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Case Report

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# An Infant with Generalized Erythematous Cutaneous Lesions, Lymphadenopathy, Persistent Vomiting and Failure to Thrive: A Case Report

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## Abstract

Omenn's syndrome is an exclusive form of primary immunodeficiency quite different from Severe Combined Immunodeficiency (SCID) in its clinical and hematological presentation. It characteristically differs from SCID with its presentation of generalized erythroderma, lymphadenopathy and peripheral eosinophilia. The diagnosis of Omenn's Syndrome is based on the clinical, hematological and biogenetic features. This is a case report of an atypical presentation of a baby referred to a Neonatal Intensive Care Unit (NICU) of a teaching hospital.

## Case Report

### Presenting Complaints

A 34 days old female baby, Baby M, was transferred to the NICU of a children's hospital, for recurrent vomiting and failure to thrive. The NICU physicians after their initial assessment and blood work referred the baby to the Clinical Immunology division to rule out immunodeficiency, for the issues of failure to thrive, generalized redness of the skin with desquamation, and lymphadenopathy.

### Prenatal History

The baby's parents were both immigrants from the Middle East. There was no history of consanguinity. The mother was G5 P2 A2. She has two children a female and a male child, 11 and 2 years old respectively born through normal vaginal delivery. The mother had two spontaneous abortion 10 years and 2 years back. The fetal ultrasound of current pregnancy was normal at 8 and 24 weeks. The GBS, HBV, HIV and VDRL serology tested negative in mother. The mother is a non-smoker and never consumed alcohol. There is no history of drug abuse. She is unemployed. There was no significant family history of congenital diseases, early deaths or unexplained deaths in the family.

### Birth History

The baby was born at 38 weeks 3 days of gestation, post epidural anesthesia. The duration of labour was 2.5 hours. The Apgar score (Appearance, Pulse, Grimace, Activity, and Respiration) at birth and 5 minutes was 8. Baby had a hoarse cry and dusky skin at birth. The birth weight of the baby was 3.070 kg. Baby was taken to the mother's room 4 hours after birth. Baby had very poor suckling effort. After several attempts the baby took some feeds but vomited every one of the feeds.

### Clinical Examination

On examination, the heart rate was 118 beats/minute, temperature was 36.5 degrees centigrade, oxygen saturation was 99% on room air and the respiratory rate was 54 breaths/minute. The general examination revealed no pallor, cyanosis, jaundice, pedal edema or clubbing. Examination of the skin revealed generalized redness all over the body and face and somewhat edematous in the face with greyish flaking of skin on the scalp. Examination of the nails revealed white periungal lesions mainly of the hands and moderately on the feet. The facies had low set ears (right more than

left) with up slanting eyes and retro micrognathia. Examination also revealed axillary and inguinal lymphadenopathy. The baby had a hoarse cry. The baby had a wound of the right ankle of size 1.5 x 0.5cm with minimal depth at the site of previous intra venous use. Auscultation of the heart revealed normal heart sounds with no extra heart sounds and a grade 2 systolic murmur. Examination of the respiratory system revealed bilateral normal vesicular breath sounds and some transmitted sounds from upper airways. There were no other adventitious sounds. Abdominal examination revealed a soft abdomen with no hepatosplenomegaly and normal bowel sounds.

### Results of Investigations

The white blood cell count was 14.4 x $10^9$/ L with a differential count of neutrophil 3.5 x $10^9$/ L, lymph 7.4 x $10^9$/ L, basophils: 2.2 x $10^9$/ L. The eosinophil count was elevated in the differential with a count of 2.1 x $10^9$/ L (0.0 x $10^9$/ L - 0.7 x $10^9$/ L). The hemoglobin was 106 g/l and platelet count were 488 x $10^9$/ L. Flow cytometry showed CD3 count was 3.406 x $10^9$/ L, which was normal. The CD4 count was 1.055 x $10^9$/ L (1.600 x $10^9$/ L -4.000 x $10^9$/ L). CD8 was 2.091 x $10^9$/ L (0.560 x $10^9$/ L - 1.700 x$10^9$/ L) and CD4/ CD8 ratio 0.5 x $10^9$/ L (1.0 x $10^9$/ L -3.2 x $10^9$/ L). Immunoglobulin and complement levels were normal. Chest X-ray revealed the absence of thymic shadow. Ultrasound of the chest failed to demonstrate thymic tissue. Ultrasound abdomen showed some sludge in the gall bladder with questionable biliary atresia. Genetic analysis was ordered.

