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Original Article

A Case Series of Omenn Syndrome in Iranian Children

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Abstract

Background: Severe combined immunodeficiencies (SCIDs) are a group of disorders with variable clinical phenotypes, usually presenting with life-threatening infections. This type of immunodeficiency results from defective differentiation of hematopoietic stem cells into mature T lymphocytes leading to various identified affected genotypes of severe immunodeficiency. Omenn syndrome is an autosomal recessive immunodeficiency disorder characterized by generalized erythroderma, lymphoadenopathy, and eosinophilia. The aim of this study was to provide specific information about the clinical, immunological, and genetic characteristics in this context.

Methods: A retrospective case review was conducted at Shahid Beheshti, Children Medical Center and Azad University Hospitals of Tehran so that the patients with a previously diagnosis of Omenn syndrome, admitted between years 2016 and 2023, were selected and included in this study.

Results: Eleven patients with known Omenn syndrome were included in our study. The mean age of onset in the patients was 45 days old. Six (54.5%) were female and 5 (45.5%) were male. There was a history of parental consanguinity in 10 out of 11 studied children (91%). BCG dissemination, erythroderma, hepatosplenomegaly, lymphadenopathies, failure to thrive, recurrent infections, and gastrointestinal manifestations were more prominent. Other presentations in order of frequency were failure to thrive (90.9%), recurrent infections (63.6%), erythroderma (63%), hepatosplenomegaly (45.5%), lymphadenopathy (36.4%), and BCG dissemination (27.3%).

Conclusion: As Omenn syndrome is a type of SCID and a pediatric immunologic emergency, awareness about the various clinical manifestations of the disease among people of different ethnicities is highly essential for timely and accurate diagnosis, treatment, and family counseling.

Keywords: Omenn Syndrome; Primary Immunodeficiency; Severe Combined Immunodeficiency; SCID

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Introduction

Severe combined immunodeficiencies (SCIDs) are a genetically heterogenous group of disorders with variable clinical phenotypes, usually presenting with life-threatening infections (1). This type of inborn error of immunity results from defective differentiation of hematopoietic stem cells into mature T lymphocytes with or without involvement of other lymphoid lineages, leading to various identified affected genotypes of severe immunodeficiency. Depending on the gene and the affected pathway, SCIDs are characterized by absent / low or dysfunctional T cells along with affected B or NK cell numbers. Omenn syndrome is classified as a type of SCID because of recurrent viral and fungal infections, chronic diarrhea, and failure to thrive (2). Omenn syndrome is caused by an incomplete block of T cell development (3). Features, such as lymphadenopathies, increased IgE levels, eosinophilia, and normal or elevated T cell counts, may initially complicate SCIDs diagnosis. The underlying defect typically results from hypomorphic mutations in V(D) J recombination, leading to a downstream effect on abnormal T and B cell development (4) and oligoclonal expansion of autologous T cells with end-organ infiltration and damage (3). The first genetic causes associated with the classical form of Omenn syndrome were hypomorphic RAG1 or RAG2 mutations as well as DCLRE1C and LIG4. However, some leaky SCID patients have been identified with hypomorphic mutations in other genes, including ADA, IL2RG, IL7R, AK2, or RMRP, which may lead to the clinical features of Omenn syndrome with severe impairment of T cell development, yet without the characteristic B-cell deficiency (5).

The autoimmune features of Omenn syndrome emphasize the potential role of T cell tolerance impairment in inducing the immune dysregulation. The pathogenesis of autoimmune manifestations is attributed to the defective thymic epithelial cell maturation, impaired AIRE protein expression, and poor generation of regulatory T cells (6). Furthermore, serum autoantibody is suggestive of defaults in B cell selection and tolerance, and therefore showing the concomitant role of B cells in the pathology of autoimmunity caused by Omenn syndrome (6).

In this study, the presentations of Omenn syndrome in Iranian children were evaluated to provide specific information about the clinical, immunological, and genetic characteristics in this context.

