Case Report/รายงานผู้ป่วย

Exfoliative Dermatitis in a 7-month-old Girl with Severe Combined Immune Deficiency.

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Abstract

Background: Severe combined immunodeficiency (SCID) is a rare, fatal syndrome with profound deficiencies of T and B cells function. Clinically, the patients have serious infection caused by bacterial, viral or opportunistic organisms. Exfoliative dermatitis is an uncommon manifestation induced by graft-versus-host disease (GVHD) from maternal lymphocytes.

Objective: We report a case of SCID who presented with exfoliative dermatitis without evidence of GVHD.

Case Report: A 7-month-old girl presented with exfoliative dermatitis since one month of age. She had oral candidiasis, pneumonia, chronic diarrhea and failure to thrive. She was found to have markedly low level of immunoglobulin G, A and M. T and B cells enumeration revealed CD4 cells, 13%, CD8 cells 1%, CD19 cells, 83% and CD16/56 cells, 3.8%. The lymphocyte proliferation to mitogen (phorbol myristate acetate) assay was poorly-responded. DNA typing analysis from her skin biopsy could not demonstrate the maternal DNA. She died from serious infection after starting bone marrow transplantation. The autopsy revealed severe depletion of both lymphoid and thymus gland with multinucleated giant cells and intracytoplasmic inclusion bodied in lung pathology.

Conclusion: We have demonstrated a case of SCID presented with dermatosis, which did not induce by GVHD. The patient needed early recognition to prevent uncontrolled infection, leading to death unless immunological reconstruction was done.

Key words: Severe combined immunodeficiency, Immune deficiency, SCID, Primary immune deficiency

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Severe combined immune deficiency (SCID) is a rare, fatal syndrome with profound deficiencies of adaptive immune response, particularly T and B cell function. Clinical signs and symptoms usually present with serious infections caused by bacterial, viral or opportunistic organisms and include failure to thrive, oral thrush, septicemia, recurrent respiratory tract infection, chronic diarrhea and dermatological manifestations. The major skin involvements of SCID are skin and mucosal infection, eczematous rash / dermatitis and graft-versus-host disease (GVHD). Some SCID patients have problems of GVHD from trans-placental transfer of maternal T-lymphocyte engraftment that can be varied from asymptomatic to (rarely) lethal, systemic multi-organ dysfunction. Exfoliative dermatitis is an uncommon cutaneous manifestation of GVHD.

CASE REPORT

A 7-month-old girl, presenting with exfoliative dermatosis, was referred to our hospital due to recurrent pneumonia unresponsive to aggressive systemic antibiotics treatment for several weeks. She had oral candidiasis, chronic diarrhea and failure to thrive.

PAST MEDICAL HISTORY

The patient was born from a healthy mother at full term (birth weight 2,100 grams). At one month old, she developed generalized erythroderma with no response to topical drugs treatment. Then, she was treated as cow's milk protein allergy by changing to a soy-based infant formula, a partial whey-hydrolysated formula and an extensive casein-hydrolysated formula, respectively, with no improvement of her skin rashes. She had one hospitalization with pneumonia at 6 months old requiring a 10-day course of broad-spectrum systemic antibiotics. After discharge, she still had intermittent diarrhea and exfoliative dermatitis.

FAMILY HISTORY

Her father and mother were 31 and 28 years old, respectively, healthy and were not consanguineous. Her older brother died at one month old with severe pneumonia.

PHYSICAL EXAMINATION

The patient was malnourished with weight of 4,920 grams (< 3rd percentile) and height of 65 centimeters (25th percentile). The temperature was 37.1°C, pulse rate 140/min, and respiratory rate, 48/min, and blood pressure, 110/70 mmHg. She had oral thrush, mild respiratory distress with secretion retained, normal tonsils, small size lymph nodes and no hepatosplenomegaly. Her skin was generalized erythema and exfoliated at head, face, trunk, all extremities and buttock. All nails were dystrophic. (Figure 1 A and B) The other systems were normal.

