International Journal of Contemporary Pediatrics
Fadnis MP et al. Int J Contemp Pediatr. 2019 Nov;6(6):2700-2701
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20194758

Case Report

A case of primary immunodeficiency: hyper IgM syndrome

Madhura P. Fadnis*, Pratibha B. Shamkuwar

Department of Pediatrics, Yashwantrao Chavan Memorial Hospital, Pimpri, Pune, Maharashtra, India

Received: 28 July 2019
Revised: 10 September 2019
Accepted: 03 October 2019

***Correspondence:**
Dr. Madhura P. Fadnis,
E-mail: Madhura.Fadnis1@gmail.com

ABSTRACT

Hyper IgM syndrome are group to disorders characterized by elevated serum level of IgM and low or absent serum levels of IgG, IgA and IgE the mechanism of HIGM is immunoglobulin Class-Switch Recombination (CSR) failure and Somatic Hyper Mutation (SHM). This diagnosis should be considered in any patient presenting with hypogammaglobulinemia, with low or absent IgG and IgA and normal or elevated IgM level. In the present case report, this was a 6-year-old male child who had history of recurrent respiratory tract infections who presented with otitis media and persistent fever spikes. Immunoglobulin studies revealed a pattern consistent with hyper IgM.

Keywords: Citrobacter, Class-switch recombination, CSOM (Chronic Suppurative Otitis Media), HIGM (Hyper-IgM syndrome), IVIG (Intravenous Immunoglobulin), Tuberculosis

INTRODUCTION

The hyper-IgM syndromes (HIGMs) are a group of rare primary immune deficiency diseases characterized by a normal or elevated serum level of IgM and low or absent serum levels of IgG, IgA and IgE with normal peripheral blood B lymphocyte counts.[1] The mechanism of HIGM is immunoglobulin class-switch recombination (CSR) failure and somatic hyper mutation (SHM). Most patients with HIGM syndrome develop clinical symptoms during their first or second year of life. The most common problem is an increased susceptibility to infection including recurrent upper and lower respiratory tract infections with encapsulated bacteria example *Streptococcus* and *H. influenza*. The HIGM results from a variety of genetic defects that affect this interaction between T and B-lymphocytes. There are 8 main sub-types described, depending on the mutation responsible. The first described, and most common defect, is X-linked hyper IgM syndrome due to deficiency of CD40 ligand (CD40LG), which affects only male patients. Early diagnosis helps in prompt initiation of treatment in the form of IVIG. We present a case of hyper IgM in a 6 year old male child with history of recurrent infections.

CASE REPORT

A 6 years old male child 2nd by birth order born of 3rd degree consanguineous marriage was admitted in view of not gaining weight adequately for 1 year of age. The child also had high grade intermittent fever for 1 month. There was also a history of cough cold and bilateral ear discharge since 1 month. The child had a significant past history of recurrent infections. First at 2 year of age, child was diagnosed with pulmonary tuberculosis for which he received treatment for 6 months. A year later child had ear discharge followed by multiple hyperpigmented skin lesions diagnosed as lichenoid lesions (pityriasis chorea).

Physical examination revealed pallor, moderate hepatomegaly and splenomegaly of 6 cm, firm liver and spleen. Anthropometric parameters showed height and weight for age below the third centile. The ear examination showed bilateral chronic suppurative otitis media (CSOM). Ear swab was sent for culture sensitivity.

blood culture was also sent in view of persistent high grade fever spikes. Ear swab showed a growth of Citrobacter Freundii sensitive to only Polymyxin B. Blood culture had a growth of Ecoli sensitive to amikacin and ceftazidime.

Following these reports a differential diagnosis of bacteremia with underlying primary immunodeficiency was suspected other differential was acute lymphoproliferative syndrome (ALPS) and leukemia. The peripheral blood smear did not show any blasts and the double negative T cell work up for ALPS was negative. The primary immunodeficiency work up showed a immunoglobulin pattern of high IgM(14.3g/l) and low levels of IgE(<4.4IU/ml), IgG(<0.067g/l) and IgA(<0.239g/l). Thus, a diagnosis of hyper IgM was made, and child was started on IVIG.

