
CASE REPORT**Acute Disseminated Encephalomyelitis in a case of Hyper IgM Syndrome***Devdeep Mukherjee^{1*}, Ritabrata Kundu¹, Prabal Niyogi¹, Joydev Tudu¹**¹Department of Pediatric Medicine, Institute of Child Health, Kolkata - 700019 (West Bengal) India*

Abstract:

Hyper IgM syndrome is a rare genetically heterogenous syndrome and is characterized by an elevated or normal serum IgM and decreased IgG, IgA and IgE, indicating a defect in the class – switch recombination (CSR) process. Patients are prone to recurrent infections. X linked variety occurring in males is the most common form of the disease. Acute Disseminated Encephalomyelitis (ADEM) in a case of Hyper IgM syndrome has never been reported. Here we report a 10 years old female with hyper IgM syndrome, possibly autosomal form of the disease, who was admitted with recurrent vomiting, seizures, encephalopathy, expressive aphasia and bladder bowel dysfunction and diagnosed to have ADEM.

Keywords: Acute Disseminated Encephalomyelitis (ADEM), Hyper IgM syndrome

Introduction:

Hyper-IgM syndrome (HIGM) is a rare primary immunodeficiency disorder which is characterized by elevated or normal serum IgM and decreased IgG, IgA, and IgE due to defective immunoglobulin class switching. Acute disseminated encephalomyelitis (ADEM) is traditionally considered a monophasic inflammatory demyelinating disorder with pleiotropic clinical manifestations, which usually includes encephalopathy, but variably includes other focal or multifocal symptoms suggestive of a central nervous system (CNS) inflammatory demyelinating disorder. We report a 10 years female child having Hyper IgM syndrome who developed Acute Disseminated Encephalomyelitis.

Case Report:

10 years old female, was admitted with the chief complaint of recurrent fever and vomiting since the last 3 days. She was having recurrent convulsions – gener-

alized tonic clonic in variety (3 episodes) since the previous evening and had obtunded sensorium. She had simultaneously developed expressive aphasia along with loss of control over her bowel and bladder functions.

She had a past history of recurrent infections since the age of 3 years resulting in frequent hospital admissions for pneumonia (3 times), empyema, and chronic suppurative otitis media, generalized lymphadenopathy, multiple neck abscesses due to *Staphylococcus aureus* and Herpetic Whitlow and had been treated with various antibiotics. Lymph node biopsy on a previous admission was suggestive of reactive hyperplasia. Mantoux test was negative.

Her development milestones were appropriate for age. There was no history of siblings or family members having a history of recurrent infections. She had received all the vaccines as per the National Immunization Schedule. There was also no history of receiving vaccines over the last 1 year.

On clinical examination, she had stable vitals with cervical and inguinal lymphadenopathy. She had no organomegaly. She had no neck rigidity. Deep tendon jerks were diminished on the right side. She also had extensor planter response on the same side.

Following admission on this occasion, blood count showed a leukocyte count of 12,300/cumm with 73% neutrophils and 23% lymphocyte. Hemoglobin was 11.4 gm/dl. Her erythrocyte sedimentation rate, C reactive protein, electrolytes, blood sugar and other blood biochemistry were normal. Her plasma ammonia and lactate levels were within normal limit. Lumbar puncture had 20 cells/cumm in her cerebrospinal fluid (CSF) with protein 22.6mg/dl and sugar 65mg/dl. No organisms were isolated from blood and CSF

culture. Her immunoglobulin profile was showed IgG < 30mg/100ml, IgA <20mg/100ml, IgE <0.1 IU/ml and significantly elevated IgM of 1314/100 ml (normal 31 - 208 mg/100 ml for age). The levels of CD4 + T cells were also demised.

Magnetic Resonance Imaging Scan of brain showed features suggestive of multiple hyper intensities in the cortical and subcortical region (bilateral fronto parietal lobes, left cerebellar hemisphere) and periventricular white matter due to Acute Disseminated Encephalomyelitis (Fig. 1).