LABORATORY AND DIAGNOSTIC STUDIES

CBC showed hemoglobin 9.5 g/dL, WBC 17,000 /mm^3 (lymphocytes 43%, neutrophils 40%, monocytes 1%, eosinophils 15% and basophils 1%) and platelets 422,000 /mm^3. No thymic shadow was seen on chest radiography. Pertinent details of the immunologic evaluations revealed very low serum immunoglobulin level (IgG < 33 mg/dL; IgA < 7 mg/dL; and IgM 18 mg/dL), blood group O with no anti-hemaglutinin antibody. T and B cell enumeration showed very low T-lymphocyte counts (CD4 13%, 713/ mm^3; CD8 1%, 55/mm^3; CD4/CD8 ratio 13), relatively high B-lymphocytes (CD19 83%, 4,549/mm^3) and NK cells (CD16+CD56 3.9%, 78/mm^3). Delayed type hypersensitivity skin test to Candida, purified protein derivative (PPD), Diphtheria and Tetanus antigens were negative. Lymphocyte transformation to phorbol myristate acetate (PMA) was not responsive. Nitroblue tetrazolium test (NBT) was normal and CH 50 was 100%.



Fig.1 *A, and B shows exfoliative dermatosis of face, body, legs, and dystrophic nails.*

Skin biopsy was done for histologic diagnosis, showed chronic granulomatosis, and for DNA typing analysis, which could not detect the mother's DNA in the skin of the patient. Serum fatty acid profiles were normal.

HOSPITAL COURSE

The clinical phenotype of this patient was compatible with SCID. She was treated by changing from formula milk to an amino acid based formula for her skin problem with no improvement, but responded to oral prednisolone. For treatment of the SCID, she was transplanted with haploidentical marrow from her father, but failed to show any evidence of engraftment. The patient died 30 days after transplantation from severe acquired respiratory distress syndrome.

Autopsy findings revealed severe depletion of the thymus gland. No germinal center was seen in any lymphoid follicles. Microscopic lung tissues showed groups of multinucleated giant cells with intracytoplasmic inclusion bodies.

DISCUSSION

Severe combined immune deficiency can be classified into two forms: x-linked and autosomal recessive. This patient had a clinical phenotype compatible with autosomal recessive form. There are many genetic and molecular bases of SCID, for examples mutation in the genetic encoding of common γ-chain receptor, Janus kinase 3 (Jak3), adenosine deaminase (ADA), ζ-associated protein-70 (ZAP-70) and recombinase-activating gene-1 and -2 (RAG-1, RAG-2).[1-2]

The major manifestation of this patient was an early development of skin problems, presenting with severe exfoliative dermatitis. This can be an uncommon manifestation of SCID as evidence of GVHD from transplacental-derived maternal T-lymphocyte engraftment. The confirmatory diagnosis can be made based on the variable numbers of tandem repeat (VNTR) analysis (the same as microsatellite analysis) and/or in situ hybridization.[3-5] Other techniques are cytofluorography using monoclonal antibody to non-

inherited maternal A locus antigen, and HLA testing by microcytotoxicity. As these methods were not available, we used the DNA fingerprint analysis technique to detect maternal DNA on the patient's skin biopsy, which failed to demonstrate any evidence of GVHD.

The differential diagnosis of neonatal erythroderma is large including infections (staphylococcal scalded skin syndrome, toxic shock syndrome and candidiasis), viral exanthems, immunodeficiency disorders (Omenn's syndrome, SCID with GVHD), ichythyoses (non-bullous ichthyosiform erythroderma, bullous ichthyosiform erythroderma, Netherton's syndrome), metabolic disorders (disorders of biotin metabolism, essential fatty acid deficiency), drug eruptions, and others (infantile seborrheic dermatitis, atopic dermatitis, psoriasis, pityriasis rubra pilaris, generalized mastocytosis).6 It is essential for physicians to recognize erythroderma, distinguish it from eczema and to search for underlying disorders. Some underlying disorders have specific therapies, esp. primary immunodeficiency diseases, which need early recognition for the best treatment results and to prevent mortality and morbidity.

The treatment of choice for SCID is bone marrow transplantation[7,8]. Our patient was underwent bone marrow transplantation with a poor result, possibly due to the late diagnosis of SCID, the complications of severe infection contracted before and during transplantation, and/or from the high number of NK cells present.

Autopsy findings showed severe depletion of the thymus gland and lymphoid follicles with no germinal centers seen. The microscopic lung histology revealed multinucleated giant cells with intracytoplasmic inclusion bodies possibly caused by an infection of measles, herpesvirus or respiratory syncytial virus, however, we did not have monoclonal antibodies to these pathogens to make a definitive diagnosis.

In conclusion, early recognition of the diagnosis of SCID may have led to immunological reconstitution by bone marrow transplantation, which in this case may have prevented extreme susceptibility to infection and death.

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