An Analysis of Omenn Syndrome– A Rare Combined Immunodeficiency Syndrome

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Abstract

Omenn Syndrome is a rare combined immunodeficiency syndrome manifested mainly by generalised erythroderma, alopecia, loss of eyebrow and eye lashes, generalised oedema and metabolic disturbances. Poor prognosis is reported as it mimics the appearance of severe eczema and immunodeficiency and is under noticed as there is presence of circulating lymphocytes. Understanding the guidelines of prompt diagnosis will facilitate early treatment and improve prognosis.

Keywords: *Omenn syndrome, treatment, guidelines, prognosis.*

Introduction

Omennsyndrome is a rare combined immunodeficiency syndrome classified under 4A01.10 severe combined immunodeficiency in ICD Classification. This rare syndrome was first described by Gilbert Omenn in 1965[1]. The statistics of this disease is not clear, but 1in 58000 babies born with Severe Combined Immunodeficiency (SCID) in US each year and according to Orphanet report series of rare diseases, there are 25 cases of omen syndrome reported through publication in January 2020[2].

Clinical presentation: The babies with Omenn syndrome frequently present with : chronic diarrhoea, pneumonitis, enlarged lymph nodes, failure to thrive, hepatosplenomegaly, pustular rash on extremities, generalised erythroderma, alopecia, loss of eyebrow and eye lashes, generalised oedema and metabolic disturbances due to protein loss through the skin and gut[3].

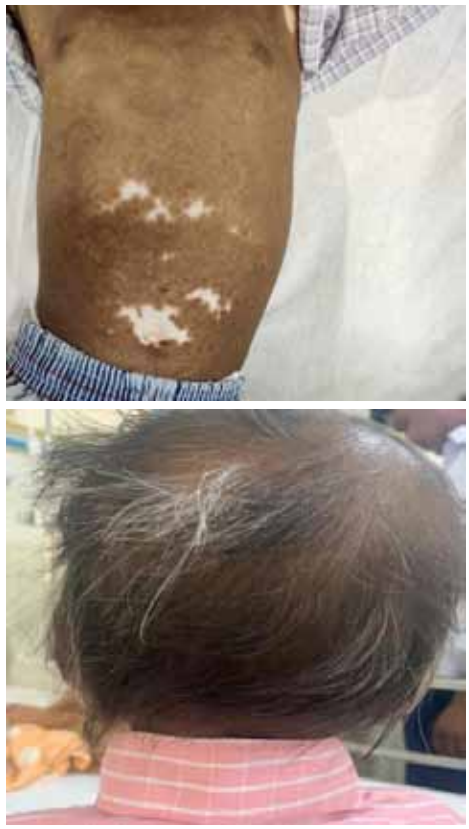

Figure 1: Characteristic clinical features of Omenn syndrome which shows generalised erythroderma and alopecia.

Atypical Omenn syndrome: Few of case reports have described on atypical Omenn syndrome which is manifested as RAG -2 gene mutations where all the

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clinical manifestations of omen syndrome appear except rash, eosinophilia, and elevated IgE. One report was presenting atypical omen syndrome with Adenosine Deaminase (ADA) Deficiency[4].

Associated Syndromes: There will be associated syndromes in babies suffering from Omenn syndrome which makes the prognosis poor. The associated syndromes reported through various case reports are:

1. Cartilage hair hypoplasia: This is an associated autosomal recessive inherited disorder manifested as short limb dwarfism, fine sparse hair and abnormal immune system[5].
2. Adenosine Deaminase Deficiency: A metabolic disorder with mutations in the ADA gene causes immunodeficiency
3. Digeorge syndrome: Digeorge syndrome involves deformity of heart, parathyroid and is a congenital anomaly characterized by defects mainly from 3rd and 4th pharyngeal pouches.
4. Colomboma of eye: Colomboma means defect is manifested by a hole in any one of structures of the eye like iris, retina, choroid, or optic disc.
5. Cardiovascular abnormalities: An infant with Omenn syndrome usually found to have biventricular hypertrophy, impaired left ventricular systolic function, and severe sinus bradycardia, possibly secondary to endomyocardial disease caused by eosinophilia[6]
6. Growth retardation
7. Sensory problems
8. CHARGE syndrome: Coloboma, Heart Defect, Choanal Atresia, Growth Or Development Retardation, Genital Hypoplasia, Ear Anomaly Or Deafness
9. Ligase 4 deficiency: A mutation in LIG 4 Gene affects the major mechanism of DNA double strand break repair.

Diagnostic Measures:

Type of evaluation	Major findings
Laboratory evaluation	Normal or high lymphocyte count
	Eosnophilia is invariably present[7,8]
	Flow cytometry shows presence of an oligoclonal set of activated antigen-stimulated Th2 cells, B cells are absent and natural killer cells are present. Normal distribution of CD4/CD8 or predominant CD8.
	Elevated IgE and IgG levels

Type of evaluation	Major findings
Imaging studies	Thymus is absent
Other findings	Mutational analysis for RAG-1 and RAG-2 to permit genetic counseling and prenatal diagnosis in subsequent pregnancies[9]
	Serum interleukin 4 (IL-4) and interleukin 5 (IL-5) levels are typically increased. In vitro cells produce decreased levels of IL-2 and interferon-gamma (IFN-γ) compared with the elevated IL-4 and IL-5 production by Th2 cells.

Skin biopsy, lymph node biopsy, fluorocytometric analysis of peripheral blood lymphocytes, lymphocyte mitogen assays and Bronchoscopy can be done further for diagnosis[10].

Treatment: Symptomatic treatment can be done but the prognosis is reported as poor in many of the case reports. The only treatment modalities which can be adopted arebone marrow transplantation and stem cell transplantation[11].

Why poor prognosis is reported: Many times the symptoms of Omenn syndrome mimic the appearance of severe eczema and immunodeficiency are under noticed as there is presence of circulating lymphocytes. These children will be treated with steroids and referral services are assured properly due to the wrong diagnosis. A case report of a 5 year old boy with symptoms of diffuse erythrodema and pustular rash on extremities reports that the rash was incorrectly diagnosed as erthyema toxicum versus transient neonatal pustular melanosis. This case

was later identified as Omenn syndrome through the diagnosis of T-B-NK1 SCID and Chimerism testing[12,13].

Guidelines to be followed for better prognosis:

- If a newborn baby manifests signs associated with Omenn syndrome, evaluate T cells, B cells and natural killer cells (NK).
- Determine the origin of T cells using Chimerism studies
- Prompt immunosuppressive therapy
- Define the genetic aetiology

These guidelines will help the health professionals for prompt diagnosis and facilitate early treatment[14].

Conclusion

Early newborn screening, prenatal counselling and genetic counselling play an important role in preventing and early identification of SCID's. It is important to understand regarding Omenn syndrome by the health care professionals and able to diagnose them accurately at the earliest. It will enhance the initiation of treatment at the earliest and improve the prognosis.

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