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Case report

SINUS HISTIOCYTOSIS AND MASSIVE LYMPHADENOPATHY (ROSAI-DORFMAN DISEASE) IN AN 8 YEAR OLD FEMALE CHILD: A RARE CASE REPORT

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ABSTRACT

Introduction: Sinus histiocytosis with massive lymphadenopathy is an infrequent, self-resolving histo-proliferative disorder of benign nature, also known as Rosai–Dorfman Disease. The typical manifestation of this disease includes bilateral, progressive cervical lymphadenopathy along with pyrexia. Laboratory manifestations consist of raised erythrocyte sedimentation rate, leukocytosis and hypergammaglobulinemia. **Case report:** An 8 year old female child presented with progressive, painful cervical and submandibular lymphadenopathy of three months duration. There was polymorphic leukocytosis and anemia along with raised Erythrocyte sedimentation rate and hypergammaglobulinemia. Fine Needle Aspiration cytology revealed sinus histiocytosis with massive lymphadenopathy, which was confirmed by the cervical lymph node biopsy. The histopathology revealed dilated sinuses filled with lympho plasma cells, large histiocytes and engulfed neutrophils (Emperipolesis). **Conclusion:** Massive, progressive bilateral cervical and sub mandibular lymphadenopathy, suggesting Sinus histiocytosis and massive lymphadenopathy-Rosai–Dorfman Disease. This was confirmed by Cytology, histopathology and immuno- histochemistry.

Keywords: Emperipolesis, Hypergammaglobulinemia, Lymphadenopathy, Fine needle aspiration cytology

INTRODUCTION

The Rosai-Dorfman disease (RDD), also known as Sinus histiocytosis with massive lymphadenopathy (SHML) is a lympho phagocytic disorder first described in 1969[1]. It usually occurs in children and young adults and males are more frequently affected than females[2]. The most frequently affected lymph nodes are cervical lymph nodes and the usually involved extranodal sites are upper respiratory tract, skin, nasal cavity and bone[2]. SHML also involves eyes, ocular adnexa, head and neck, subcutaneous tissue and skeletal muscle (including heart and breast). Even the central nervous system, gastrointestinal tract, including liver, salivary glands, genitourinary tract (kidney and uterine cervix) and thyroid may be affected[2]. The characteristic presentations comprise febrile onset multiple, painless, bilateral cervical lymphadenopathy. Raised erythrocyte sedimentation rate (ESR), elevated white blood cell count and hypergammaglobulinemia are distinct features of SHML. Though, the fine needle aspiration cytology (FNAC) identifies majority of the SHML, biopsy is indicated in some, where the cytomorphology is inconclusive.

CASE REPORT

An 8 year-old female child presented with progressive cervical lymphadenopathy of three months duration. It was associated with fever spikes

and profound sweating for one month. The lesions initially started over the posterior aspect of the neck which gradually extended all over the neck in three months. These were accompanied by pain which subsided with antimicrobial administration. No history of contact with tuberculosis and there was no weight loss. Clinical examination revealed multiple, bilateral, cervical and submandibular lympadenopathy of 1.5cm to 3 cm size (as shown in figure 1). They were non-tender, discrete, firm and immobile. The skin over the lesions was smooth and shiny. This was not accompanied by lympadenopathy in other regions or organomegaly. The peripheral blood cell count showed anemia (hemoglobin-10.8gms %), polymorphic leukocytosis (21,000/cu. mm) and Erythrocyte sedimentation rate (ESR) was elevated (75 mm at the end of one hour). Likewise, serum gamma globulins were raised. Abdominal ultrasongraphy delineated mesenteric lymphadenopathy, but there was no organomegaly. Also, there was no mediastinal lympadenopathy on Chest radiograph. Retro-viral serology was negative and hepatits B surface antigen was also negative. Important causes of massive lymphadenopathy in children contain tuberculosis, lymphoreticular malignancy and reactive histiocytosis. Hence the child was subjected to FNAC of cervical and submandibular lymph nodes. This was done with multiple passes from different sites and some of the smears were highly cellular consisting of many large histocytes, along with lymphophagocytosis (emperipolesis) by these histiocytes. There were reactive polymorphs, lymphocytes and few plasma cells in the background (as shown in figure-2, (H&E 400X)). This distinct cytomorphology is phathognomic of SHML/RDD. The child was further investigated with cervical lymph node excision biopsy for additional confirmation. Histopathology disclosed thickened capsule, perinodal fibrosis and dilated sinuses upon reactive lymphoid background. These sinuses were distended with lympho plasma cells, large histiocytes containing vesicular nuclei and engulfed lymphocytes and polymorphs (emperipolesis) (as shown in figure-3, H&E 200X). Some of the histiocytes showed nuclear debris, however, there were no eosinophils, granulomas and necrosis was absent. Immunohistochemistry, S100 highlights histiocytes (SHML cells) in the distended sinuses (as shown in figure-4, (400X, S100)), ascertaining the diagnosis of RDD. The child showed a dramatic response to oral steroids in follow-up in the form of lymphnodes regression.

