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Case Report

A Case Report of Neonatal Omenn Syndrome Presenting as Striking Erythroderma

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Abstract

Background: Omenn Syndrome (OS) is a kind of Serious Combined Immunodeficiency Disease (SCID). A variety of genetic defects responsible for lymphocyte or thymic development can give rise to OS, of which the Recombinase-Activating Genes (RAG1 and RAG2) being the best characterised. It is often misdiagnosed and progressively deteriorated due to the limit knowledge in early life of children.

Case Presentation: We present herein a typical case of Omenn syndrome that initially manifested as diffuse erythroderma in a 2-day-old newborn.

Conclusions: The age of Omenn syndrome onset was earlier. Typical clinical features include erythroderma and immune dysfunction. Immunodeficiency must be considered in every case of neonatal erythroderma and immunological evaluation should be performed as soon as possible. Genetic study confirms the diagnose. We found two novel mutations in RAG1 could cause Omenn syndrome.

Keywords: Neonate; Omenn syndrome; SCID; Erythroderma

Introduction

Omenn Syndrome (OS) is a form of Severe Combined Immunodeficiency Disease (SCID) characterized by erythroderma, hepatosplenomegaly, lymphadenopathy, and alopecia. It is reported that the incidence of the disease is 1/500,000~1/100,000 abroad. Puzenat E [1] et al. reported that the incidence ratio of male to female was about 1:1. In patients with OS, B cells are mostly absent, T cell counts are normal to elevated, and T cells are frequently activated and express a restricted T-Cell Receptor (TCR) repertoire [2]. In recent years, with the increasing awareness of Omenn syndrome, more and more cases have been reported, but few cases have been reported in neonates to date. We herein present a very rare case of Omenn syndrome whose most outstanding manifestation is erythroderma and which was diagnosed in a short period of time after birth by gene detection. At the same time, two novel mutations of Recombination-Activating Gene Complex 1(RAG1) c.3072-c.3073 insT and c.2190 delT were found, which enriched the RAG1 gene mutation database.

Case Presentation

A 2-day-19-hour-old baby boy at full term was admitted to our Neonatology Ward II in our hospital on an emergency basis because of "polypnea and dermatological abnormalities for 2 days". At birth, he had unusual-looking skin characterized as rough skin, diffuse erythema, and yellow-white secretions over his body, mainly in the head and face, then progressed to dry and partial cracked skin with oily colloidal substance covering his entire body, accompanied by jaundice and slight eyelid edema. The whole thing looks like parchment (Figure 1 A,B). In the meantime, he had polypnea without fever, cough, foaming, cyanosis and progressive dyspnea. In the course of the disease, he had no screaming, seizures, vomiting and diarrhea. Since the onset of disease, his spirit and reaction are normal, crying and sucking force are good, bowel movement and urination are as usual. The child was the 4th fetus and the 2nd birth, cesarean delivery due to "giant", birth weight was 3575g, apgar score was normal, formula milk feeding, no history of blood transfusion, and no similar medical history in the family.

On arrival, physical examination showed: T 36.^{0}C, R 55t/min, HR 132t/m, BP 68/42mmHg, average growth and development, medium nutrition, fine complexion, diffuse large areas of redness over the whole body with scattered yellow-white desquamate over it, no ulceration and bleeding spots. Marked swollen lymph nodes in the neck and axilla could be touched. Double lung breathing sounds thick without wheezes and rales. Soft abdomen without hepatosplenomegaly. No obvious abnormalities were found in the heart and nervous system.

Laboratory examination revealed: White Blood Cell up to 36.33x10^{9}/L. Absolute lymphocyte and eosinophil counts peaked at 14.64x10^{9}/Land 13,81x10^{9}/L, respectively. Lymphocyte count by classification showed high numbers of T-cells (21630.16 cells/mL)), absent B-cells (3.28 cells/mL), and normal natural killer cells (414.86 cells/mL). TBNK showed CD3+% was high (89.24%) and CD19+% =0.00. The CD4:CD8 ratio was high (4.59, 0.98-1,94). Immunological examination showed slightly high IgE (7.1IU/ml) and level of IgA, IgM, C3 and C4 decreased significantly. The collective clinical manifestations and laboratory findings all suggested SCID (Figure 2). So we conducted genetic test which demonstrated biallelic mutations in RAG1 (Figure 3).

