Hyperimmunoglobulin E syndrome and multiple brain abscesses

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ABSTRACT

Hyperimmunoglobulin E (HyperIgE) syndrome is a rare primary immunodeficiency disease characterized by recurrent skin and pulmonary infections and an elevated serum IgE level. We report a female neonate with hyperIgE syndrome who presented with multiple brain abscesses and superficial cold abscesses caused by Staphylococcus aureus and also developed pneumonia later on. On follow-up, she developed pneumonia twice and cold abscess once. She responded well to conservative management.

Key words: *HyperIgE, Staphylococcus aureus, Brain abscess*

Hyperimmunoglobulin E syndrome is a rare (incidence $<10^{-6}$) primary immunodeficiency disorder [1]. It is characterized by elevated serum levels of IgE, recurrent staphylococcal skin abscesses and sinopulmonary infections [2]. However, brain abscess in neonatal life is a rare clinical presentation of hyperIgE syndrome. Therefore, we describe a neonate with multiple brain abscesses and cold abscesses caused by Staphylococcus aureus and pneumonia.

CASE REPORT

An 18-day-old girl presented with high grade fever and recurrent convulsions for one day. Antenatal and early postnatal periods were uneventful. The baby was a product of non consanguineous marriage. She was born at term by normal delivery with a birth weight of 2900 gms. She was exclusively breastfed. On admission, her temperature was 38.5^0C, heart rate - 158/min, respiratory rate – 42/min, blood pressure – 62/42 mm-Hg, and SpO2 on room air was 94%. The baby was conscious and there was no active convulsion at the time of admission.

On general examination, there were coarse facial features (prominent forehead, wide-spaced eyes, broad nasal bridge and fleshy nasal tip) along with left sided facial palsy (Figure 1) and a fluctuant swelling (2 cm x 1.5 cm) over occipital area of scalp. CNS examination revealed hypertonia and left sided facial palsy. Respiratory and cardiovascular system examination revealed no abnormality.

Figure 1 - Coarse facial features and left sided facial palsy

On investigations, her random blood glucose was 103 mg%, and her serum calcium (11 mg/dl), serum electrolytes and arterial blood

gases were normal. Total leukocyte counts were high (24300/mm^3) with normal platelet counts and positive CRP but normal CSF study. Her initial absolute eosinophil count was 930/mm^3. She was given intravenous fluids, intravenous antibiotics (vancomycin and meropenem) and intravenous phenobarbitone. She responded to this treatment, fever subsided and alertness improved. Scalp abscess was drained and pus was sent for gram-stain and culture-sensitivity. Gram-staining showed gram-positive cocci. Both cultures of the blood and pus grew methicillin resistant Staphylococcus aureus showing sensitivity to vancomycin, meropenem and linezolid. A plain CT scan of brain was done which showed multiple abscesses in both cerebral hemispheres, in left frontal and right parietal regions (Fig2).

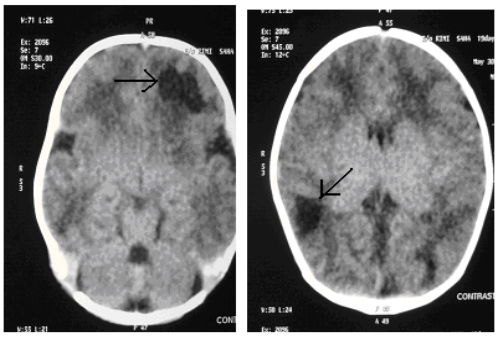

Figure 2 - Brain abscesses in left frontal and right parietal regions (Arrows)

While on treatment, she started developing multiple superficial abscesses in different sites like nape of neck, dorsum of left hand, left foot and right thigh. These abscesses were non-tender and there was no rise of local temperature or redness suggesting cold abscesses. All abscesses were drained in time. On day 25, she developed respiratory distress for which chest x-ray was taken. It showed patchy pneumonitis. Subsequent serial blood counts showed normal total leukocyte counts and platelets but eosinophilia was still present.