DISCUSSION

The hyper-IgM syndrome (HIGM) is one of the rarest primary immunodeficiencies.[2] It is characterized by a deficiency in switching from production of IgM to IgG, IgA and IgE, with the presence of elevated or normal serum IgM levels, and low levels of other immunoglobulin classes. B-lymphocytes can produce IgM antibodies on their own, but they require interaction with T-lymphocytes in order to switch antibody production from IgM to the other immunoglobulin classes.[3] This diagnosis should be considered in any patient presenting with hypogammaglobulinemia, with low or absent IgG and IgA and normal or elevated IgM level. In the present case the child had hepatosplenomegaly with low counts and low platelet counts. Hence, a differential of leukemia was kept in mind, but peripheral smear and bone marrow did not show any blast cells.

Most of the patients of hyper IgM present with recurrent bacterial infections.[4] In the present case the child had previous history of pulmonary Koch for which he was given treatment. This indicates the defect in T cell function. They are prone for many opportunistic infections like *pneumocyctis carnii* an important finding noted in the present case was that child had recurrent chronic suppurative otitis media which showed a growth of Citrobacter and blood culture showed *E. coli*.[5] The patients are also prone to various complications. Lymphoid hyperplasia, caused by the presence of giant germinal centers, is a frequent complication.[6] Adenocarcinomas of the liver, biliary tract and other parts of the GI system are other complications of chronic GI disease, and require periodic screening to allow for an early diagnosis. There is also an increased incidence of autoimmune diseases.[7,8] Pulmonary function tests are essential at diagnosis and yearly thereafter to monitor for chronic lung disease. follow up of these patients is very important. The further diagnosis of a specific subtype of HIGM depends on the identification of a mutation analysis of the genes known to cause these disorders. There are 8 subtypes of which type 1 due to defect in the CD 40 ligand is the most common.[9] It is X linked. Treatment consists of IVIG 500 mg/kg every 4 weeks. It is especially useful for the treatment of recurrent bacterial infections. At present, stem cell transplantation remains the most effective method of HIGM treatment. Genetic therapy for HIGM is currently in the experimental stages.[1] Thus prompt diagnosis is extremely vital for the early detection of hyperigm syndrome as treatment can be instituted timely

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Qamar N, Fuleihan RL. The hyper IgM syndromes. Clini Rev Aller Immunol. 2014 Apr 1;46(2):120-30.
2. Silva R, Da Costa JT. Hyper-IgM syndrome-a case report and a clinical perspective. Eur Ann Aller Clin Immunol. 2010;42(5):194-6.
3. Davies EG, Thrasher AJ. Update on the hyper immunoglobulin M syndromes. Br J Haematol. 2010;149:167-80.
4. Guo L, Chen B, Xu B, Lu M, Ning B, Chen Z. X-Linked Hyper-Igm Syndrome with Eosinophilia In A Male Child: A Case Report Exp Ther Med. 2015;9(4):1328-30.
5. Davies EG, Thrasher AJ. Update on the hyper immunoglobulin M syndromes. Br J Haematol. 2010;149:167-80.
6. Cabral-Marques O, Klaver S, Schimke LF, Ascendino ÉH, Khan TA, Pereira PV, et al. First report of the Hyper-IgM syndrome Registry of the Latin American Society for Immunodeficiencies: novel mutations, unique infections, and outcomes. J Clini Immunol. 2014 Feb 1;34(2):146-56.
7. Winkelstein JA, Marino MC, Ochs H, Fuleihan R, Scholl PR, Geha R, et al. The X-linked hyper-IgM syndrome: clinical and immunologic features of 79 patients. Medicine. 2003 Nov 1;82(6):373-84.
8. Jesus AA, Duarte AJ, Oliveira JB. Autoimmunity in hyper-IgM syndrome. J Clin Immunol. 2008;28(1):S62-S6.
9. Al-Herz W, Bousfiha A, Casanova JL, Chatila T, Conley ME, Cunningham-Rundles C, et al. Corrigendum: Primary immunodeficiency diseases: An update on the classification from the International Union of Immunological Societies Expert Committee for primary immunodeficiency. Frontiers Immunol. 2014 Sep 24;5:460.

Cite this article as: Fadnis MP, Shamkuwar PB. A case of primary immundeficiency-hyper IgM syndrome. Int J Contemp Pediatr 2019;6:2700-1.