Rosai Dorfman Syndrome - A rare clinical entity

S.S. Bist • Saurabh Varshney • Manisha Bisht • V.P. Pathak • Anuradha Kusum • Nitin Gupta

Abstract

Sinus histiocytosis with massive lymphadenopathy (also known as Rosai Dorfman syndrome) is a unique disease of unknown etiology with a childhood predilection. It is an uncommon benign condition, often confused with lymphoma. Patients usually present with massive, painless, bilateral cervical lymphadenopathy and clinical course is variable. This condition has been sporadically reported in Indian literature¹. Here we report a 26-year-old women presenting with a painless bilateral cervical lymphadenopathy. A FNAC from cervical lymph node was compatible with Rosai Dorfman syndrome and confirmed histopathologically.

Keywords Sinus histiocytosis • Massive lymphadenopathy • Rosai Dorfman syndrome.

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML) was initially described by Azoury and Reed in 1966, later it was described to have a benign course by Rosai and Dorfman in 1969 and is now widely known as Rosai Dorfman syndrome². SHML is a histopathological entity consisting of cervical lymphadenopathy, which shows marked dilatation of the lymph node sinuses containing histiocytes. It is a rare cause of cervical lymphadenopathy, usually seen in the first decade of life and should be considered in the differential diagnosis. Castleman's disease, dermatopathic lymphadenitis, mucocutaneous lymph node syndrome (Kawasaki's disease), histiocytic necrotising lymphadenopathy (Kikuchi's disease), vascular transformation of lymph nodes and inflammatory pseudotumor of the lymph node are among the other rare causes of lymph node enlargement. SHML is an important addition to this list. A clinician may rarely encounter a clinical picture indistinguishable from lymphoma. However, histopathological report as SHML may come as a surprise. At the same time it comes as a relief to the clinician and the patient, as the disease has a benign course.

Case Report

A 26-year-old female presented with bilateral, painless cervical lymphadenopathy with accompanying history of intermittent low-grade fever for past three years. According to the patient, she had undergone tonsillectomy for the same problem two and half years ago. But contrary to the expectation, the neck swelling did not regress even after tonsillectomy and was progressively increasing in size and number. She also received anti tubercular therapy for 4 months prescribed by a private practitioner without any improvement. On local examination she had bilateral multiple cervical lymph node enlargements, which were grossly enlarged, firm, non-tender and matted with smooth surface (Fig.1). Rest of ENT and systemic examination was normal. Investigations showed a HB-10 gm/dl, total WBC count -7560/cu mm, differential WBC count -N 67, L32, E01 and ESR-

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Fig. 1 Clinical photograph of the patient showing bilateral cervical lymphadenopathy

Fig. 2 Microphotograph showing characteristic emperipolesis with abundant histiocytes (H & E X 40).

65 mm 1st/hr. Peripheral blood film showed microcytic, hypochromic red blood cells. Chest x-ray and USG scan of the whole abdomen was revealed normal. FNAC of right and left cervical node showed sheets of sinus histiocytes with many of these showing lymphocytophagocytosis and erythrophagocytosis (emperipolesis) (Fig. 2). Lymph nodes biopsy showed markedly dilated sinuses containing sheets of histiocytes with eosinophilic cytoplasm and small nuclei, some of the histiocytes show lymphocytes in cytoplasm. There was no evidence of malignancy or granulomatous lesion. These features were consistent with a diagnosis of sinus histiocytosis with massive lymphadenopathy. Bone marrow examination was reported normal. The patient was treated with oral prednisolone 60 mg / day for a period of 6 weeks and then tapered off. On follow up the lymph nodes enlargement regressed in size and the fever subsided. The patient is still under follow up.

