Case Reports

Severe Combined Immunodeficiency

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Severe combined immunodeficiency syndrome (SCID) is a rare life threatening primary immunodeficiency. Absent tonsils and absent thymus are key clinical markers that may point to the diagnosis. We report a series of 3 cases of SCID who presented with recurrent infections and failure to thrive.

Keywords: *Immune, Deficiency.*

Severe combined immunodeficiency syndrome (SCID) is a rare genetic disorder (incidence of 1 in 5,00,000) characterized by defective or absent T cell and B cell function(1,2). Children with SCID usually present in the first 6 months of life with sepsis, disseminated tuberculosis following BCG vaccine, candidiasis, *Pneumocystis carinii* pneumonia, severe viral infections, chronic diarrhea, failure to thrive and malabsorption(3,4). SCID is often fatal within the first year of life unless bone marrow transplant or hematopoietic stem cell transplant is done(5). SCID is classified into 2 major groups: those without T cells and B cells (T-B-) and those with B cells (T-B+)(5). T-B+ SCID is usually inherited as X-linked recessive disorder but rarely can be an autosomal recessive due to Jak 3 kinase deficiency(6). However, T-B- SCID occurs equally in boys and girls(5). We report a series of 3 cases of SCID who presented to us in infancy with severe, multiple infections and diagnosis of SCID was confirmed by serum immunoglobulin levels and enumeration of T, B and NK cell numbers.

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Case Reports

Case 1

A 3-month-old boy third in birth order born of non-consanguineous marriage presented with recurrent diarrhea and failure to thrive requiring 3 hospitalizations in past. He was born at full term with a birth weight of 3.25 kg and was on exclusive breast feeds. He had received BCG and 1st dose of OPV and DPT. The index case had two elder sisters. The eldest of them was small for gestational age, had chronic diarrhea, failure to thrive and died at 2 months of age. The other sister died at 9 months of age due to pneumonia.

On examination, weight was 2.7 kg and length was 49 cm. He had triangular facies, tonsils were absent and no BCG scar was seen. There was no rash, lymphadenopathy or organomegaly. His hemogram showed total leucocyte count of 6,300 cells/cumm with absolute lymphocyte count of 1575 cells/cumm. *X*-ray chest showed no evidence of thymus. HIV ELISA was negative. In view of borderline lymphocyte counts, absent tonsils and recurrent infections with failure to thrive, a primary immunodeficiency was suspected. His lymphocyte subsets and serum immunoglobulins were suggestive of T-B+NK- SCID

(*Table I*). He had three more episodes of diarrhea and succumbed to the disease at 9 months of age.

Case 2

A 4-month-old boy born of third degree consanguineous marriage presented with breathlessness since eight days and failure to thrive. He was hospitalized twice for pneumonia. He was third in birth order and other two children were asymptomatic. On examination, weight was 3.5 kg, length was 52 cm, rectal temperature was 100ºF and respiratory rate was 46/minute and he had bilateral crepitations. He had a perianal candidial rash with no organomegaly. Tonsils were absent. His *X*-ray chest was suggestive of interstitial pneumonia and thymus was not seen. Blood, stool and urine culture grew *Candida albicans*. His hemogram showed total leucocyte count 10,500 cells/cumm with absolute lymphocyte count of 3,780 cells/cumm. His HIV ELISA, TORCH IgM and IgG were negative. In view of systemic candidiasis, a primary immuno-deficiency was considered. His investigations suggested T- B+NK- SCID (*Table I*). He was treated with IV amphotericin B and discharged on oral flucanozole, trimethoprim sulphamethoxazole prophylaxis and advised to avoid live vaccines.

TABLE I–*CD Panel and Immunoglobulin Profile of all 3 Patients*(9).

	Patient 1	Patient 2	Patient 3
Age	3 months Male	4 months male	8 months male
Tonsils	Absent	Absent	Absent
Clinical Features	Recurrent diarrhea, Failure to thrive	Recurrent pneumonia, Failure to thrive	Recurrent pneumonia, Failure to thrive
Lymphopenia	Present	Absent	Present
CD3 (cells/cumm)	172 (Normal for age = 2300-6500)	1846 (Normal for age = 2300-6500)	899 (Normal for age = 2400-6900)
CD4 (cells/cumm)	121 (Normal for age = 1500-5000)	670 (Normal for age = 1500-5000)	327 (Normal for age = 1400-5100)
CD8 (cells/cumm)	2 (Normal for age = 500-1600)	895 (Normal for age = 500-1600)	282 (Normal for age = 600-2200)
CD19 (cells/cumm)	454 (Normal for age = 600-3000)	731 (Normal for age = 600-3000)	1920 (Normal for age = 700-2500)
CD20 (cells/cumm)	ND	Absent	1419
CD16 (cells/cumm)	5	Absent	Absent
CD56 (cells/cumm)	5	Absent	Absent
HLA DR (cells/cumm)	375	ND	ND
IgG (mg/dL)	310 (N = 162-601)	414 (162-601)	>2400 (530-1063)
IgM (mg/dL)	<20 (N = 18-39)	255 (33-126)	>240 (65-110)
IgA (mg/dl)	160 (N = 52-117)	60 (44-840)	48 (38-93)
SCID	T-B+NK-	T-B+NK-	T-B+NK-

ND = Not done.

