

Case Report

A Female Infant with Severe Combined Immunodeficiency

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ABSTRACT

We report a case of a female infant with autosomal recessive severe combined immunodeficiency. She presented early in life with recurrent severe chest infection,

opportunistic infections and failure to thrive. This is a serious life-threatening disorder. The child will die with severe infection within two years of life, if left untreated.

KEY WORDS: bone marrow transplantation, gene therapy, severe combined immunodeficiency

INTRODUCTION

Severe combined immunodeficiency (SCID) is a life-threatening disorder due to severe T and B cell dysfunction^[1]. Most patients present by the age of three months with recurrent infections, diarrhea, dermatitis and failure to thrive. It is an immunological emergency as the patients' life depends on early precise diagnosis and team approach in management. Bone marrow transplantation is the specific treatment while gene therapy still under trial^[1]. Genetic counseling is an essential part in the management and prenatal diagnosis is available through chorionic villus sampling early in pregnancy.

CASE REPORT

A six-month-old Kuwaiti girl was admitted with severe bronchopneumonia. She was a product of full term, normal vaginal delivery with a birth weight of 2.5 kg. She was the third child born to healthy first degree consanguineous parents with two healthy elder brothers. Her physical examination showed failure to thrive with weight and length below the 3rd centile. She was toxic, febrile, having tachycardia with signs of respiratory distress.

The routine hemogram and biochemical investigations were normal. Plain X-ray chest showed bronchopneumonia. Intravenous fluid and antibiotic were started and she responded well and was discharged after seven days in good general condition. She was readmitted after two days with severe bronchopneumonia. Further investigations were done for recurrent pneumonia including barium-swallow which showed gastro-esophageal reflux. Sweat chloride was normal and serum immunoglobulin showed panhypoglobulinemia (Table 1). A CT chest showed bilateral pneumonic

infiltrate with no congenital anomalies.

As a result of low immunoglobulins the patient was referred to immunologists who diagnosed the case as SCID, subclass MHC class II antigen deficiency and recommended daily oral antibiotic prophylaxis and monthly i.v immunoglobulin until stem cell transplantation could be arranged .

One month later she was readmitted and transferred to ICU in poor general condition with respiratory failure due to severe bronchopneumonia (Fig. 1 and 2). During her stay in the ICU a multidisciplinary team was involved in her management (pediatrician, pulmonologist, immunologist, gastroenterologist and infectious disease control specialist). A repeated septic profile including cultures from blood, urine, and broncho-alveolar lavage (BAL) showed: positive urine culture for *Klebsiella pneumoniae* and multiple organisms in BAL including RSV, *Pseudomonas* and *Pneumocystis carinii*. She was ventilated and started on total parenteral nutrition. She also received fluconazole, trimethoprim/sulphamethoxazole, piperacillin/tazobactam (tazocin), ribavirin, cimetidine, methylprednisolone and immunoglobulin. Unfortunately, she died due to uncontrollable sepsis resulting multiorgan failure at eight months of age .

DISCUSSION

SCID represents a group of rare, sometimes fatal, congenital disorders characterized by little or no immune response and can occur in all races with frequency of 1 in 100,000 births. This disease usually presents within the first three months of life, as chronic diarrhea, failure to thrive, pneumonia and sepsis without specific