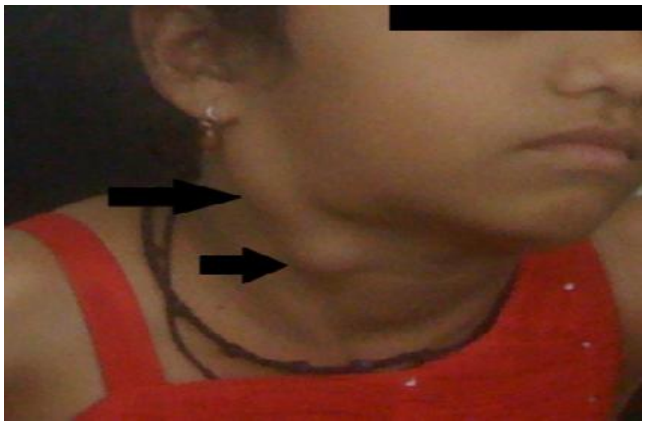

Fig 1: Clinical photograph revealing cervical lymphadenopathy- as shown with arrows.

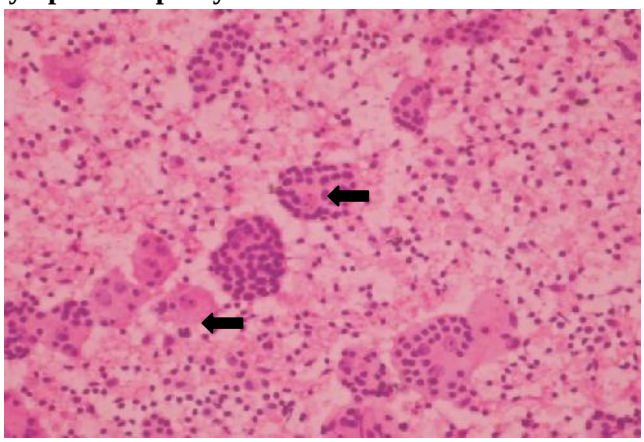

Fig2: Cytology smear (H&E 400X) revealing many large histocytes, with lymphophagocytosis (emperipolesis) (As shown with arrows. Background showed reactive polymorphs, lymphocytes and few plasma cells)

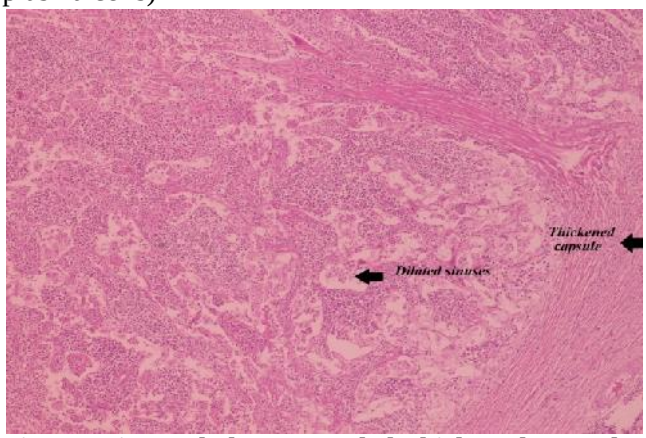

Fig 3: Histopathology revealed thickened capsule, perinodal fibrosis and dilated sinuses. Background shows reactive lymphoid population. These sinuses were distended with lympho plasma cells, large histiocytes with vesicular nuclei and engulfed lymphocytes and polymorphs (emperipolesis) - as shown with arrows. (H&E 200X)