Methods

A retrospective case review was conducted at Shahid Beheshti, Children Medical Center and Azad University Hospitals of Tehran so that the patients with a previously diagnosis of Omenn syndrome, admitted between years 2016 and 2023, could be selected and included in this study. The study was approved by the Ethics Committee of Islamic Azad University of Medical Sciences with the referral code of IR.IAU.TMU.REC.1402.175. Only eleven patients had been diagnosed according to IUIS criteria to be included in the current study. Chart reviews were prepared for demographic information, past medical history, clinical manifestations, laboratory tests, genetic evaluations, available therapies, and the patients' status up to the time of the study.

Results

Eleven patients with known Omenn syndrome were included in our study. The age of onset in all the patients was before the third month of life with a mean age of 45 days. Six (54.5%) were female and 5 (45.5%) were male. There was a history of parental consanguinity in 10 out of 11 studied children (91%) with Omenn syndrome.

Among the clinical manifestations of the children admitted with the diagnosis of Omenn syndrome, the following signs and symptoms were recognized or reported more frequently. BCG dissemination, erythroderma with or without peeling, hepatosplenomegaly, lymphadenopathies, failure to thrive, recurrent infections, and gastrointestinal manifestations, including non-bloody watery diarrhea, vomiting, oral food intake intolerance and bloating, were more prominent. From the above-mentioned presentations, gastrointestinal manifestations were the most frequent with a 100% occurrence in the studied patients in our study. Other presentations in order of frequency were failure to thrive (90.9%), recurrent infections (63.6%), erythroderma (63%), hepatosplenomegaly (45.5%), lymphadenopathy (36.4%), and BCG dissemination (27.3%).

The first presentations of the disease were skin involvements of various types (including rash, erythroderma, and staphylococcal scalded skin syndrome), gastrointestinal manifestations, or BCG lymphadenitis.

The evaluation of the final outcome of the studied children showed that unfortunately six patients passed away, one received hematopoietic stem cell transplantation and was alive at the time of the study, one in the waiting list of stem cell transplantation, and the remaining three were missing in their follow-up course.

The initial immunodeficiency work-up revealed leukocytosis and eosinophilia (5% to 50%) in all the patients. Serum immunoglobulins levels, including IgG, IgA, and IgM, were lower than those of healthy individuals at the same age range. IgE, as a diagnostic marker in Omenn syndrome, was high in most of the patients (**Figure 1**).

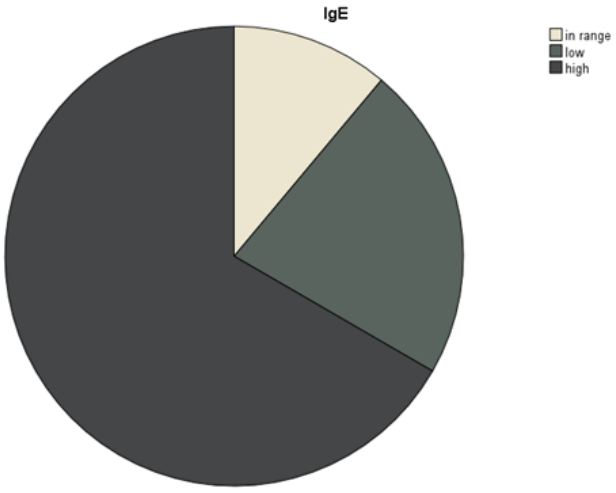

Figure 1. The distribution of IgE values in the studied patients

By flow cytometry analysis, the CD markers for immunophenotyping of T cells and their subtypes were evaluated in these patients. Among the patients in the current study, only three showed T lymphocytosis with CD3 predominance and the other patients revealed a lower CD3 T cell counts compared to healthy children in the same age group. This was also true for CD4 T cell counts in the patients as 6 of them showed significant decrease in these cell types. Likewise, CD8 T cell counts were also significantly decreased and only three patients had normal counts (**Table 1**).