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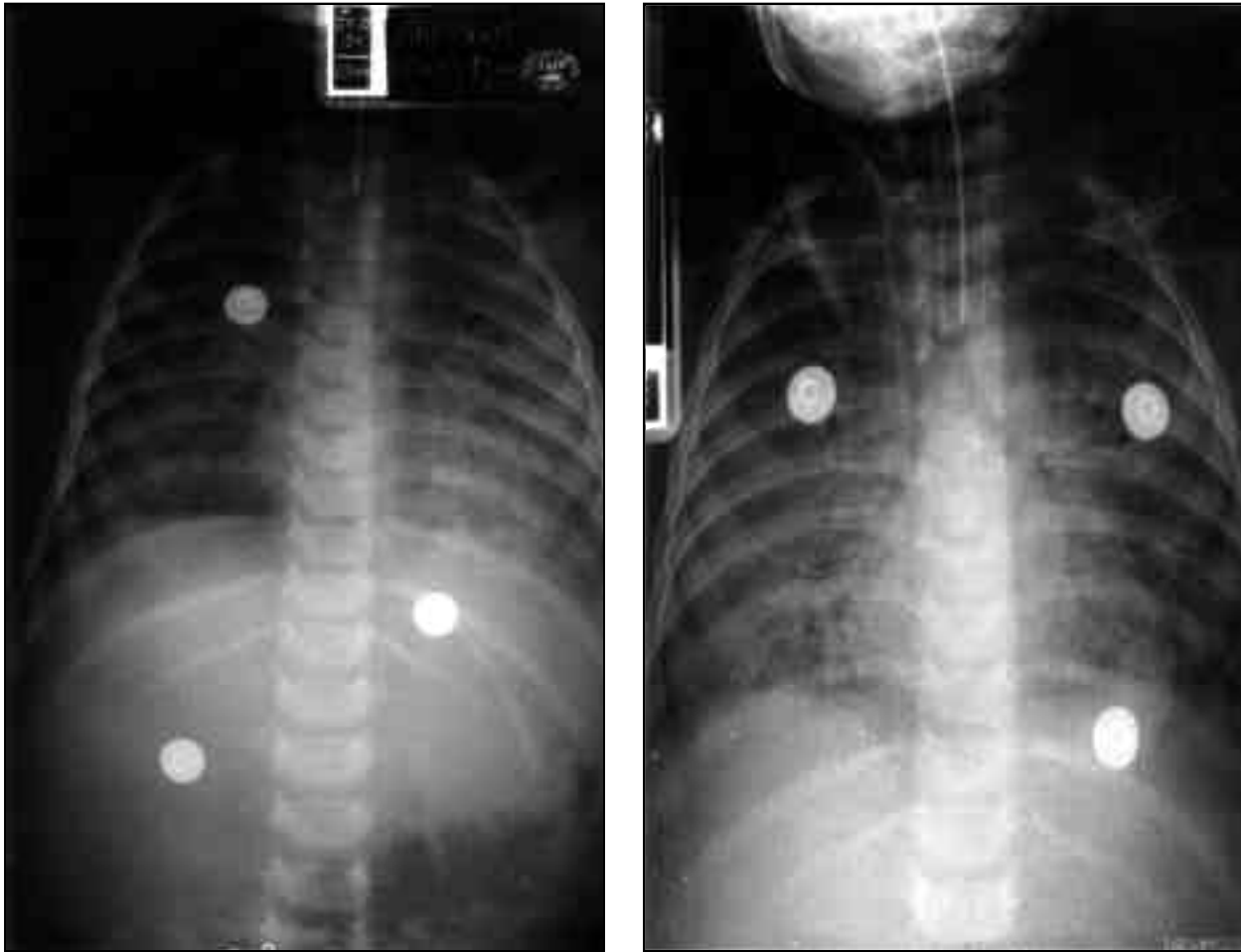


Fig. 1 and 2: Showing bilateral diffuse parenchymal infiltrates of *Pneumocystis carinii* pneumonia.

abnormalities on physical examination. The defining feature of SCID is a defect in specialized white blood cells (B and T lymphocytes) that defend us from infection by viruses, bacteria and fungi^[1]. All forms of SCID are inherited. Almost 50% cases of SCID are linked to the X chromosome passed on by the mother. X linked SCID lymphopenia occurs primarily from the absence of T cells (CD3+) and natural killer (NK) cells^[2]. X linked SCID results from a mutation of the common gamma chain of the interleukin (IL) receptor for IL-2, IL-4, IL-7, IL-9, IL-15 and this protein is encoded on the X chromosome.

Defective IL receptors and IL receptor pathways prevent the proper development of T-lymphocytes^[3]. T-lymphocytes play a key role in identifying invading agents as well as activating and regulating other cells of the immune system (B cells). So in this condition no functional antibody is produced. Autosomal recessive types are Adenosine deaminase (ADA) deficiency, Janus associated kinase 3 (JAK 3) deficiency, purine nucleoside phosphorylase (PNP) deficiency, defective expression of major histocompatibility (MHC) complex antigen, IL-2 deficiency, Zap-70 protein tyrosine

kinase (PTK) deficiency, reticular dysgenesis and Omenn syndrome.