Case 3

An 8-month-old boy born of non-consanguineous marriage presented with recurrent pneumonia and failure to thrive requiring four hospitalizations in past. He was born at full term with birth weight of 2.5 kg. He was third in birth order and both elder sisters were asymptomatic. He had received BCG and 3 doses for OPV and DPT. On examination, his weight was 5.7 kg and length was 68 cm. He had respiratory rate of 66/ minute with bilateral coarse crepitations. There was no rash and systemic examination was normal. Milk scan for gastroesophageal reflux showed no reflux. Sweat chloride was 17 meq/L (normal range = 0-30 meq/L). *X*-ray chest showed right upper zone consolidation and thymus was not seen. High resolution CT scan of the chest showed focal areas of fibrosis and patchy consolidation. Arterial blood gas showed hypoxia (PO_2 = 60 mm of Hg, Oxygen saturation = 92%) with normal pH. Broncheo-alveolar lavage culture and smear were negative for bacterial, mycobacterial and fungal infection. Hemogram showed total leucocyte count of 10,400 cells/cumm with absolute lymphocyte count of 936 cells/cumm. HIV ELISA was negative. In view of lymphopenia, recurrent pneumonia and failure to thrive, a primary immunodeficiency was suspected and investigations confirmed T-B+NK- SCID (*Table 1*). He was treated with IV amoxycillin/clavulanic acid and trimetho prim sulphamethoxazole (20 mg/kg/d of trimethoprim) along with chest physiotherapy for 21 days and discharged on trimethoprim sulphamethoxazole prophylaxis.

Discussion

SCID was first reported in 1950 by Swiss pediatricians Glanzmann and Riniker(7) and rarely reported in India. Most patients with SCID have thymic hypoplasia and small, poorly developed lymph nodes and tonsils as was seen in our patients. The clinical presentation may differ. One of our patients presented with repeated diarrhea whereas the other two had respiratory symptoms. Patients with SCID usually succumb to recurrent viral, bacterial or fungal infections in infancy as was seen in first patient. Patients with graft versus host disease (GVHD) due to engrafted maternal T cells may present with erythematous maculopapular rash and hepatosplenomegaly which was not seen in any of our patients(4). Diagnosis can be established by enumeration of lymphocyte subsets and immunoglobulins. Most patients with SCID have persistent lymphopenia (<1500 lymphocytes/cumm), CD3+ T lymphocytes count of less than 500 cells/cumm and hypogammaglobulinemia(4) as was seen in 2 of our patients. Serum IgA and IgM levels range from absent to normal to high for age(4). Despite the presence of detectable serum immunoglobulins in some patients, antigen specific antibody production is absent(1).

A diagnosis of SCID is a medical emergency. A high degree of suspicion is essential to suspect SCID. The immediate concern is to bring any current infection under control and to ensure adequate nutrition. Intravenous immunoglobulin may be used to bolster the immune response(8). Prevention of infections is a major step in managing patients with SCID. Prophylactic antibiotics especially trimethoprim sulphamethoxazole to prevent *Pneumocystis carinii* pneumonia may be useful. Children with SCID should not receive live virus vaccines such as oral polio, measles vaccine, chickenpox vaccine and BCG vaccine as such vaccines can cause serious illness or even death. Curative therapy is bone marrow transplant.

REFERENCES

1. Elder ME. T-cell Immunodeficiencies. Pediatr

Clin North Am 2000; 47: 1253-1274.

2. Stephan JL, Vlekova V, Le Deist F, Blanche S, Donadieu J, De Saint-Basile G *et al*. Severe combined immunodeficiency: a retrospective single-center study of clinical presentation and outcome in 117 cases. J Pediatr 1993; 123:564-572.
3. Altare F, Lammas D, Revy P, Jouanguy E, Doffinger R, Lamhamedi S, *et al*. Inherited interleukin- 12 deficiency in a child with Bacille Calmette – Guerin and Salmonella enteritidis disseminated infection. J Clin Invest 1998;102: 2035-2040.
4. Buckley RH, Schiff RI, Schiff SE, Market L, Williams LW, Harville TO, *et al*. Human severe combined immunodeficiency: genetic, phenotypic and functional diversity in one hundred eight infants. J Pediatr 1997; 130: 378-387.
5. Rosen FS. Severe combined immunodeficiency: A pediatric emergency. J Pediatr 1997; 130: 324-325.
6. Macchi P, Villa A, Giliani S, Sacco MG, Frattini A, Porta F, *et al.* Mutations of JAK-3 gene in patients with autosomal severe combined immune deficiency SCID. Nature 1995; 377: 65-68.
7. Glanzmann E, Riniker P. Essentielle lymphocytophthise: Ein neues Krankheitsbild aus der Säuglingspathologie. Ann Paediatr 1950; 175: 1-32.
8. Fasano MB. Risks and benefits of intravenous immunoglobulin treatment in children. Curr Opin Pediatr 1995; 7: 688-694.
9. Gunn VL, Nechyba C. Immunlogic reference values in Harriet Lane Handbook. !6th ed. Mosby, St. Louis, 2002: 313.

Acrodysostosis : Autosomal Dominant Transmission

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We describe a 2½-year-old male child with acrodysostosis, presenting with nasal hypoplasia, peripheral dysostosis (gross shortening of hands and feet), cone-shaped epiphysis, advanced bone age, and mental retardation. He and his mother also had bilateral first ray hyperplasia of the feet thereby expressing the autosomal dominant inheritance pattern.

Key words: *Acrodysostosis, Peripheral dysostosis, First ray hyperplasia of foot.*

Acrodysostosis is a rare skeletal dysplasia, first described by Maroteaux and Malamut in 1968, and since then around 40 cases have been published in the literature(1). Though most case reports have occurred sporadically, it is believed to be an autosomal dominant condition. In this report we are presenting the first case with autosomal dominant inheritance pattern of acrodysostosis from India.

Case Report

A 2½-year-old male child with psychomotor delay was referred for evaluation. He was born to a 24-year-old primigravida mother and a 37-year-old father and weighed 2500 g at birth. There was no history of consanguinity.

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