Hemoglobin was evaluated next, the results of which showed lower levels compared to normal children. The lowest detected hemoglobin was 4.30 with a mean of 9.8±2.14. However, the interpretation of this finding should be carried out with caution. Since all infants in this age group physiologically suffer from an age dependent anemia, this finding cannot necessarily be attributed

Table 1. CD markers (%) in the studied patients.

		CD3	CD4	CD8	CD16	CD56	CD19	CD20
N	Valid	10	11	10	7	6	10	7
	Missing	1	0	1	4	5	1	4
Mean		42.6410	32.0845	9.7520	24.8171	20.2867	17.6780	14.2529
Range		91.50	81.00	28.66	72.18	40.22	59.00	59.13
Minimum		1.50	3.00	.34	5.27	1.20	.60	.87

to Omenn syndrome as the cause of this chronic disease.

Discussion

This study is a report of eleven patients presenting with an Omenn syndrome phenotype. Omenn syndrome is rare and inherited in an autosomal recessive pattern with an early onset in young infants and children (7). Considering the autosomal recessive pattern of the inheritance, an equal distribution of this disease is expected in both genders. However, the number of female patients was slightly more than males in this study, which could be simply attributed to the small sample size. Since Omenn syndrome is an inherited genetic disorder, it is expected to occur in children with a family history of parental consanguinity which was detected in all patients except one. Therefore, in the case of such diagnosis, not only the patients' index case samples but also those of their parents as well as siblings should be subject to genetic analysis. All the patients in this study were under three months of age at the onset of the disease, which was in line with previous studies (8).

Since Omenn syndrome is categorized as a severe combined immunodeficiency, these patients typically present with early onset opportunistic infections (5, 9). The patients of the present study were mainly admitted to hospitals due to recurrent severe infections and their complications (e.g. pneumonia, otitis media, and dehydration). Gastrointestinal involvement presenting with persistent watery non-bloody diarrhea, vomiting, poor feeding, failure to thrive, hepatosplenomegaly, and lymphadenopathy were found in these patients in order of frequency. These gastrointestinal presentations were attributed to lymphocyte infiltration of the gut (10) as the major cause along with secondary infections of the organ due to the underlying primary immunodeficiency.

Severe skin involvements presenting with erythrodermic scaly eruptions with the typical rash development due to the same pathologic lymphocyte infiltration of the skin is usually found in the first few weeks of life in children with Omenn syndrome (11). The same was found in most of the (63.6%) patients of the current study along with recurrent infections and various gastrointestinal involvements.

One of the most common presentations in our studied patients was the development of unusual reactions to BCG immunization. This vaccine is routinely administered to newborns in endemic settings at birth for the prevention of meningitis and disseminated TB and has proved to be highly effective against these infections. The high rate of BCG infection in the patients of this study was attributed to this routinely administered vaccine at birth when the immune system health status of babies is still unknown. Studies from other parts of the world where this vaccine is not routinely administered have not reported such complications.

The complications observed in our studies patients after this immunization were suppurative or non-suppurative lymphadenitis, lymphadenopathies, and disseminated tuberculosis infection as the most severe presentation. Poor wound healing after surgical resection of lymphadenopathies was another complication in these patients. In addition, disseminated tuberculosis necessitating multi-drug prescriptions further aggravated the course of the disease due to the medication adverse effects, such as drug allergy and transaminitis.

Another finding of this study was autoimmune manifestations presenting with erythroderma and hepatosplenomegaly. Alopecia was not common among the patients, which could be attributed to their young age at the onset of the syndrome.

The lab tests results showed that anemia was the most common abnormality, which could be explained as physiologic anemia, commonly expected in this age group of infants, and not as the anemia of chronic disease. Consistent with previous findings, Eosinophilia and higher IgE levels were significant in the patients of this study as well (2). Most of the patients in this study had normal (54.5%) or increased (45.5%) lymphocyte counts and only one of them was lymphopenic (WBC=3000). Omenn syndrome in the studied patients was substantiated based on the number of T cells. Since Omenn syndrome is an inherited disorder, Omenn phenotype can be attributed to various genotypes. Therefore, genetic analysis appears to be helpful in confirming the diagnosis by revealing defective genomic rearrangement of genes in T cell and B cell receptors (10). Unfortu-

nately, further genetic tests were carried out only in two of the patients, the results of which showed a missense mutation in IL-7R in both infants with their parents having a heterozygous mutation. This mutation has been previously identified in other studies as well (12, 13).

