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A Case Report of a 10-Month-Old Girl with EBV Related Hemophagocytic Lymphohistiocytosis Syndrome Co-Infected with Measles

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Abstract

Objective: The main objective of this article was to study a 10-month-old girl with EBV related hemophagocytic lymphohistiocytosis syndrome (HLH) co-infected with measles and analyzed the cause of the case.

Materials and Methods: We had recorded clinical manifestations of the patient, laboratory tests, pathogenic tests and morphology detection.

Results: Laboratory studies of the patient suggested the existence of measles virus infection after the measles vaccination, EBV infection, combined with its iron protein, abnormal level of lipid, and hemophagocytes in the bone marrow smear indicated that the patient caught a EBV related hemophagocytic lymphohistiocytosis syndrome co-infected with measles.

Conclusions: We reported a rare case of an infant girl diagnosed of sever EBV-associated HLH with measles virus infection, a life threatening hematological disorder. Comprehensive analysis of laboratory tests, etiology and morphology were important for the diagnosis of HLH.

Keywords: Measles; EBV; Hemophagocytes; Hemophagocytic lymphohistiocytosis syndrome (HLH)

Presentation of Case

A 10-month-old infant was admitted to Shenzhen Children's hospital with four day history of fever as high as 39.7℃ and measles for two days. Pulse is 132/minutes; Rate is 40/min, weight: 6.5 kg, the conscious was clear and easy to be agitated and cry. The whole body skin elasticity, scattered visible rash millet grain samples, pressure of color fading, no leakage, hips with a little desquamation, superficial lymph nodes not touch obviously enlarged; The size of the head is normal, and there is no secretion in the eye circumference. The lips were slightly cracked, the left buccal mucosa suspected measles mucosa, pharyngeal hyperemia. Temperature can drop to normal after oral drug, but fever again and again. No chills, convulsions, without shortness of breath, no cough, no vomiting. The heart sounds strong, the law firm, the valve of each valve is not heard and the murmur, the unintentional bal of friction; Abdominal paipation, bowel sound normal; The limbs move freely, muscle strength and muscle tone are normal symmetry. No abnormality was found in the nervous system.

Its diagnostic consideration for admission: fever and measles as the main performance. Heat is given priority to with high fever, easy relapse, scattered all visible rash millet grain samples, analysis of the cases are as follows: 1) measles: for babies, children with fever, rash, as the main performance, 10 days prior to the onset of leprosy vaccine, the body: the left buccal mucosa suspected measles mucosa spot, on high alert, but no obvious catarrh symptoms, is not supported. Prevention of inoculation history: measles vaccination at 8th month.The laboratory test was below in Table 1:

Table 1: Laboratory Values

	29th Oct	30th Oct	1th Nov	3th Nov	18th Nov
WBC*109/L	6.01	8.32	10.26	7.83	12.95
Neu%	52.5	22.7	12.6	28	30.7
Lymph%	37.6	71.8	80.3	59.9	63.1
Hb g/L	106	107	95	92	94
PLT *109/L	326	336	257	477	645
CRP mg/L	20.8	29	11.3	2.5	<0.5
Fib g/L	2	1.9	1.8	1.5	1.45
TG mmol/L	3.66	2.92	4.45	4.53	-
CHOL mmol/L	2.7	3.18	5.73	6.73	-
HLDL mmol/L	0.41	0.43	0.59	0.95	-
VLDL mmol/L	1.98	2.36	3.73	4.65	-
FER g/L	14388	12270	5679	1429	470

The pathogenic screenings are as below (Table 2), the diagnosis of measles is obvious and combined with the four results of EB-V-DNA and antibody, EBV infection in children should be infected with previous, and recently activated. Children with etiology detection suggest the existence of measles virus infection, EB virus infection, all are secondary HLH reasons.

Table 2: The Pathogenic Detection

Sample type	Throat swab		Blood		
Testing Items	MP-DNA	EB-DNA	VCA-IgG	EBNA-IgG	Measles-IgG
Results	<5.00E＋2	1.74E＋5	Positive	Positive	Positive

In the end, we applied the bone marrow biopsy and detect the morphology of bone marrow smear by Wright staining, as shown in figure 1, there were some hemophagocytes could be seen in the bone marrow smear in different fields of view. Considering together, HLH syndrome diagnosis conforms to 4 within 8 standard, including (1) fever more than 1 week, temperature is >38.5 ℃; (2) Hypertriglyceridemia was more than 3mmol/L and (or) low-fibrinogenemia (< 1.5 g/L); (3) The serum ferritin is more than 500ug/L; (4) There are hemophagocytes in bone marrow, cerebrospinal fluid or lymph nodes[1]. There were some other supporting evidences: brain symptoms accompanied by increased number of CSF cells and (or) protein increases, transaminase and blood bilirubin elevation, LDH > 1000U/L. The treatment of IVIG was effective treatment in the early stage through blocking the immune response [2].