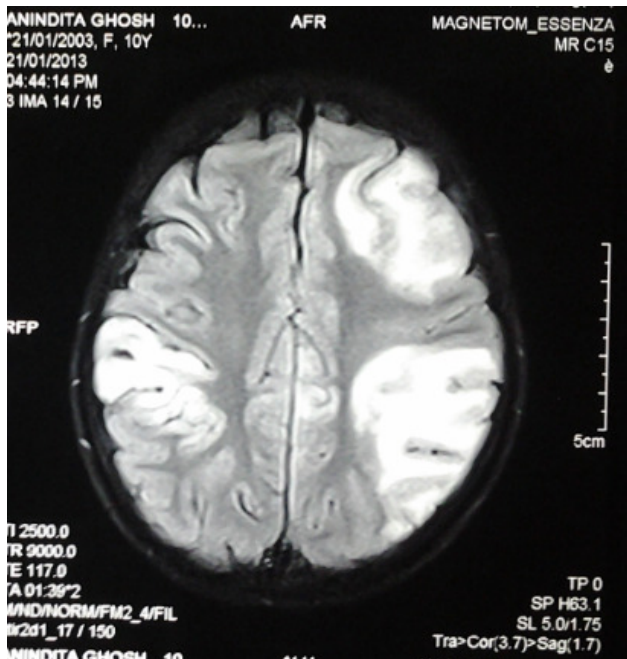


Fig. 1: Multiple hyper intensities in the cortical and subcortical region (bilateral fronto parietal lobes, left cerebellar hemisphere) and periventricular white matter due to ADEM.

On being diagnosed with Hyper IgM syndrome, she was given 500mg/kg of intra venous Immunoglobulin (Immunoglobulin replacement therapy). Thereafter she was also treated with IV methylprednisolone at 30mg/kg/day for 5 days for ADEM. This was followed with oral prednisolone at 2mg/kg/day. Inj Phenytoin was given for controlling her seizures. Gradually over the next 72 hours her sensorium improved and her symp-

toms subsided. She was discharged after 14 days with oral steroids and is presently receiving monthly infusion of Immunoglobulin and is in regular follow up. She is also on prophylaxis with cotrimoxazole.

Discussion:

Hyper-IgM syndromes are a group of primary immunodeficiency's whose molecular basis is still unknown. The most common variant is the X-linked form of disease (XHIGM), due to mutations in the CD40 ligand-encoding gene (CD40LG). Mutations in CD40, activation-induced cytidine deaminase (AICDA), and uracil glycosylase (UNG) are responsible for autosomal recessive forms of HIGM [1, 2]. Our patient being a female child is unlikely to be the X linked recessive form of the disorder and is more likely to be autosomal recessive.

There is normal B cell count, but abnormal interactions between B and T cells leading to impaired class switching mechanism. The immune defect extends beyond the CSR defect and also involves maturation of dendritic cells and T cell priming. Recurrent infections in the respiratory tract and gastrointestinal problems are the most common clinical manifestation. They also have a high risk of opportunistic infections with *Cryptosporidiosis*, *Pneumocystic jiroveci*, *Cytomegalovirus* and *Mycobacterium*. Our index case had been admitted several times with pneumonia. She also had *Staphylococcus aureus* isolated from abscesses in the neck. There was also a history of herpetic whitlow. Some patients are also prone to autoimmune disorders like anemia, thrombocytopenia, hepatitis etc. Immunoglobulin replacement is the mainstay of treatment of all forms of HIGM, and may improve clinical outcome [1, 2]. In spite of this treatment, prognosis remains poor. About half the patients will die by the third decade of life, and many others develop chronic morbidities during childhood.

Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system that typically follows a febrile infection

or a vaccination. Children are predominantly affected [3]. A plethora of viral and bacterial pathogens and a number of vaccinations have been associated with ADEM [4, 5].

There are reports of association of ADEM in patients with common variable immunodeficiency [6]. There is also a report of ADEM being the first manifestation in a patient with CVID (7).

However, to our knowledge there is no reported case of patients with Hyper IgM syndrome developing acute disseminated encephalomyelitis though the tendency to develop autoimmune disease is common in them.

Based on the presumed autoimmune etiology of ADEM, the common treatment approach consists of

intravenous methylprednisolone at a dosage of 20 to 30 mg/kg per day (maximum 1 g/day) for 3 to 5 days, followed by an oral corticosteroid taper of 4 to 6 weeks [8]. We applied a similar treatment protocol for treating our patient, to which she has responded. In case of insufficient response or contraindications to corticosteroids, intravenous immunoglobulin G (IVIg) at a dosage of 2 g/kg divided over 2 to 5 days is a therapeutic option [8].

Immunoglobulin replacement therapy also reduces the incidence of infections in patients with Hyper IgM syndrome [1]. It also reduces the likelihood of lymphoid hypertrophy. Our patient is presently being given immunoglobulin every month.

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