### Specialists Opinion

The NICU physicians noted that the baby had some abnormal facies with low set ears, up slanting eyes and retrognathia. Baby was started on TPN after several failed attempts of feeding. The baby also started to develop a dry skin rash, which looked parched in appearance all over the body. Baby was transferred to the NICU at the peripheral hospital for specialist opinion and management. Baby M was seen by a geneticist and was confirmed to have some abnormal facies that did not fit into any predefined syndrome. CGH (Comparative Genomic Hybridization) study was ordered by genetics. The baby was referred to the pediatric cardiologist for a grade 2 systolic murmur. The echocardiogram confirmed a small patent foramen ovale. The pediatric gastroenterologist was consulted for persistent vomiting and failure to thrive. Abdominal X-rays and esophago-gastro duodenoscopy was normal. A G-tube was inserted, and J extension was attempted but was not successful. A barium study through the G-tube showed moderate reflux with minimal amount. Baby M was seen by the pediatric neurologist to rule out neurological problems. MRI of the brain showed cyst-like lesions of the periventricular white matter. The neurological opinion was that they were porencephalic cysts probably due to late fetal anoxia or perinatal cerebral injury leading to a pseudo bulbar picture. Baby M was also found to have axillary and inguinal lymphadenopathy. The skin lesions on the baby started spreading all over the body and the rash on the scalp started to flake as grey flakes, without erythema. Baby also had periungal white lesions of the fingers and toes secondary to fungal infections.

### Diagnosis

After 6 weeks from the initial presentation, the results of the genetic analysis by CGH (Comparative Genomic Hybridization), revealed RAG1 (Recombination-Activating Gene 1) and RAG2 (Recombination-Activating Gene 2) hypomorphic mutations with a leaky defect. Hence the baby was diagnosed with Omenn Syndrome.

### Management

The medical conditions, clinical findings, risks and benefits of investigations and procedures, results of the investigations and the diagnosis of the baby were clearly explained to the parents of the baby every step of the hospitalization, by the NICU (Neonatal Intensive Care Unit) team and the specialists. Emotional and social support was provided to the parents by the physicians and allied health team. Baby M was referred to specialized pediatric hospital for bone marrow transplantation. The baby had bone marrow transplantation and is currently 1year old and doing well with appropriate weight gain, and no infections.

## Discussion

Omenn's syndrome is a genetically explicit form of immunodeficiency with leaky defects. The syndrome occurs due to hypomorphic mutations in RAG1, RAG2, DCLRE1C (DNA Cross-Link Repair 1C), LIG4 (DNA Ligase 4), RMRP (RNA component of Mitochondrial RNA Processing endoribonuclease) and ADA (Adenosine Deaminase genes [1]. These mutations reduce the functions of the enzymes encoded by these genes but do not totally stop the enzymes from being produced, resulting in a variable leaky defect[2]. The increase in the clone of T cells, specifically the TH2 (T- Helper Lymphocyte Type 2) type, is believed to cause the inflammation and eosinophilia, which is noted in these patients [2]. The features of clinical and investigative presentation in infants with generalized erythroderma, generalized lymphadenopathy, eosinophilia and severe immunodeficiency warrants further investigation by physicians. The diagnosis is reached usually with genetic analysis. Prompt diagnosis of this syndrome can expedite the treatment with bone marrow transplant and thereby reduce morbidity and mortality. It is imperative that family physicians and community pediatricians who provide care to neonates and infants with the presentation of failure to thrive and persistent vomiting to consider primary immunodeficiency in their differential diagnosis. These patients need early referral to institutions that are capable of managing these conditions [3-5].

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