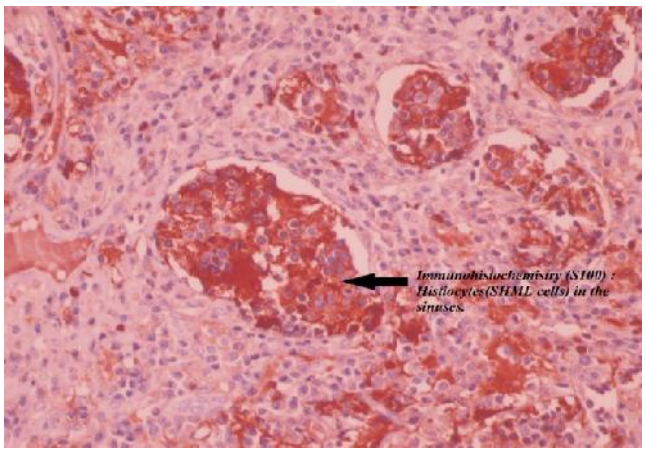

Fig 4: Immunohistochemistry, S100 (400X, S100) highlights histiocytes (SHML cells) in the distended sinuses- as shown with arrows.

DISCUSSION

The RDD is an unusual disorder of bone marrow stem cell origin[3]. Although, any age group can be affected, majority of these cases are reported in second decade of life. Males are more commonly affected than females[4].The index case being a female child and manifesting before first decade of life makes this case a rare presentation. The salient clinical features include painless, bilateral, progressive cervical lymphadenopathy. This is frequently associated with fever, anemia (66%) leukocytosis (59%), neutrophilia (68%), elevated ESR (88 %), and hypergammaglobulinemia (90%) which were noted in the index case. Also, a varied extranodal manifestation has been reported[4] in SHML, the most common being eyed, ocular adnexa, salivary glands and gastrointestinal tract. Likewise, central nervous system and genitourinary tract can also get affected[4]. There was associated mesenteric lymphadenopathy in this case, but mediastinal lymphadenopathy and organomegaly were absent. Although the accurate etio-pathogenesis of SHML is unknown, infectious etiology coupled with immuno compromised status have been implicated. Human herpes virus (HSV) 6 (as detected by fluorescent in situ hybridization (FISH)), Epstein-Barr virus and cytomegalovirus (CMV) have been reported to be the etiological factors. Likewise, bacterial pathogens like Klebsiella and Brucella also have been attributed[4, 5]. The index case had polymorphic leukocytosis with elevated ESR, but the blood culture was sterile and the viral markers were negative for retrovirus and CMV. However, Epstein -barr virus and HSV-6 viral assay could not be done due to financial constrains. The characteristic cytological features of SHML include abundant large histiocytes with plentiful, phagocytosed lymphocytes (emperipolesis) and pale cytoplasm lymphocytes, plasma cells, and occasional neutrophils in the background[3,6,7]. This emperipolesis, a hallmark of SHML/RDD was seen in our case[8]. Humble et al., in 1956 defined emperipolesis as a biological phenomenon in which an intact cell is penetrated by another. It is different from phagocytosis as the viable engulfed cell exists within another cell, can exit with no morphological and physiological consequence for either of them[9]. These histiocytes reveal positive immunostaining for various markers like S100 protein, which was seen in the index child. Immunostaining for other proteins as CD11c, CD14, CD33, and CD68[4] have also been reported. Presence of positive immunohistochemistry for S100 protein in our case makes it a unique entity. Characteristic histological features are well reported in the literature; however the cytomorphology on FNAC is less defined[6]. Along with histology, cytology was also characteristic of SHML in our case, which makes it further special.