Investigations like echocardiography, coagulation profile and follow-up CT scan of brain after 7 days were done, and a neurosurgeon was involved in the management. Echocardiography and coagulation profile were normal. Follow-up CT scan showed resolving abscesses. Though the baby was on culture-sensitive antibiotics, still she was suffering from new crops of abscess in different sites and pneumonia. These findings led us to think of hyperIgE syndrome and immuno-globulin profile was done which showed elevated level of IgE (666.80 IU/ml). It was 12.7 times upper normal range (1.40 – 52.30 IU/ml). Raised serum IgE levels further supported our diagnosis of hyperIgE syndrome; however, we could not confirm our diagnosis by genetic mutational study due to non-availability of the facility in our center. She responded well to conservative management. After a course of 4 weeks of IV antibiotics, she was discharged on oral phenobarbitone and linezolid.

On follow-up, there was complete resolution of brain abscesses and no recurrence of convulsion. EEG done at 3 months was normal. Phenobarbitone was tapered and then omitted. Her growth and neurological development was normal. But she required two more hospitalizations – one at 6 months for pneumonia and other at 8 months for pneumonia and a cold abscess on right forearm. Repeat serum IgE levels at 6 and 8 months were very high (more than 15 times normal).

DISCUSSION

HyperIgE syndrome is a relatively rare primary immunodeficiency syndrome characterized by recurrent severe staphylococcal abscesses of the skin, lungs and other viscera as well as upper and lower airway infections and markedly elevated levels of serum IgE. Most cases are sporadic, but both autosomal dominant (AD) and recessive (AR) inheritance have been described [3]. Abnormal neutrophil chemotaxis due to decreased production of gamma interferon by T-lymphocytes is thought to cause the disease [4]. The skeletal, dental and soft tissue abnormalities are seen in AD forms, while severe viral infections and neurological complications are seen in AR hyperIgE syndrome [2,3]. Mutations in STAT3 gene are found in AD cases while AR

cases are due to mutation in DOCK8 gene [5]. Genetic mutation study was not done in this case due to non-availability of the facility in our center.

There are no diagnostic criteria for hyperIgE syndrome. The lack of specific blood tests, other than elevation of serum IgE levels (>2000 IU/ml or >10 times the age-specific upper norm) and eosinophilia (>2SD above norm), makes the diagnosis of hyperIgE syndrome difficult, requiring compilation of symptoms which develop over years. A typical presenting sign is a newborn rash [6] that was not present in our baby. She presented with neurological complications like left sided facial palsy, multiple brain abscesses and convulsion – a very unusual presentation reported in newborn life. Facial appearance (asymmetric facial appearance, coarse skin, prominent forehead, deep-set eyes, broad nasal bridge and bulky nasal tip), fractures with minor trauma, retained primary teeth, scoliosis and hyperextensibility of joints are observed in hyperIgE syndrome. Scoliosis and hyperextensibility of joints are seen in AD form but these were not seen in our patient. Pneumonia is typically caused by Staphylococcus aureus, Streptococcus pneumoniae or Haemophilus influenzae. Recurrent pneumonias are complicated with pneumatoceles or brochiectasis [7].

Though the baby was on culture-specific antibiotics, she continued to develop multiple cold abscesses one after another. There was persistent eosinophilia (>700/cmm). This led us to think about hyperIgE syndrome. Moreover she had 3 episodes of pneumonia in her infancy. Treatment of hyperIgE syndrome consists of long-term anti-staphylococcal antibiotics, respiratory physiotherapy and IVIG to antibody-deficient patients. Antifungal drugs are useful in cases of fungal infection. Thoracic surgery is needed for superinfected pneumatoceles or those persisting for more than 6 months [8]. Other therapeutic options like methotrexate, cyclosporinA, interferon gamma, plasmapheresis and bone marrow transplant have been tried in several studies with variable results [9].

CONCLUSION

HyperIgE syndrome, a multisystemic disorder with a compilation of clinical manifestations, is a big challenge for clinicians in establishing a diagnosis in suspected cases. Patients with hyperIgE syndrome require multidisciplinary care under the supervision of clinical immunologist.

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