A case report on severe combined immune deficiency: A rare inherited pediatric disorder

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ABSTRACT

Severe combined immune deficiency (SCID), also known as alymphocytosis, Glanzmann-Rinker syndrome, and thymic alymphoplasia, is characterized by impairment in the differentiation of T, B lymphocytes, and natural killer cells. Adenosine deaminase deficiency is the most common cause of SCID, as it leads to dysfunction of T, B lymphocytes and severe lymphopenia. Due to the severity of the disease, early diagnosis is essential to provide desired treatment and get a good therapeutic outcome. They need special treatment to strengthen the immune system and improve the chance of survival such as hematopoietic stem cell transplantation and enzyme replacement therapy (ERT). We present the case of a 4-month baby, born to a consanguineous couple with altered vitals and symptoms pertaining to immunodeficiency, and were on empirical antibiotic therapy and supportive care therapy to control opportunistic infections and stabilize the patient. This case report gives a brief insight into SCID.

Key words: *Bone marrow transplant, Deficiency, Enzyme replacement therapy, Immune, Lentiviral gene therapy, Severe combined immune deficiency*

Severe combined immune deficiency (SCID), also known as alymphocytosis, Glanzmann-Rinker syndrome, and thymic alymphoplasia, is the most severe form of primary immunodeficiencies. There are now at least nine different known genes in which mutation leads in the form of SCID. It is also known as the bubble boy disease because its victims are extremely vulnerable to infectious diseases [1]. SCID is the result of a compromised immune system that is considered almost absent. X-linked SCID (X-SCID) is an immunodeficiency in which the body produces very few T-cells and natural killer (NK) cells [2]. In ADA deficiency 16% of cases were autosomal recessive with profound lymphopenia. Purine nucleoside phosphorylase (PNP) deficiency related to the PNP gene leads to elevated deoxyguanosine triphosphate levels resulting in T-cell toxicity and deficiency. ZAP70 deficiency characterized by the lack of CD8+ and the presence of circulating CD4+ which are unresponsive to a T-cell receptor-mediated stimuli. Janus kinase-3 is an enzyme that mediates the transduction downstream of the gamma chain signal [3,4]. Signs and symptoms like congestion, airway infection, oral ulcers , ear infections and Lung infections like pneumonia causing breathing problems can even lead to death. Whereas digestive problems like vomiting and diarrhea are observed. SCID may cause bone-related problems [5].

CASE REPORT

A male patient of age 4 months born to second-degree consanguineous parents was admitted in the hospital with complaints of cold, cough (dry intermittent) more sensitive during the night, difficulty in breathing, poor feeding, and decreased urine output for 2 days.

On examination, the patient was febrile (TEMP – 100.6*F), maintaining saturation with 60% of oxygen, his heart rate was170 bpm, and blood pressure was 96/68 mmHg. Pallor and respiratory distress were present. On auscultation of the chest, air entry was bilateral equal with crept. Weight on admission was 4.3 Kg and the blood group was “B” positive. At various sessions of the treatment, complete blood picture (CBP), peripheral smear test, and liver function tests were different. Details are shown in Tables 1-3.

In Fig. 1, the first and second chest X-rays were taken during the first session of treatment. Here, the first X-ray shows mild lower respiratory tract infection (LRTI) and the second X-ray shows bilateral patchy infiltration. The third X-ray was taken in the second session in which perihilar infiltration was observed. Hyperinflated lungs and interstitial pneumonitis were seen in the fourth X-ray, considered during the third session. In 4th session through X-rays 5 and 6 spur like appearance of scapula,widening

Table 1: Session-wise variability in major complete blood picture components

Investigation (normal range)	1st session	2nd session	3rd session	4th session
Hemoglobin (10–13 g%)	6	9.5	9.1	13.5
Red blood cells (4.5–5.5 mill/mm^3)	2.7	3.8	3.6	4.6
White blood cells (4500–10,000/mm^3)	43,000	73,000	6800	10,400
Packed cell volume (40–48 vol%)	20	30.1	27.9	38.3
Platelet (140,000–450,000/mm^3)	340,000	87,000	69,000	27,000

Table 2: Session-wise variability in peripheral smear test

Components	1st session	2nd session	3rd session	4th session
RBC	*Microcytic *Polychromasia+*Occasionally nucleated	*Normocytic *Norm chromic	*Normocytic *Norm chromic *Anisocytosis	*Normocytic *Hypochromic
WBC	Leukocytosis	Neutrophilic leukocytosis	Normal	Normal
Platelets	Adequate	Mild thrombocytopenia	Moderate thrombocytopenia	Chronic thrombocytopenia

