Case Report

Sinus histiocytosis with lymphadenopathy-a case report

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Abstract

Sinus histiocytosis with lymphadenopathy is a rare condition of unknown etiology that is characterized by the overproduction of histiocytes accumulating in the lymph node sinuses and in the lymphatics of extranodal sites if involved. Lymph nodes of the neck are the most common place of histiocyte accumulation, although other lymph nodes and organs may involve, as well. The common sites of the disease outside the lymph nodes are skin, soft tissues, upper respiratory tract, the sinuses, kidney, thyroid, small bowel, breast, and bone. Hepatosplenomegaly is uncommon. The symptoms of this disease vary with the site of involvement. It is often referred to as sinus histiocytosis with massive lymphadenopathy (SHML). In this article an adult male of 38 years, has been described who presented with bilateral cervical and axillary lymphadenopathy clinically suspected of infectious (tubercular-in the context of our country) or hematological malignant etiology. However on fine needle aspiration cytology, the smears showed many histiocytes, lymphocytes and plasma cells. Biopsy of cervical lymph node showed dilated sinuses filled with histiocytes and lymph node architecture showing inflammatory cells having lymphocytes and histiocytes. These findings were considered consistent with sinus histiocytosis with chronic lymphadenitis.

Keywords: *Histiocytosis, Sinus; Lymphadenopathy, Massive; Rosai-Dorfman Disease*

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML), also known as Rosai-Dorfman Disease (RDD), is a rare entity of lymph nodes and was first described by Rosai and Dorfman in 1969[1]. Painless massive lymphadenopathy is the most frequent presenting symptom and involves the cervical lymph node in up to 90% of patients. The most often affected extranodal sites include skin and soft tissues, upper respiratory tract, orbit, testicle, kidney, thyroid, small bowel, breast, and bone[2]. Extranodal involvement of at least one site is identified in 43% of RDD cases and only 23% exclusively have extranodal disease[3]. Typically, the lymph node sinuses are expanded by a proliferation of histiocytes with abundant pale eosinophilic cytoplasm[4].

The etiology and pathogenesis of this disorder is unknown. There is no evidence to support immunodeficiency, autoimmune disease or a neoplastic

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process for the etiology of the disorder. Molecular studies have found no evidence of clonal rearrangement implying that this disease is a reactive or neoplastic condition. An association with Epstein-Barr virus (EBV), cytomegalovirus (CMV), Brucella, Klebsiella, or human herpes virus 6 has been suggested but not proven[5]. SHML involving extranodal sites shows similar morphologic features to its nodal counterpart although more fibrosis and fewer histiocytes are encountered and less prominent emperipolesis (the phagocytosis of lymphocytes and plasma cell by the histiocytes)[6]. SHML is generally regarded as a benign disorder inspite of its propensity to form large masses and to disseminate to both nodal and extranodal sites. It usually shows a prolonged clinical course with occasional exacerbation and remission phases and a patient may experience recurrent or persistent but stable lymphadenopathy. Prognosis is generally good but clinical or laboratory evidence of immune dysfunction tends to predict a poorer outcome. In most cases the disease undergoes spontaneous resolution. In others, an insidious course develops for years or decades. In rare cases, the disease follows an aggressive course and may be fatal 6 and involvement of kidney, lower respiratory tract, or liver has been found to be a poor prognostic sign 3. Occasionally, RDD may be associated with autoimmune disorders and hematopoietic malignancies [7,8,9,10].

Case report

Mr Zakir Hossain, 38 years old male hailing from Gashala village of Sirajgong district, presented to Khwaja Yunus Ali Medical College & Hospital at Sirajgonj on 04th December 2010 (R01102035615, C0110012070799) with firm, nontender, discrete, multiple small sized (ranging as 1-4 cm) palpable lymph nodes in both sides of the neck and axilla (Fig-A). He had low grade fever off and on with malaise and general weakness for the last one year or more.

