Sinus Histiocytosis with Massive Lymphadenopathy – Its Rare Immunological Complication

Jagabandhu Ghosh* and Joydeep Ghosh1

1Department of Paediatrics, I.P.G.M.E.R & S.S.K.M Hospital, Kolkata, West Bengal, India
2Department of Biotechnology, Heritage Institute of Technology, Kolkata, West Bengal, India

Abstract

A 3-year-old boy presented with irregular fever, multiple painless swelling over neck, axilla and inguinal region for one and half year. The child developed progressive palor for one to two months. Examination revealed generalized lymphadenopathy including massive cervical lymphadenopathy, hepatosplenomegaly, severe anaemia and absence of jaundice. Here, a case of sinus histiocytosis with massive lymphadenopathy complicated by a rare autoimmune haemolytic anaemia is reported.

Keywords: Sinus; Histiocytosis; Autoimmune; Lymphadenopathy

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML) is a nonneoplastic, usually self limiting disease of unknown aetiology [1]. SHML most commonly presents as painless cervical lymphadenopathy with frequent involvement of other lymph nodes. In 30% of patients extranodal sites such as skin, bone, eye, and breast are involved [2]. Evidence of various immunological dysfunctions has also been documented in few case studies [3]. The authors report here one uncommon interesting case of generalised lymphadenopathy with autoimmune haemolytic anaemia.

Case Report

A 3-year-old boy presented with complaints of irregular fever, painless swelling over neck, axilla and inguinal region for one and half year. The neck swelling started with involvement on left side followed by right side. Subsequently the swelling appeared on left axilla followed by both inguinal regions. The mother noticed progressive palor for last two months. There were no histories of bleeding manifestations, arthralgia, polyuria, jaundice, skin lesion.

Physical examination revealed body weight 14.5 kg (50th centile), height 94 cm. (50th centile), pulse rate 90/minute, blood pressure of 90/60 mm of Hg, respiration rate of 28/minute, moderate pallor. Jaundice and oedema were absent. Multiple cervical, submandibular lymph nodes of 2-2.5 cm. in diameter, firm, not tender, few matted were noted. Few left sided axillary and bilateral inguinal lymph nodes of 2.5/3.5 cm. were found. There was no evidence of sternal tenderness. Abdominal examination revealed liver 5 cm. below right costal arch and midclavicular line (span 11 cm.), firm, not tender and spleen 2 cm. below left costal arch, firm in consistency.

Laboratory investigations showed haemoglobin of 5.4 gm%, total leucocyte count-31000/cu mm, differential- neutrophil 90%, lymphocyte 6%, monocyte 3%, eosinophil 1%, platelet count-3,89000/ cu mm. The corrected reticulocyte count was 3%. Peripheral blood smear showed normocytic normochromic, microcytic hypochromic red blood cell, anisocytosis, few target cells and spherocytes. Direct Coomb’s test was strongly positive. Biochemical profile revealed:- serum total bilirubin 1.8 mg/dl, unconjugated 1.2 mg/dl, conjugated 0.6 mg/dl, S.G.O.T- 20 U/L, S.G.P.T-24 U/L, alkaline phosphatase 290 units/L, total protein 8.2 gm/dl, albumin 3.5 gm/dl, globulin 4.7 gm/dl. The tuberculin test was negative. Chest x-ray showed mediastinal widening.

CT scan of abdomen showed retroperitoneal lymphadenopathy of sizes varying from 1.5x2.5 cm. to 2.5x3.5 cm. Fine needle aspiration cytology of cervical lymph node showed sheets of sin histiocytes with some evidence of emperipolesis which means active penetration by a smaller cell into a larger cell. Lymph node biopsy showed massive enlargements of sinuses with prominent histiocytic infiltrations. There was no evidence of malignancy or granulomas. Bone marrow aspiration showed no evidence of malignant infiltration or granuloma. Electron microscopy from cervical lymph node biopsy showed no birbeck granules. Immunohistochemically, histiocytes were positive for S100 protein but negative for CD 1a.

The patient was started on prednisolone in the dose of 2 mg/kg/day in three divided doses. The neck swelling started regressing within 3–4 days of therapy. Fever subsided on 6th day of therapy. Considerable regression of neck swelling and other lymph nodes was noticeable in about three weeks of treatment. Patient received two units of packed red blood cells at interval of seven days during initial part of therapy because of severe anaemia.

Discussion

SHML, without any definite established aetiology, usually presents with massive painless lymphadenopathy. Extraneous involvement is common and found mainly in the head and neck [4]. However, it may also involve the skin, orbit, salivary glands, pancreas, central nervous system, bone [5].

Pathological differential diagnosis of SHML includes reactive sinus hyperplasia, Langerhans cell histiocytosis (LCH), malignant lymphoma. Acute leukaemia, autoimmune lymphoproliferative syndrome (ALPS) may also be included clinically. LCH was excluded in the present case by the absence of birbeck granules and CD1a positivity.

*Corresponding author: Jagabandhu Ghosh, Consultant Pediatrician, Ex-Professor & HOD, I.P.G.M.E.R & Ushashi Housing Society, 245 Vivekananda Road, Kolkata-700006, West Bengal, India, Tel: 9434239336; E-mail: jbgghosh@yahoo.com

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Acute leukaemia was rejected by long history, absence of blast cells in peripheral blood smear and bone marrow aspirate examination. Bone marrow aspiration and lymph node biopsy examination not revealing any malignant cellular infiltration ruled out the possibility of malignant lymphoma also.

The presence of severe anaemia was unusual for SHML. It may be explained by the association of autoimmune haemolytic anaemia (AIHA) which was also reported by earlier workers [3,6]. AIHA has been well reported in malignant lymphoma. AIHA in childhood acute lymphoblastic leukaemia, a very rare entity has been found in one case (unpublished personal observation). Despite the presence of AIHA the possibilities of malignant lymphoma and acute lymphoblastic leukaemia were excluded. ALPS were an important consideration in view of the presence of AIHA. In ALPS autoimmune phenomenon like immune thrombocytopenic purpura, AIHA, vitiligo, hypothyroidism may be present. Lymphoproliferative phenomenon like lymphadenopathy, hepatosplenomegaly, hypersplenism may be evident [7]. In the present case ALPS was excluded by the presence of S100 positivity, and conspicuous emperipolesis. The classical finding of emperipolesis differentiates it from other diseases though emperipolesis may not be present in all cases of SHML [8]. On the other hand emperipolesis may be seen occasionally in malignant lymphoma, LCH also. SHML has also been associated with various other immune abnormalities like uveitis, systemic lupus erythematosus [9]. AIHA, the immune abnormality in the present case is just a coincidence or is caused by SHML is unclear here. In view of the fact that histiocytes are not commonly responsible for immune dysregulation, the pathogenetic mechanism of AIHA in SHML needs future study. Maric et al. in their study found some of the histopathological features of SHML in lymph nodes of ALPS patients (41%) including S100 positive histiocytes and emperipolesis [10]. Therefore further studies are warranted to establish the relationship between SHML and ALPS or to know whether they are the different facets of a single disease.

This case report, therefore, concludes that the possibility of SHML should be considered while evaluating AIHA or the cause for massive lymphadenopathy.

State of informed consent

Parents were informed about the suitability of publication of the case in the journal. They gave verbal consent in this regard.

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