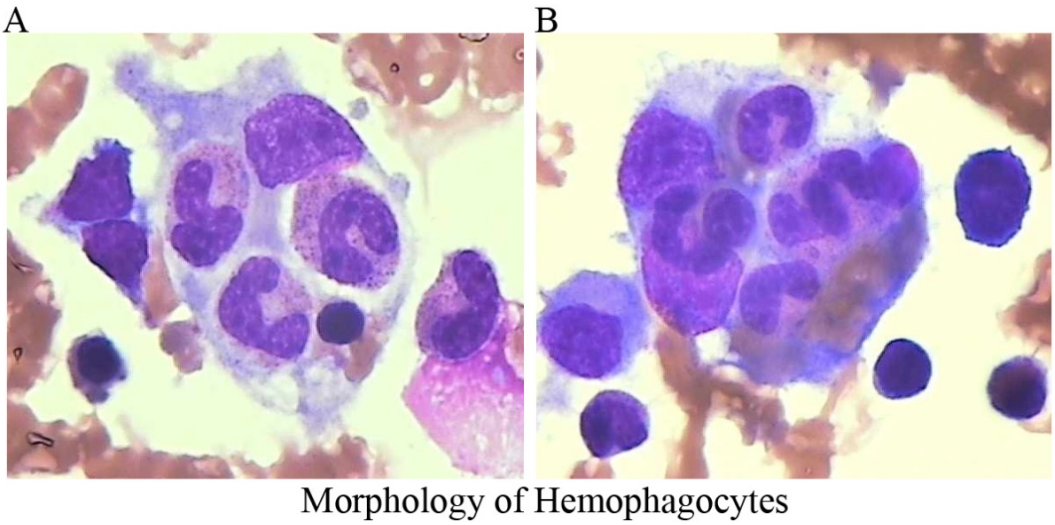

Figure 1: The morphology of hemophagocytes A and B, Bone marrow biopsy were applied for the detection of morphology of the patient, hemophagocytes was detected in different fields of view of the bone marrow smear with Wright staining. Magnification was 400 times.

Discussion

Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis syndrome (EBV-HLH) is a serious disorder in which monoclonal growth of T cells infected with EBV and macrophage activation cause pancytopenia, high fever and acute liver failure[4, 5]. It is a life threatening hematological disease associated with severe systemic inflammation caused by an uncontrolled and ineffective immune response, such as activation and aberrant proliferation of macrophages, lymphocytes and dendritic cells resulting in cytokine storm. Epstein-Barr virus (EBV) is the most infectious agent in patients with the viral-associated HLH [6]. Hyper level of inflammatory cytokines by activated cytotoxic T lymphocytes and macrophages plays an important role in the pathogenesis of HLH, and phagocytosis by macrophages of erythrocytes, leukocytes and their precursors in the bone marrow is a hallmark of HLH. Limited numbers of cases with measles virus infection have been demonstrated in viral-associated HLH patients. Herein, we reported a pediatric case of sever EBV-associated HLH with measles virus infection.

HLH is divided into two types based on its etiology: primary (genetic) and secondary (acquired) HLH. Primary HLH is due to genetic defects in cellular cytotoxicity, whereas secondary HLH is associated with viral infections including Epstein-Barr (EBV), autoimmune diseases, malignant diseases, or acquired immune deficiency conditions [7]. In our report cases, the ten--month girl was diagnosed as EBV-related HLH co-infected with measles, it is hard to say she belongs to primary or acquired HLH, because we didn't get the genetic data such as mutations in the gene encoding perforin which was a limitation of this study. However, EBV and measles infection were both confirmed at this study as well as the morphology of hemophagocytes. Her parents didn't have a consanguineous marriage and didn't have family medical history. Therefore, it was hard to be diagnosed as primary HLH.

Despite the difficulty of diagnosis, the treatment of EBV-HLH is also a big challenge to doctors. Despite the various intensive treatments, more than 30% of the patients diagnosed with EBV-HLH died because of the disease or its complications [8, 9]. The most important key point of HLH treatment is remediation of hypercytokinemia, for which immunosuppressant medication. HSCT (Hematopoietic stem cell transplantation) is the only possible treatment for immunosuppression -resistant HLH, including for EBV-HLH. In pediatric patients, there was no significant difference between myeloablative conditioning regimen (MAC) and RIC, bone marrow transplantation and CBT[10]. Interestingly, an initial course of a rituximab treatment resulted in a dramatic decrease of EBV DNA to undetectable levels, suggested that the rapid decrease of EBV-DNA load following rituximab treatment was beneficial for the patient's survival[9, 11]. In conclusion, how to cure HLH is also a difficult problem in the world field which need us to do more effort in diagnose and treatment of HLH patient, to decrease the mortality of this disease.

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Ethical Approval Statement

This study was approved by the ethics committee of Shenzhen Children's Hospital, informed consent for publication was obtained from her parents of the individual participant in the study

Conflict of Interest

The authors declare no competing financial interests.

Informed Consent

All guardians of the subjects included in this study provided appropriate informed consent.

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