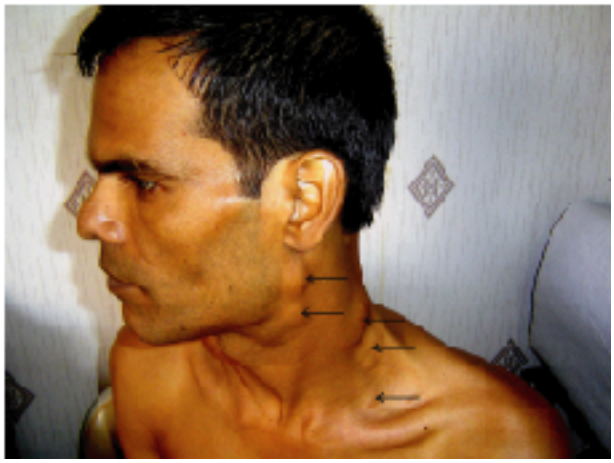

Figure-A

The patient had no past significant medical history or any family history of tuberculosis. His pulse was 96/minute, temperature: 980F (370C), blood pressure: 110/70mm Hg, weight; 47 kg, and height 163.5 cm, he was found mildly anemic, liver and spleen were just palpable. Routine laboratory investigations revealed hemoglobin: 8.9gm/dL, WBC count was 22.18 x 109/L with neutrophil leucocytosis, neutrophil % being 87.1%, platelet count: 306 x 109/L, Erythrocyte Sedimentation Rate: 118 mm at the end of 1st hour. Chest skiagram showed nothing significant. Routine test of the urine was unremarkable. Ultrasonographic study of the whole abdomen revealed mild hepatosplenomegaly. Tuberculin test showed an induration of 13 mm. Immunochromatographic tests for tuberculosis were negative, and chromatographic immunoassay of antibody to Leishmania in serum was found negative. Fine needle aspiration smear cytology (FNAC) of lymph node repeated twice showed lymphocytes at various stages of development and maturation, histiocytes and plasma cells. No granuloma, Reed Sternberg or malignant cells were seen. FNAC in both times however reported chronic nonspecific lymphadenitis. The patient received a course of antibiotic without any response. Biopsy of cervical lymph node revealed dilated sinuses filled with histiocytes and lymphocytes, architecture of the lymph node was partially preserved with follicular hyperplasia showing inflammatory cells having neutrophils, lymphocytes and histiocytes. No granuloma or malignancy was seen. These findings were considered consistent with sinus histiocytosis with chronic lymphadenitis. The patient refused to do bone marrow study. He was given a course of prednisolone to which he showed response and his fever subsided with feeling of well being. He was advised for regular follow up but the individual failed to report.

Discussion

Sinus histiocytosis with massive lymphadenopathy is a rare disorder characterized by a nonmalignant proliferation of histiocyte within lymph node sinuses and lymphatics in extranodal sites. Most cases occur in the first or second decade of life. The patient reported here was an adult. Most patients with SHML tend to have a chronic massive enlargement of cervical lymph

nodes frequently accompanied by fever, elevated ESR, neutrophilia, and polyclonal gammopathy 5. In addition to lymphadenopathy our patient had history of chronic recurrent fever with mild hepatosplenomegaly and laboratory investigations showed elevated ESR, neutrophilic leucocytosis. Biopsy of cervical lymph node showed dilated sinuses filled with histiocytes and lymph node architecture showing inflammatory cells having lymphocytes and histiocytes. These findings were considered consistent with sinus histiocytosis with chronic lymphadenitis. The morphological feature of smears of affected lymph node in a patient with SHML includes a histiocytic proliferation with presence of large histiocytes showing fine vacuoles in the cytoplasm and large vesicular nuclei. The phagocytosis of lymphocytes and plasma cell (emperipolesis) is characteristic[11]. The background population predominantly consists of lymphocytes, plasma cells, and neutrophils. On immunocytochemistry, the histiocytes are positive for S-100 and CD-68 and, negative for CD-1a, which confirms the diagnosis of RDD 12. Immunohistologic, flow cytometry & marker studies could not be done in our case. Immunoglobulin levels and serologic tests for CMV, HIV, and PCR of mycobacteria were also not done in our patient. We had some limitations to do those investigations. When compared to surgical core or excision biopsy, FNA can at times be misinterpreted due to limited or non-representative sampling and, as FNA does not permit examination of the tissue architecture, diagnosis can be further confounded. Despite these potential limitations, FNA is still a very useful tool for the diagnosis of RDD[12].