In regard with the limitations of the current study, this was a retrospective study by analyzing the patients' previous records at hospitals and some of the records were not comprehensive enough. The sample size was also small for such a case series study.

Conclusion

As Omenn syndrome is a type of SCID and a pediatric immunologic emergency, awareness about the various clinical manifestations of the disease among people of different ethnicities is highly essential for timely and accurate diagnosis, treatment, and family counseling. This study stresses the fact that this syndrome is fatal if untreated. It also emphasizes the importance of neonatal screening for early detection of primary immunodeficiencies as it is currently performed in many developed countries. Furthermore, in newborns in endemic countries deferring BCG immunization until obtaining the screening results may greatly prevent the infant from the dissemination of BCG infection and also the adverse side effects of its medications.

Conflict of Interests

There is no conflict of interest.

References

1. Cirillo E, Cancrini C, Azzari C, Martino S, Martire B, Pession A, et al. Clinical, immunological, and molecular features of typical and atypical severe combined immunodeficiency: report of the Italian Primary Immunodeficiency Network. Front Immunol. 2019;10:1908.
2. Villa A, Notarangelo LD, Roifman CM. Omenn syndrome: inflammation in leaky severe combined immunodeficiency. J Allergy Clin Immunol. 2008;122(6):1082-6.
3. Tsilifis C, Spegarova JS, Good R, Griffin H, Engelhardt KR, Graham S, et al. Omenn syndrome in two infants with different hypomorphic variants in Janus kinase 3. J Clin Immunol. 2024;44(4):98.
4. Roifman CM. Severe combined immunodeficiency. In: Rich RR, editor. Clinical Immunology: Principles and Practice. Elsevier Saunders; 2013.
5. Fuchs S, Rensing-Ehl A, Pannicke U, Lorenz MR, Fisch P, Jeelall Y, et al. Omenn syndrome associated with a functional reversion due to a somatic second-site mutation in CARD11 deficiency. Blood. 2015;126(14):1658-69.
6. Somech R, et al. Reduced central tolerance in Omenn syndrome leads to immature self-reactive oligoclonal T cells. J Allergy Clin Immunol. 2009;124(4):793-800.
7. Khan U, Ahmad RU, Aslam A. An infant with Omenn syndrome: a case report. Ann Med Surg (Lond). 2022;74:103319.
8. Al Aboud A, Al Aboud K. Gilbert Omenn and his syndrome. Our Dermatol Online. 2012;3(1):55-6.
9. Hsu CC, Lee JYY, Chao SC. Omenn syndrome: a case report and review of literature. Dermatol Sin. 2011;29(2):50-4.
10. Elnour IB, Ahmed S, Halim K, Nirmala V. Omenn's syndrome: a rare primary immunodeficiency disorder. Sultan Qaboos Univ Med J. 2007;7(2):133.
11. Zafar R, Ver Heul A, Beigelman A, Bednarski J, Bayliss SJ, Dehner LP, et al. Omenn syndrome presenting with striking erythroderma and extreme lymphocytosis in a newborn. Pediatr Dermatol. 2017;34(1):e37-9.
12. Giliani S, Bonfim C, De Saint Basile G, Lanzi G, Brousse N, Koliski A, et al. Omenn syndrome in an infant with IL7RA gene mutation. J Pediatr. 2006;148(2):272-4.
13. Mazzucchelli RI, Riva A, Durum SK. The human IL-7 receptor gene: deletions, polymorphisms and mutations. Semin Immunol. 2012;24(4):225-33.