INTRODUCTION
The hyper-immunoglobulin E (IgE) Syndrome (HIES), also known as Job's syndrome is a rare primary immunodeficiency characterized by the clinical triad of recurrent staphylococcal abscesses of skin, recurrent cyst-forming pneumonia, and an elevated serum IgE level of > 2000 IU/ml. Although, most cases are sporadic, families with autosomal dominant (AD-HIES) and recessive (AR-HIES) traits have been reported. Very few articles were published previously on central nervous system abnormalities with definite neurologic manifestations which may vary from partial facial nerve paralysis to hemiplegia in children but Acute Disseminated Encephalomyelitis (ADEM) in a child with HIES hitherto has not been reported. Here we describe a 5-year-old male child with HIES who presented with neurologic manifestations of ADEM.

CASE REPORT
A 5 years old boy was admitted with complaints of fever, headache and vomiting for one day, one episode of generalized convulsion and altered consciousness on the day of admission. He had Glasgow coma scale of E2M1V3 and decerebrate posturing without signs of meningeal irritation. His cranial nerve examination was found to be normal. Child had exaggerated deep tendon reflexes on left side with positive Babinski response. General examination revealed few scar of healed abscess over left side of nasal bridge, eczema over left cubital fossa and necrotic ulcer over dorsal aspect of left forearm. Examinations of other systems were unremarkable.

Initial investigations revealed hemoglobin level of 9.2 gm/dL and total white cell count of 18400/mm³ with an absolute eosinophil count 3312/mm³. Other investigations like liver function test, renal function test, serum electrolytes and random blood sugar were within normal limit. CSF examination showed pleocytosis (78 cells/µl) with mild elevation of protein (50 mg/dl). CSF culture was sterile. Serology for herpes simplex, Japanese encephalitis, measles and mumps virus was found to be negative. Polymerase Chain Reaction (PCR) analysis of viral nucleic acid in CSF was not done as the facility for the same was not available at our centre. Acyclovir and broad spectrum antibiotics were started keeping in view of the possibility of viral encephalitis or bacterial meningitis. Her consciousness level was further deteriorated in spite of treatment over the next 3 days. Magnetic Resonance Imaging (MRI) was done at 96 hours which revealed bilateral asymmetrical multiple hyper-intensities predominantly involving subcortical white matter in both fronto-parietal lobes (Figure 1a and b). In view of the scattered distribution of hyperintense lesions, screening MRI spine was done and found normal. A provisional diagnosis of ADEM was made and intravenous methylprednisolone was started. Acyclovir and antibiotics were withdrawn. Patient showed dramatic response to above therapy and on day 3, he started moving limbs spontaneously. But he developed two large cystic swellings, one (10 x 10 cm) over left upper thigh and another (6 x 6 cm) over anterior chest wall having characteristically no signs of inflammation, which revealed pus on surgical exploration. Coagulase positive Staphylococcus aureus was detected on both pus and blood culture which was sensitive to vancomycin and cloxacillin. Chest X-ray and ultrasonography of abdomen showed normal finding. Mantoux test was negative.
Due to disseminated infection, hypereosinophilia and the complexity of his clinical course, the question of primary immunodeficiency was raised and he was investigated accordingly. The findings of further laboratory workup included serum IgA (233 mg/dl, reference range: 17 - 318 mg/dl) and serum IgE (3040 IU/ml, reference range: 0 - 230 IU/ml). IgM and IgG concentrations were within the normal range. Screening for human immunodeficiency virus antibody and antineutrophil antibody were negative. Past medical record revealed repeated hospitalization due to radiologic proven pneumonia and treated aggressively. In view of recurrent skin and lung infections, eczema, and elevated serum IgE level, a final diagnosis of HIES with ADEM was made. Genetic analysis could not be performed for HIES as the facility for the same was not available at the study centre.

The child was treated with a 5-day course of intravenous methyl prednisolone (30 mg/kg/d) followed by oral Prednisolone (1.5 mg/kg/d for 4 weeks, tapered over next 2 weeks) along with sensitive antibiotics and supportive measures. Child was advised about antimicrobial prophylaxis during discharge and kept under periodic follow-up. After 3 months of follow-up, patient was normal with no neurological deficits. His repeat MRI brain, done after 6 months, showed resolution of changes seen in previous MRI.

DISCUSSION

A spectrum of abnormalities on brain MRI, ranging from focal hyperintensities, Chiari-1 malformations, occlusion of the central retinal artery, bilateral berry aneurysms at the internal carotid bifurcation with subarachnoid hemorrhage, thrombosis involving left middle cerebral artery and left posterior inferior cerebellar artery to lacunar infarcts, venous angioma, capillary telangiectasia, arachnoid cysts, colloid cyst and CNS infections were reported previously in patients with HIES. But, in most of the cases, non-vascular abnormalities were detected as an incidental finding and remained asymptomatic. Altered sensorium, seizure, ataxia, ophthalmoplegia, facial nerve palsy, and hemiplegia are the reported neurologic complications, found in patients with HIES. Although, the exact mechanism is still unclear, it has been proposed that hypereosinophilic vasculitis or occult infections might be the underlying etiology of those neurologic manifestations.3-7

The underlying pathology of ADEM in index case remains unclear but seems to be immunologically mediated. Studies have shown that in HIES patients there is suppression of both humoral and cellular immunity, leading to superinfection with other microorganisms.4 Characteristics bilateral asymmetric multifocal subcortical white matter involvement on MRI; remarkable improvement after steroid therapy with resolution of MRI changes on repeat imaging study favours the diagnosis of ADEM in this case. ADEM can be difficult to distinguish from the first attack of multiple sclerosis as both share common clinical and pathophysiologic aspects, but later these two can be distinguished based on clinical course of the disease, lack of relapses, and resolution of lesions on repeat MRI.9 Like other primary immunodeficiency, there is as yet no cure for HIES. Therapy for HIES is directed at anti-staphylococcal antibiotic prophylaxis and management of infections by using sustained systemic antibiotics and antifungal agents along with topical therapy for eczema and drainage of abscesses. Interferon-gamma, immunoglobulin supplementation, low-dose cyclosporine and histamine-2 receptor have been reported to be beneficial in selected patients, but they are not generally indicated.10

REFERENCES


