LETTER TO EDITOR (VIEWERS CHOICE)

AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)-A RARE CASE WITH COMMON CLINICAL MANIFESTATION

S M Jali, Abhilasha Sampagar, Prakash R Malur, Mallikarjun Jali

An 8 years old boy presented with progressive swelling over the neck and groin for 4 years. There was history of pallor, distension of upper abdomen and easy fatigability for one year. Parents and three siblings of this child were in good health. On examination he was malnourished (height=110cms, weight=16kg), had pallor, icterus, splenohepatomegaly and non-tender, discrete generalized lymphadenopathy. The cervical group of lymphnodes measured between 6-8 cms whereas axillary and inguinal group of lymphnodes measured between 3-5 cms. Other systems were normal. Investigations revealed hemoglobin of 5.3gm%, white cell count of 10900 cells/cumm. (neutrophils 34%, lymphocytes 64%, eosinophils 2%), platelets 90000 cells/cumm. Peripheral smear revealed a hemolytic picture (fragmented red blood cells, polychromatophilic cells and target cells). Reticulocyte count was 7% and direct coomb's test was positive. Mantoux test and gastric lavage for acid fast bacilli was negative. Abdominal ultrasonography showed hepatosplenomegaly but no lymphnodes. Cervical lymph node biopsy revealed scattered reactive germinal centres and a markedly expanded paracortex composed of medium sized lymphocytes, plasma cells, histiocytes and immunoblasts. The lesional atypical cells in paracortex expressed CD3 and were immunonegative for CD20, CD30, Terminal Deoxynucleotidyl Transferase (TdT), CD34, CD4, CD8, CD68 and CD117. This was suggestive of autoimmune lymphoproliferative syndrome (ALPS). Serum IgG level was 4028mg/dL (reference range is 490-1400mg/dL). For confirmatory diagnosis of ALPS, a revised set of diagnostic criteria proposed by Oliveira et al in 2010 (1) was taken into consideration for diagnosis in this patient. Both the required criteria (a. More than 6 months of non-malignant, non-infectious lymphadenopathy and/or splenomegaly; b. Elevated α/β-DNT cells with normal or elevated lymphocyte counts) as well as two secondary accessory criteria (a. Typical immunohistologic findings; b. autoimmune cytopenias with elevated immunoglobulin G levels) were fulfilled. He was started on pulse methyl prednisolone (10mg/kg/day) for 5 days followed by oral prednisolone (2mg/kg). Easy fatigability and dyspnea on exertion improved within 10 days After 15 days of therapy, his hemoglobin increased to 8.8gm% and platelets increased to 1,60,000 cells/cumm. There was regression in the size of the lymphnodes (cervical lymphnodes measured 3-5 cms, axillary and inguinal group of lymphnodes measures 1-2cms), but there was no regression in size of liver and spleen. Prednisolone was tapered over a period of 1 month and stopped. He is on regular follow up and has no further autoimmune complications.

Generalized lymphadenopathy and hepatosplenomegaly are frequently seen in pediatric practice. When the common conditions are ruled out, a differential diagnosis of ALPS should be considered, as early intervention in this condition can prevent the life threatening autoimmune complications. ALPS is characterized by

non-malignant lymphadenopathy, splenomegaly and autoimmune cytopenias. (2) It is the first autoimmune disease with a defined genetic basis. (3) The major causes of mortality and morbidity are severe autoimmune manifestations, hypersplenism, asplenia related sepsis and the development of lymphomas. (4) This rare disorder is caused by defects in the mechanisms that induce apoptosis of lymphocytes which leads to the accumulation of polyclonal population of T cells which express CD3 but do not have CD4 or CD8 markers. (5) ALPS is managed with steroids and intravenous immunoglobulins. If there is no response then mycophenolate mofetil (1200 mg/m2/day) or rituximab can be used. These patients should be followed up for significant cytopenias and increase in size of lymph nodes. Serial PET scan and lymph node biopsy should be done if there is suspicion of lymphoma. (4)

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From: Department of Pediatrics, JN Medical College, Belgaum, India.

Address for Correspondence: Dr Abhilasha Sampagar, Department of Pediatrics, JN Medical College, Mysore, India.

Email: docabhilasha@gmail.com

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