The common differential diagnoses include infectious lesions, reactive lymphoid hyperplasia and hematological malignancies. A detailed clinical history and careful morphological asses-sment usually prevents misdiagnosis.

The course of SHML is usually benign, indolent and self-limiting in most of the patients. Treatment does not appear to be necessary in the majority of patients since the disease does not usually threaten life or organ function. Surgery is generally limited to biopsy to confirm the diagnosis or, to relieve obstructive symptoms by debulking. Patients with progressive disease have been treated with corticosteroids, chemotherapy or radiotherapy with variable results[13]. For patients with high fever without other symptomatology steroid therapy may be instituted[14]. Our patient received corticosteroids to which he responded. However all patients deserve long-term follow-up, since the natural history of the disease is quite variable, usually alternating periods of exacerbations and resolutions or, rarely, pursuing a progressive course[14].

Conclusion

In summary, RDD, a rare, benign, self-limiting histiocytic proliferative disorder, can be encountered in both nodal and extranodal locations, and recognition of this disorder is important to avoid misinterpretation and subsequent unnecessary treatment. To conclude, these types of cases, one as reported above, should alert the clinician and cytopathologist to the possibility of occurrence of SHML even in minimally enlarged lymph nodes. Careful interpretation of FNAC slides along with appropriate marker study would help in early diagnosis and timely management. Moreover, it has been suggested that the terminology of massive lymphadenopathy in SHML may be revised to Sinus Histiocytosis with Lymphadenopathy (SHL) or use of RDD should be encouraged[15].

References

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol. 1969;87:63-70.

2. Tiju JW, Hsiao CH, Tsai TF. Cutaneous Rosai-Dorfman disease: remission with thalidomide treatment. Br J Dermatol. 2003;148:1060-1061.

3. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol. 1990;7:19-73.

4. Pettinato G, Manivei JC, d'Amore ES, Petrella G. Fine needle aspiration cytology and immunocytochemical characterization of the histiocytes in sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman syndrome) Acta Cytol. 1990;34:771-777.

5. Karpas A, Worman C, Arno J, Nagington J. Sinus histiocytosis with massive lymphadenopathy: virological, immunological, and morphological studies. Br J Haematol. 1980;45:195-200.

6. Gaitonade S. Multifocal, extranodal sinus histiocytosis with massive lymphadenopathy. Arch Pathol Lab Med. 2007;131:1117-1121.

7. Maia DM, Dorfman RF. Focal changes of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) associated with nodular lymphocyte predominant Hodgkin's disease. Hum Pathol. 1995;26:1378-1382.

8. Garel L, Lucaya J, Piqueras J. Clinical quiz. Large anaplastic lymphoma coexisting with Rosai-Dorfman disease. Pediatr Radiol. 2004;34:509-510.

9. Lu D, Estalilla OC, Manning JT, Jr, Medeiros LJ. Sinus histiocytosis with massive lymphadenopathy and malignant lymphoma involving the same lymph node: a report of four cases and review of the literature. Mod Pathol. 2000;13:414-419.

10. Maia DM, Dorfman RF. Focal changes of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) associated with nodular lymphocyte predominant Hodgkin's disease. Hum Pathol. 1995;26:1378-1382.

11. Stastny J F, Wilkerson M L, Hamati H F, Kornstein M J. Cytologic features of sinus histiocytosis with massive lymphadenopathy. A report of three cases. Acta Cytol 1997;41:871-876.

12. Shi Y, Griffin A C, Zhang P JL, Palmer J and Gupta P. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman Disease): A case report and review of 49 cases with fine needle aspiration cytology. Cytojournal. 2011; 8: 3. PMCID: PMC3049239

13. Goodnight J W, Wang M B, Sercarz J A, Fu Y S. Extranodal Rosai- Dorfman disease of the head and neck. Laryngoscope 1996;106:253-256.

14. Ju J, Kwon Y S, Jo K J, Chae D R, et al. Sinus Histiocytosis with Massive Lymphadenopathy: A Case Report with Pleural Effusion and Cervical Lymphadenopathy. J Korean Med Sci. 2009; 24(4):760-762.

15. Sachdev R, Setia N, Jain S. Sinus histiocytosis with massive lymphadenopathy. Is the lymph node enlargement always massive? Med Oral Pathol Oral Cir Bucal. 2007;12:198-200.