introduction

Atypical hemolytic uremic syndrome (HUS) is a heterogeneous group of primary and secondary disorders, the pathogenesis of which is poorly understood [1, 2]. The syndrome is characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure with frequent occurrence of neurological complications. As opposed to shigella associated HUS, the atypical form is not preceded by diarrhea usually unrelated to season or geographic location and has a relapsing course. Most cases of primary atypical HUS are idiopathic but some may be inherited either as autosomal dominant or recessive traits or mutations in factor H-gene (C3 deficiency). However, the exact etiopathogenesis is still poorly understood. The prognosis of atypical HUS in terms of patient survival and renal outcome is poor. The final outcome of atypical HUS is

usually death or permanent renal or neurologic impairment [3, 4].

The four genes known to be associated with atypical HUS are: CFH (encoding compliment factor H), accounting for an estimated 30% of HUS; CD46 (MCP) (encoding membrane cofactor protein), accounting for approximately 12% of aHUS; CFI (compliment factor I) and rarely CFB (encoding compliment factor B). Atypical HUS is considered genetic when two or more members of the same family are affected by the disease at least six months apart in absence of any common triggering agent (drugs, systemic disease, viral agents or bacterial agents). Atypical HUS is considered Idiopathic, when none of the above said features are present [5, 6].

Case Report

A 6 years old male child presented with fever, weakness, polyarthralgia of 2 weeks duration. No. H/o sore throat, diarrhea or any other systemic disease or a family history could be elicited. On examination, the child was febrile, pale and irritable. No skin rash was found. Pallor was moderate with hepatomegaly (2 cm.) Laboratory investigations revealed: hemoglobin 5.98 mg/dl, DLC: N 44%, L52%, E03%, M01%, TLC: 3,700/C mm, TPC: 0.78 lacs/C mm, ESR: 48 mm in 1 h (wG); Ret count: 22%, QBC (MP): negative, peripheral smear examination revealed a large number of fragmented RBCs, helmet cells, schistocytes with 18 normoblasts/100 WBCs (Fig. 1). ANA, LE Cell, anti dsDNA and ASO were negative. LFT showed total bilirubin: 4.6 mg/dl, Direct: 1.2 mg/dl, other investigations revealed: LDH 1642u/l, sickling: negative, HPLC: normal, Coombs test: negative, G6PD: normal, Sr urea: 105 mg/dl, creatinine: 6.0 mg/dl. Blood, urine, stool and

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Fig. 1 PS showing helmet cells, fragmented rbc's (Leishman, 1000 $\times$)

Fig. 2 BM Aspiration showing trilineage dysplasia (Leishman, 1000 $\times$)

throat swab, cultures were sterile. Urine analysis revealed numerous erythrocytes and 4+ protein on dipstick and granular casts. Chest X-ray was normal. Renal sonography revealed normal size and increased echogenicity of the kidneys.

The clinical presentation and the laboratory features of microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure were consistent with the diagnosis of non-diarrhea associated atypical HUS.

Bone marrow aspiration study and biopsy revealed a hypocellular marrow with features of trilineage myelodysplasia (Fig. 2, 3).

Fig. 3 BM biopsy showing ALIP(H&E, $\times 400$)

Subsequently the patient rapidly developed vomiting, with worsening acute renal failure and died.

Discussion

Hemolytic uremic syndrome (HUS) is characterised by hemolytic anemia, thrombocytopenia and acute renal failure caused by platelet thrombi in the microcirculation of the kidney and other organs. Typical (acquired HUS) is triggered by infectious agents such as strains of *E. coli* (Stx. *E. Coli*) that produce powerful shiga-like exotoxins, whereas atypical HUS (aHUS) can be genetic, acquired or idiopathic. Onset of atypical HUS ranges from prenatal to adulthood. 60% of genetic of HUS progress to end stage renal disease. a HUS has been associated with defective regulation of the alternative complement pathway [7, 8]. Predisposition to atypical Hus is inherited in an autosomal recessive or autosomal dominant pattern with incomplete penetrance. Some individuals diagnosed with autosomal dominant aHUS have an affected parent or an affected close relative, but in the majority the family history is negative.

Atypical HUS is quite rare the number of cases in the world are unknown. Recent research studies confirmed the hereditary trait of HUS by reporting low C3 levels and factor H abnormalities (H-gene mutations).

Hence, all cases of acute renal failure in pediatric patients must be critically analyzed for non diarrhea associated atypical HUS. Trilineage myelodysplasia in bone marrow study of our patient has never been described in atypical HUS. In contrast to progression of atypical HUS patients to relapse and chronicity, our patients had a rapid and downhill course culminating in death.

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