Adenosine Deaminase (ADA) is the most common cause (20% of all SCID, 30-50% of autosomal recessive SCID) of SCID. The gene for ADA is located on chromosome 20 q. Accumulation of adenosine and 2-deoxyadenosine and its derivatives is toxic to lymphocytes^[4].

JAK3 deficiency is associated with lymphopenia due to absent or reduced T cells and NK cells. In PNP deficiency there is lymphopenia due to death of T cells from accumulation of toxic metabolites in the purine salvage pathway and differs from ADA deficiency as there are circulating B cells that are unable to produce antibodies. In IL-2 deficiency T cell numbers are rarely affected but fail to proliferate *in vitro* with mitogen stimulation unless IL-2 is added to the medium and is often associated with other cytokine production defects; the functional antibody production is reduced. In Omenn syndrome there are normal or elevated T cells of maternal origin, undetectable B cells^[5], poor antibody production, eosinophilia, high immunoglobulin E and TCR recombinase genes (Rag 1, Rag 2 genes) are believed to be responsible. MHC deficiency is

Table 1: Shows a summary of investigations and normal values

Investigations	Results	Normal values
Hematological:		
Hb	101 gm/l	105 - 120 gm/l
Total WBC count	14.3 x 10 ⁹ /l	6 - 17x 10 ⁹ /l
Polymorphs	75%	32%
Lymphocytes	19.7%	60%
Monocytes	4.9%	5%
Eosinophils	0.2%	3%
Basophils	0.2%	0 - 0.75%
Platelets	606 x 10 ⁹ /l	150 - 300x10 ⁹ /l
Immunological:		
IgG	< 0.33 g/l	2.85 - 7.6 g/l
IgM	< 0.07 g/l	0.14 - 0.76 g/l
IgA	0.11 g/l	0.28 - 1.1 g/l
T-cell, B-cell function and detailed immunological study	MHC class II deficiency	
Biochemical:		
AST	28 IU/l	15 - 55 IU/l
ALT	18 IU/l	5 - 45 IU/l
Urea	2.2 mmol/l	1.8 - 6.4 mmol/l
Creatinine	23 umol/l	18 - 35 umol/l
Calcium	2.4 mmol/l	2.2 - 2.7 mmol/l

associated with defective T and B cell immunity and belongs to class I (HLA-A,-B,-C) and class II (HLA-DR,-DQ,-DP) antigen deficiency. Isolated class I deficiency also known as bare lymphocyte syndrome can be milder and may present at a later age. MHC class II (the deficiency that our patient was suffering from) can present in early infancy with persistent diarrhea, pneumonia and septicemia due to virus, bacteria, *Pneumocystis carinii*, or *Candida*. Lymphocytopenia if it occurs is only moderate and has very low number of CD4+ T cells with normal or even elevated CD8+ T cells^[6]. The MHC class II antigens are undetectable on B cells and monocytes and patients are hypoglobulinemic due to impaired antigen-specific response caused by the absence of these antigen presenting molecules. The thymus and other lymphoid organs are severely hypoplastic.

Without stem cell transplantation, death from infections usually occurs within the first two years of life^[7].

The clinical features of our patient were typical of autosomal recessive SCID. She presented to us

with repeated severe pneumonia needing frequent admissions and panhypoglobulinemia on investigation.

A diagnosis of agammaglobulinaemia was considered. However, a flow cytometry immediately distinguishes between B cell deficiencies and lack of mature T cells which supports the diagnosis of SCID^[8]. Our patient was investigated further by the pediatric immunologist and was found to have MHC type II deficiency. She was started on daily oral antibiotic prophylaxis, monthly IV immunoglobulin until stem-cell transplantation could be done. The hallmark of treatment of SCID is either bone marrow or stem cell transplantation early in life to reconstitute the defective immune system. Patient needs stabilization with antibiotics, antifungals, immunoglobulins and nutritional support prior to bone marrow transplantation.

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