The important histological differential diagnoses include tuberculosis, hemophagocytic syndrome; Langerhans cell histiocytosis, reactive sinus histiocytosis and lymphoma[4]. Granulomatous epithelioid cells and caseous necrosis, histological features of tuberculous lymphadenitis are absent in SHML, in our case. Presence of hemophagocytosis, pancytopenia, hepatosplenomegaly and absence of emperipolesis, suggest hemophagocytic syndromes which were absent in our case. Langerhans cells with pathognomnic Birbeck granules and eosinophilic microabscess were absent in our case[4,6,10]. Reed-Sternberg cells and eosinophils, characteristic histological features of Hodgkin's lymphoma were also absent in RDD, our case[4,6].

The mainstay of treatment is supportive and symptomatic as there is no ideal treatment. However, various treatment modalities include surgery, radiotherapy, steroids and chemotherapy[11]. The usual course of this disease is indolent with 50% of the patients showing a complete resolution without squeale and one third of the patients have persisting asymptomatic lymphadenopathy. Very few (17%) continue to be symptomatic after 5 to 10 years[11]. The

index child showed resolution of lymphadenopathy with steroid therapy, within three months.

CONCLUSION

SHML/RDD in an 8 year old female child presenting with massive progressive cervical, sub mandibular lymphadenopathy and typical laboratory findings. The presence of characteristic cytomorphology, emperipolesis and positive immune reactivity for S100 protein in the first decade of life makes this case unique.

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Conflict of interest: Nil

REFERENCES

1. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinicopathological entity. Arch Pathol. 1969; 87:63–70.
2. Warnke RA, Weiss LM, Chan JK, Cleary ML, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). In: Rosai J, eds. Atlas of Tumor Pathology, 3rd Series: Tumors of the Lymph Nodes and Spleen. Washington: Armed Forces Institute of Pathology; 1995:349–60.
3. Das DK, Gulati A, Bhatt NC, Sethi RG. Sinus histiocytosis with massive lymphadenopathy (Rosai–Dorfman disease): Report of two cases with fine needle aspiration cytology. Diagn Cytopathol. 2001; 24:42–45.
4. Kumar B, Karki S, Paudyal P. Diagnosis of sinus histiocytosis with massive lymphadenopathy (Rosai–Dorfman disease) by fine needle aspiration cytology. Diagn Cytopathol. 2008; 36:691–95.
5. Lampert F, Lennert K. Sinus histiocytosis with massive lymphadenopathy: Fifteen new cases. Cancer. 1976; 37:783–89.
6. Deshpande AH, Nayak S, Munshi MM. Cytology of sinus histiocytosis with massive lymphadenopathy (Rosai–Dorfman disease) Diagn Cytopathol. 2000; 22:181–85.
7. Iyer VK, Handa KK, Sharma MC. Variable extent of emperipolesis in the evolution of Rosai Dorfman disease: Diagnostic and pathogenetic implipications. J Cytol. 2009; 26:111–16.
8. Snehalatha R, Senthilnathan P, Prathiba Ramani, Sherlin J Herald. The rosai dorfman syndrome-the report of a rare case. Journal of Clinical and Diagnostic Research. Available from http:// www. jcdr. net// back_ issues.asp2014.
9. Humble JG, Jaynee WHM, Pulvertaft RJ, Biological interaction between lymphocyte and other cells Br J Hematol 1956; 2:283.
10. Eisen RN, Buckley PJ, Rosai J, Immunophenotypic characterization of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) Semin Diagn Pathol 1990; 7(1):74-82.
11. Raveenthiran V, Dhanlaxmi M, Hayavadana Rao PV, Vishwanathan P, Rosai dorfman disease: report of a 3 year old girl with review of treatment options Eur J Paediatric Surg 2003; 13:350-54.