Case Report

Rosai Dorfman disease- a rare entity report of two cases with nodal and extranodal involvement

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Abstract

Rosai Dorfman Disease (RDD) also known as Sinus Histiocytosis with Massive Lymphadenopathy (SHML) is a very rare variety of reactive histiocytoses. It commonly involves cervical lymph nodes, although involvement of other lymph node regions, skin and other organ involvement can occur. It has a good prognosis so there is a need to differentiate it from other lympho proliferative disorders of poorer prognosis. We present two cases of this rare disorder illustrating its clinical spectrum; a 22 years old woman with involvement of submandibular lymph nodes, nasal septum and sub-glottic region and a 45 years old male with prominent skin involvement.

Introduction

Histiocytic proliferative disorders are classified into three main types. Type 1 also known as Langerhan cell histiocytosis is due to reactive proliferation of langerhan cells; type2 (a) is due to reactive proliferation of dermal dandrocytes; type 2 (b) due to reactive proliferation of histiocytes other than Langerhan cells or dermal dandrocytes; and type 3 is due to malignant proliferation of histiocytes.[1] Rosai Dorfman Disease (RDD) also known as Sinus Histiocytosis with Massive Lymphadenopathy (SHML) is a very rare disorder belonging to type 2(b) histiocytosis and was first described by Rosai and Drofman in 1969.[2] Its clinical presentation is varied and usually presents with lymphadenopathy which most of the time reaches massive proportions. Skin is the most common site of extra nodal involvement. Other documented sites are gastrointestinal tract, genitourinary tract, bones and brain. We present two cases of this rare disorder; a 22 years old lady only with involvement of submandibular lymph nodes, nasal septum and sub-glottic region and a 45 years old male with prominent skin involvement. As it is a self-limiting disease in most cases and has a good prognosis, there is a need to differentiate it from other lympho proliferative disorders with poorer prognosis.

Case 1

A 22 years old woman presented with history of progressive nasal blockade, stridor, hoarseness of voice and multiple swellings in the neck for the last 5 years. Nasal blockade and stridor were the initial symptoms. The neck swellings appeared about one year after the above symptoms. These were painless but kept increasing in size gradually. There was also a history of significant weight loss. As tuberculosis being prevalent in this part of the world, she was provisionally diagnosed as a case of tuberculosis and was given anti tuberculosis therapy for 9 months but there was no response. She had taken multiple other treatments but no record was available.

On examination she had 3 large lymph nodal swellings in the sub-mandibular region, one on right and two on the left side (Figure 1). These were firm and non tender. The margins were well defined and discrete. The overlying skin was normal and not attached to the underlying masses. The swellings were mobile and not attached to the underlying tissues. There were no other swellings on the rest of the body. Rest of the systemic and dermatological examination revealed no abnormality. Examination of the nose showed thickened nasal septum. Indirect laryngoscopy showed a bulge in the subglottic region with intact mucosa and narrowed lumen.

Biopsy was taken from the swelling in left sub mandibular region which on histopathology showed extensively dilated sinuses with lymphocytes, plasma cells

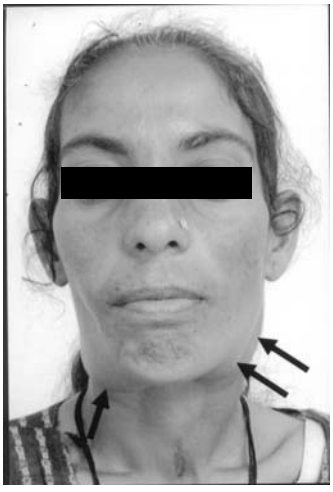

Figure 1. Three large lymph nodal swellings in the neck.

and scattered multinucleated foamy histiocytes showing lymphophagocytosis (emperipolisis).. The multinucleated histiocytes had mild to moderate atypia. Immunohistochemical staining was positive for S-100. These findings confirmed the diagnosis of SHML. CT Scan of brain, chest and abdomen was done but no other lesions were detected.

Considering the self limiting course of the disease in most of the cases she was reassured. The patient is on follow up for last 9 months without any medication. The progression of disease has stopped. There has been reduction in stridor and hoarseness of voice has also decreased. However, nasal blockade and swellings persist.

Case 2

A 45 year old male presented with hoarseness of voice, and multiple swellings on the skin for the last five years. The lesions had been persistent despite various treatments. Examination of the skin revealed multiple brown to skin colored nodules and plaques of various sizes distributed over trunk (Figure 2). Cervical lymph nodes were enlarged firm, discrete and mobile. Skin biopsy on histopathology revealed a polymorphous infiltrate of lymphocytes, plasma cells and scattered multinucleated foamy histiocytes showing lymphophagocytosis (emperipolisis). Immunohistochemical staining was positive for S-100. CT scan of brain, chest and abdomen was done but no other lesions were detected. On these findings a diagnosis of SHML with skin involvement was made. The patient had been previously tried on various chemotherapeutic agents including methotrexate and cyclophosphamide but with no improvement. We observed the patient for two years without any treatment but his symptoms and signs remained unchanged without any improvement or deterioration. The patient was lost to follow up.