Table 3: Session-wise variability in liver function test

Investigations (normal range)	1st session	4th session
Serum glutamic-oxaloacetic transaminase (20–60 IU/L)	246 IU/L	462 IU/L
Serum glutamic pyruvic transaminase (5–45 IU/L)	55 IU/L	85 IU/L
Protein (5.9–7 g/dl)	4.1 g/dl	3.9 g/dl
Albumin (3.4–4.2 g/dl)	2.2 g/dl	1.9 g/dl
Albumin/globulin ratio (1.4–3.4)	1.1	1.1

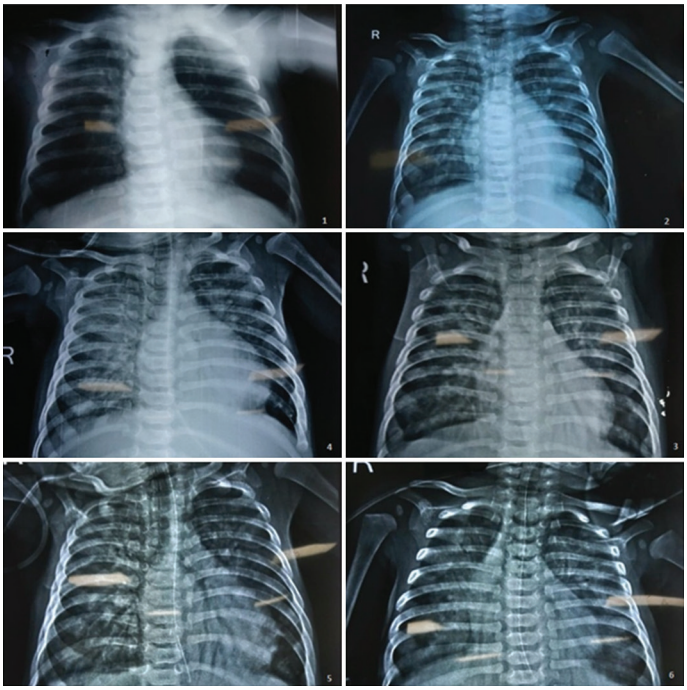

Figure 1: Chest X-rays 1and 2 were taken during the 1st session of treatment. Here, X-ray-1 shows that there is mild lower respiratory tract infection and X-ray-2 shows bilateral patchy infiltration. X-ray-3 was taken in the 2nd session in which perihilar infiltration was observed. Hyperinflated lungs and interstitial pneumonitis were seen in X-ray-4 considered during the 3rd session. In the 4th session through X-rays 5 and 6, spur-like appearance of scapula, widening of costochondral junctions, heart contours obliterated by bilateral interstitial opacities, and absence of thymic silhouette were observed

of costo chondral junctions, heart contorus obilaterated by bilateral interstitial opacities,abscence of thymic silhouette was observed (Fig. 1). In Fig. 2, mild ascites and interstitial atresias were found. Hereditary multiple intestinal atresia (HMIA) is a rare cause of intestinal obstruction in humans which is associated with a profound combined immunodeficiency. HMIA is a presumed autosomal recessive disorder. Besides the gastrointestinal (GI) tract, HMIA also affects the thymus, lungs, spleen, and liver.

LRTI with respiratory distress, failure to thrive with severe anemia, was considered as the provisional diagnosis for the first session of the treatment and started on intravenous (IV) antibiotics (inj. Piptaz 430 mg iv 3 times daily [TID], inj. Linezolid 45 mg iv TID), IV fluids (2/3rd maintenance), oxygen support 1 l/min, frequently nebulized with Levolin (0.31 mg, 6th hourly), and normal saline 3% (2 ml 6th hourly). In view of anemia (Table 1), the baby was given one unit of leukocyte-reduced red blood cells 65 ml over 5 h, Syp. Azee (2 ml, OD), and Syp. Fluvir (1.8 ml, BD). The patient's father was counseled regarding the baby condition and intensive care requirement.

The baby was shifted to PICU in view of increased anemia, respiratory distress, and oxygen requirements for the second session of treatment. The same treatment was continued initially followed by symptomatic relief with antacid (inj. Pantop 20 mg OD) and antipyretic (inj. Pcm 1 g BD). GI study is shown in Fig. 2. Since oxygen requirement increased, 5 L of oxygen mask was used. In the third session of the treatment, probiotics were introduced as the baby developed loose stools, IV antibiotics were upgraded (inj. Meropenem and inj. Colistin), and inj. fluconazole was given. Blood parameters were regularly monitored. Immune deficiency panel showed IgG total 62.1 mg/dl (232–1411 mg/dl). The baby received 20% albumin transfusion in view of low albumin, as mentioned in Table 3. During the fourth session of treatment, the baby developed generalized seizures for which inj. Midazolam and inj. Levipil were provided. Inj. Septra was prophylactic to treat pneumocystis, as mentioned in Fig. 1.