Discussion

SHML is a well-recognized benign syndrome but a rare cause of lymphadenopathy in the adult. The disease shows a worldwide distribution and can manifest in any age group. 81% of reported cases occur during the first and second decades of life and has a 2:1 male-to-female ratio³. Our patient was a female who reported the occurrence of the disease during the third decade of life. The predominant clinical manifestation of the disease is massive cervical lymphadenopathy (87.3% of cases) that, in most cases, is painless and bilateral, affecting one or all-cervical chains. Lymph nodes are isolated, mobile, and small during the initial stages but becomes adherent with disease progression, forming a voluminous multinodular mass. The axillary (23.7%), inguinal (25.7%), and mediastinal (14.5%) regions can also be affected, but always to a lesser extent than cervical involvement⁴. In our case only bilateral cervical group of lymph nodes were involved. Extranodal manifestation of the disease is observed in 28-43% of cases, with preference for

head and neck region^{3,5} which was not seen in our case. The most common sites of extranodal involvement are skin (27.4%), nasal and paranasal cavities (26.8%), subcutaneous tissue (22.2%), orbit and eyelids (20.1%) and bone (18.4%). In extremely rare circumstances the central nervous system can also be affected. Suprasellar involvement mimicking meningioma has been reported⁶. The concomitant involvement of one or more sites in the same individual is observed in up to 44.7% of cases. According to one study⁷, the most frequent otorhinolaryngologic manifestations are found in the nasal cavity (50%), pharynx (25%), paranasal sinuses (18.7%), amygdala (12.5%) and trachea (6.3%). Fever occurs in up to 30% of cases, which was also present in our case. Anemia, leukocytosis, neutrophilia, increased ESR and hypergammaglobulinemia are other common associations. The etiology of SHML still remains obscure, but two theories exist. One associates the disease with a specific infectious process; the other attributes it to a disturbance of the immune system. However, no laboratory evidence pointing to an etiologic agent and no other clinicopathological signs suggesting a deficient humoral or cellular immunity or phagocytosis disorder have been reported⁴. The diagnosis of Rosai Dorfman disease is made on the basis of clinical suspicion and confirmed by histopathological examination and immunohistochemical studies. In lymph nodes, the sinuses are markedly dilated and crowded with histiocytes, lymphocytes and plasma cells. Histiocytes show abundant foamy cytoplasm, some of which show small lymphocytes in cytoplasm (emperipolesis). Emperipolesis means lymphocytophagocytosis, which differs from phagocytosis in that lymphocytes taken up are not attacked by enzymes and appear intact within the histiocytes. The distinctive histiocytes of SHML that exhibit emperipolesis, their association with numerous plasma cell and the distension of lymph node sinuses or lymphatics in extranodal sites distinguish SHML from a variety of benign and malignant disorders in which phagocytosis of cells may be a prominent

feature. The latter include melanoma and cancer metastatic to lymph nodes, since malignant cells have the propensity to phagocytose hematopoietic cells. Histiocytes are S-100 positive, CD 1a-negative and do not contain Birbeck granules. However, these marker studies could not be done in our patient. Even though it is considered as a benign disease, fatalities could occur due to cellular infiltrate of SHML. The causes of death due to SHML were reported to be a combination of cellular infiltration, mass forming ability of SHML and also may be due to defect in immune function⁸. In general, extranodal involvement does not determine a more aggressive character or poor outcome; however, generalized lymphadenopathy, extranodal involvement of multiple organs (kidney, lungs and liver) and immunologic alterations lead to a poor prognosis⁸. There is no specific treatment for SHML.

Treatment is necessary only when the disorder becomes organ or life threatening. The treatment modes include corticosteroids, chemotherapy with a combination of vinca alkaloids and alkylating agents, low dose interferon, antibiotics therapy, radiotherapy and surgical treatment with partial or total resection⁹. Surgical option may be reserved for compressive symptoms, like airway obstruction, neurologic or ocular compressions, or severe deformation. However, the best treatment for SHML has yet to be established. We had treated our patient with corticosteroid therapy for which the response was favourable.

Conclusion

Rosai Dorfman syndrome is a rare cause of lymphadenopathy but a well-defined clinicopathologic entity. Massive cervical lymphadenopathy is the hallmark of the disease and head-neck region is the preferred site of the extranodal involvement.

Hence otorhinolaryngologists and pathologists should always be aware of SHML in making a differential diagnosis of cervical lymphadenopathy.

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