Biological samples were collected from the baby and his family after informed consent according to institutional Helsinki committee. Genetic test results showed that RAG1 exon 2 of the children had complex heterozygous mutations of c.3072-c.3073 insT from his

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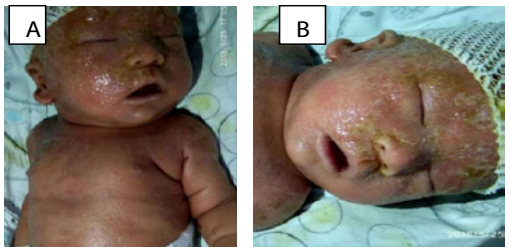

Figure 1: (A, B) Skin lesions in the child with Omenn syndrome. Generalized erythema and yellow-white secretions mainly over the head and face.

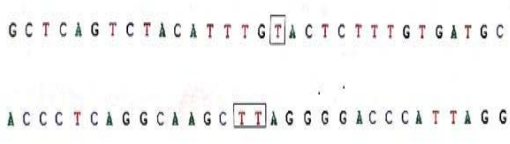

Figure 2: NCBI reference sequence. This is the normal sequence of gene RAG1.

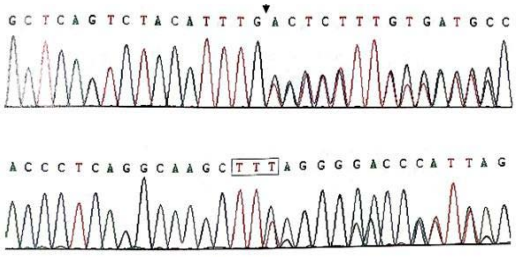

Figure 3: The child's sequence. Demonstrated biallelic mutations in RAG1, it showed that RAG1 exon 2 of the child's complex heterozygous mutations of c.3072-c.3073 insT (from his father) and c.2190 delT (from his mother).

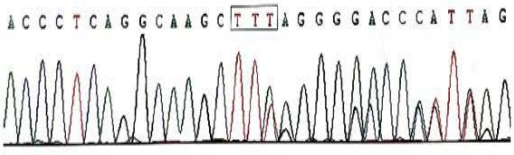

Figure 4: Father's sequence: Showed that RAG1 exon 2 of the father had only one mutation of c.3072-c.3073 insT.

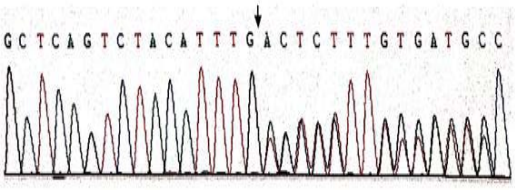

Figure 5: Mother's sequence: Showed that RAG1 exon 2 of the mother had only one mutation of c.2190 delT.

father (Figure 4) and c.2190 delT from his mother (Figure 5), which had not been reported. These two mutations resulted in the amino acid changes at Residue 1025 and 730 of RAG1 protein encoded by RAG1 respectively.

During hospitalization, the patient was given anti-infection, fluid rehydration and other supportive treatments. After the genetic test came back, the child had accomplished match test since effective treatments for the disease are bone marrow or stem cell transplants. When the child was 2-month-3-day-old, he developed fever, cough and diarrhea; 17 days after that, he developed respiratory and heart failure and was admitted to the ICU. The family gave up treatment and the patient died of multiple organ failure before the matching results came back.

Discussion and Conclusion

Omenn syndrome was first reported by Omenn in 1985. It is a rare severe combined immunodeficiency characterized by the presence of a substantial number of oligoclonal activated T cells, and the lack of B lymphocytes, associated with particular clinical features such as generalized erythroderma, lymphadenopathy, hepatosplenomegaly, and increased occurrence of life threatening infections [3]. The disease is autosomal recessive and is mainly caused by a partial defect in RAG1 or RAG2 genes involved in T lymphocyte receptor and immunoglobulin gene rearrangement, but mutations in other genes have also been described [4]. At present, there is a lack of satisfactory treatment for this disease, and children often die of severe infection or organic failure. Bone marrow transplantation or hematopoietic stem cell transplantation may be used if appropriate donors are available [5,6]. Recently, few neonate cases with Omenn syndrome were reported. Our patient demonstrates three unique aspects. Firstly, he had the very typical clinical features including skin abnormalities, marked swollen lymph nodes as well as lab profiles. Secondly, all impairments occurred right after birth especially the striking erythroderma, and immunological assessment was performed earlier which promoted the conduction of gene test. Thirdly, two novel mutations (c.3072-c.3073insT and c.2190delT) in RAG1 cause OS were reported here, bioinformatics predicts that these two mutations are highly pathogenic. The combination made him the standard neonate with Omenn syndrome. This case could remind healthcare workers that any newborn infants presenting with erythroderma or swollen lymph nodes, further immunologic function investigation and gene analysis may be needed to exclude the severe combined immunodeficiency. Early diagnosis may be helpful for the timely marrow or stem cell transplantation and the improvement of the outcome.

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