Primary immune deficiency test showed absolute leukocyte count 3.7 microL (4–12 microL), CD3% 96% (51–77%), absolute CD19+B cells count 83 cell/microL (430–3000), CD19% 2.4%

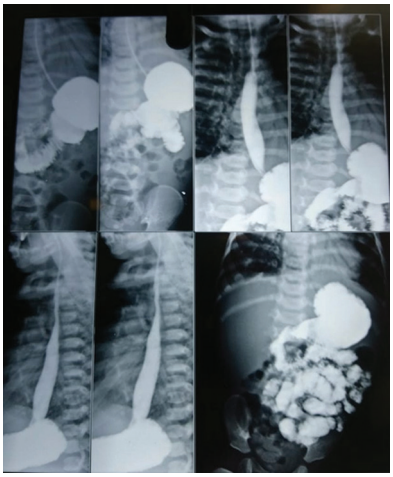

Figure 2: Gastrointestinal (GI) study of the patient in which mild ascites and interstitial atresia were found, hereditary multiple intestinal atresia is a rare cause of intestinal obstruction in humans associated with a profound combined immunodeficiency. Hereditary multiple intestinal atresia (HMIA) is presumed autosomal recessive disorder. Besides GI tract, HMIA also affects thymus, lungs, spleen, and liver

(11–41%), absolute CD56+NK cells 20 cells/microL, CD56% 0.54%(3–14%), absolute CD3+CD4 count 1280 (1800–4000), and CD8% 34.4% (12–23%) indicating severe lymphopenia. Thus, all the above-mentioned (chest X-ray, CBP, immunodeficiency test, and GI study) reports were discussed with consultant pediatric hemato-oncologist who opined it as SCID. Thus, parents and the family were counseled regarding diagnosis; also, the genetic counseling was done for future pregnancies.

The patient's oxygen saturation and hemodynamic status were regularly monitored for further hospitalization and treatment. The patient was discharged and shifted to another hospital where there was a proposal for bone marrow transplant, but the baby succumbed to death while therapy was under process.

DISCUSSION

SCID is a genetic syndrome characterized by a profound deficiency in cell-mediated and humoral immunity. Clinical manifestation begins in an early stage of life such as opportunistic infections; failure to thrive, diarrhea, etc., are common in primary immunodeficiency [6].

Pre-SCID was first reported in 1950 by Swiss pediatricians Glanzmann and Rinker [7]. The prevalence of SCID around the world is 1 in 100,000 births [8]. In the past decade, about 50 cases were noted in India [9]. Babies with SCID suffer from recurrent infections. The treatment and prevention of infections would prolong their life. They need special treatment to strengthen the immune system and improve the chance of survival. These treatments include hematopoietic stem cell transplantation (HSCT), enzyme replacement therapy (ERT), and lentiviral gene therapy.

HSCT is also called as bone marrow transplant. A bone marrow transplant works best when certain markers from donor match to a recipient. About 95% of the babies treated with HSCT are newborns who survive and develop a working immune system [10]. ERT is used in replacing the missing enzyme in the patient with a man-made version. It requires long-term therapy in such cases throughout life. ERT may vary based on so many factors but priory based on the type of SCID [11]. In the present case, the cause of SCID was genetic as the parents were the second degree consanguineous. A similar case was reported by Bobby *et al.* [12]. The initial diagnosis and treatment provided also resembled in a study done by Rosen [13]. Lentiviral gene therapy uses a harmless virus to insert a missing gene called IL2RG into bone marrow cells taken from infants with X-SCID disorder. The first X-SCID gene therapy trial two decades ago at first appeared successful, but some patients later developed leukemia because the new gene activated a cancer gene. The scientist reports that the new study used a safer virus as well as chemotherapy to make room for the repaired cells, a step that more effectively restored the infants' immune systems.

Fig. 1 explains about the variation in the respiratory tract on the progression of the disease from the first session to the fourth session, similar diagnostic report was noted in Gennery *et al.* [14] and Giraud *et al.* [15]. Fig. 2 shows multiple intestinal atresia which is associated with combined immune deficiency. This was also observed in a study done by Ali *et al.* [16]. During the fourth session, antibiotics were given prophylactically to treat pneumocystis, this resembled a study by Irashah [17]. Primary immune deficiency panel showed decreased CD4, CD8, absolute leukocyte count, etc. This kind of report was also noted in report done by Therasecole *et al.* [18]. In the end, the 653 patients had died while treatment for bone marrow transplantation was under process [19]. If there was an early diagnosis, the patient might have survived [20].

CONCLUSION

SCID is a pediatric emergency where the early diagnosis may result in a better prognosis. Early diagnosis allows adapted care before life-threatening infections or complications enable prompt referral to bone marrow transplant before the occurrence of end-organ damage or secondary infective complications.

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