Familial Hemophagocytic Lymphohistiocytosis Type 3

Yue Du¹ · Li Li¹ · Xiao Ying Wang¹ · Liang Chen¹ · Sheng Hua Jia¹ · Rong Mi¹

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To the Editor: A newborn boy was admitted to a local hospital with fever and splenomegaly. He was the mother's second pregnancy and first birth, born after an uncomplicated pregnancy, with healthy and non-consanguineous parents. The first pregnancy was voluntary abortion. Prenatal ultrasound revealed normal fetal growth and development ever before, but at 39 3/7 wk, it revealed splenomegaly, ascites and fetal cerebral ventriculomegaly. The next day, he was delivered by cesarean section with a birth weight of 3550 g and a length of 50 cm, additionally the apgar scores was 10 points. He showed no dysmorphic features. The routine blood test showed WBC $8.1 \times 10^9/L$, neutrophils $0.92 \times 10^9/L$, hemoglobin 120 g/L, platelets $33 \times 10^9/L$, CRP 21.1 mg/L, atypical lymphocyte 20%; normal liver enzymes, and ultrasound showed splenomegaly and cholestasis. He was diagnosed with infection and treated with kinds of antibiotics and blood products, but the disorder still deteriorated.

After 18 d, he was admitted to our department as his fourth hospital. Physical examination revealed fever, tachypnea, petechiae, lymphadenopathy, hepatosplenomegaly and abdominal distension. Laboratory examination revealed anemia, neutropenia, thrombopenia, elevated liver enzymes, cholestasis, high ferritin, high triglyceride and low fibrinogen. The CD107a excitation experiment showed that the degranulation function of NK cell is decreased ($\Delta CD107a < 5\%$). Inflammatory cytokines were increased, especially sCD25 (29135 pg/ml). NK cell count were 2%, NK cell's activity counts were 20.85%. The bone marrow aspirates showed hemophagocytosis. The chest CT showed lung exudation, a number of enlarged and significantly enhanced bilateral axillary lymph nodes. Thus he was diagnosed with Hemophagocytic lymphohistiocytosis (HLH), and treated

with additional dexamethasone and cyclosporine according to the HLH 2004 protocol.

On the 30th day of life, the genetic analysis from his peripheral blood, demonstrated the compound heterozygous mutations of *UNC13D* gene: c.118–308 C > T in intron 1 which was pathogenetic and inherited from his father; the other mutation c.3002 T > C, in exon 31, p.L1001P was predicted to be probably pathogenic using 2 different protein programs (PolyPhen, SIFT) and inherited from his mother. Then his diagnosis was corrected as Familial hemophagocytic lymphohistiocytosis type 3 (FHL3). But the hematopoietic stem cell transplantation (HSCT) was refused, and he died of the infection at 52 d of age [1–3].

Compliance with Ethical Standards

Conflict of Interest None.

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✉ Rong Mi
mr85695601@sina.com

¹ Department of Pediatrics, Newborn Medicine, Children's Hospital, Capital Institute of Pediatrics, 2# Yabao Road, Beijing, China