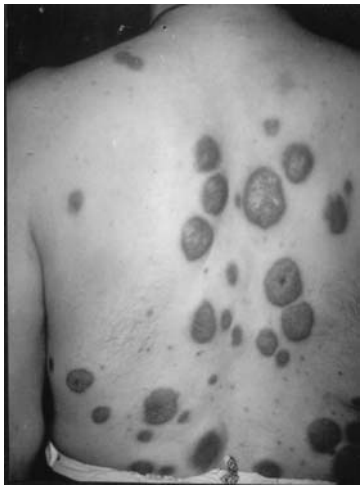

Figure 2:. Multiple brown to skin colored nodules and plaques of various sizes distributed over trunk.

Discussion

More than 600 cases of RDD had been reported, in all races but mainly in the whites (43%), in any age group but more in first and second decades (81%), and more in males than females (2:1).[3] Our first patient was a 22 year old female whereas the second was a 45 year old male.

SHML is considered to be a reactive rather than malignant histiocytosis. The disorder is due to immune dysregulation possibly in response to an infectious agent. The stimulation of monocytes/macrophages via Macrophage-Colony-Stimulating-Factor leads to proliferation of macrophages, which is the main pathogenesis of SHML.[4] Search for a possible infectious agent has been inconclusive. Some patients have shown evidence of Epstein-Barr virus, Klebsiella rhinoscleroma and Brucella, but these are not consistent findings. A recent study failed to show evidence of human herpes virus 6 and 8 in skin lesions.[5] In none of our two patients was there evidence of any preceding infection.

The most common clinical presentation of SHML is painless lymph node enlargement. The enlargement is usually massive but sometimes may be mild.[6] In 90% cases cervical lymph nodes are affected but involvement of the other lymph node regions has been reported. Our first patient had only isolated cervical lymph nodal enlargement where as second patient had involvement of cervical nodes in addition to skin lesions. Fever, night sweats, malaise and weight loss may be present at the time of presentation as was seen in our first patient who reported significant weight loss.

Forty three percent of patients have at least one extra nodal site involved. Skin is the most common region and no nodes may be affected. Pure cutaneous SHML may remain localized to skin with no systemic involvement even with long term follow up.[7] In our second patient there were prominent skin lesions with nodules and plaques. Other organs involved include bone, salivary gland, central nervous system, genitourinary system, lower respiratory tract, liver, gastrointestinal tract, heart and thyroid gland. We were unable to locate any other organs affected despite extensive clinical examination and investigations in both of our patients.

Microscopic features have been well described.[8] A polymorphous cellular infiltrate composed of neutrophils, lymphocytes, plasma cells, medium-sized mononuclear cells with indented nuclei, and, typically, numerous large and distinctive Rosai Dorfman (RD) cells expand lymph node sinuses. RD cells have abundant cytoplasm with round-to-oval, medium-to-large nuclei with a vesicular chromatin pattern. Nuclear atypia is unusual. Phagocytized intact-appearing lymphocytes are present in the cytoplasm of most RD cells (lymphocytophagocytosis or

emperipolesis: "wandering about within"), which is a diagnostic feature. The other important factor is that RD cells are S-100 protein-positive on immunohistochemistry. CD 68 staining may also be positive. In extra nodal SHML the picture is exactly similar to the nodal disease and appears to be an abnormal lymph node architecture. The histopathology of both of our patients showed all the above features along with the presence of S-100 protein on immunohistochemistry.

The common differential diagnoses include infectious lesions, reactive lymphoid hyperplasia with sinus histiocytosis, Langerhans cell histiocytosis, haemophagocytic syndrome and malignant lymphoma. A detailed clinical history and careful morphological assessment usually prevents misdiagnosis.

Many treatments have been tried, including steroids, vinca alkaloids, etoposide, ciclosporin and x-rays but no ideal therapy has been identified and the response is generally poor.[9] Our second patient did receive chemotherapy but his disease persisted with no improvement.

The prognosis of SHML is reasonably good. In 238 patients followed for more than a year, 49 were well and free from the disease, 126 had persistent disease, 3 had progressive disease and 21 died, although 4 deaths were unrelated to SHML. Poor prognostic features in this disease are immunological abnormalities and multiple extra nodal sites of the disease.[10] The lesion in our first patient was progressive for about 3 years and since then it is persistent and is now regressing. She has been followed for 9 months and during this time the stridor and hoarseness of voice have reduced although lymph node swellings persist. The disease in our second patient remained unchanged despite treatment.

Our two patients adequately illustrate the main clinical spectrum of a rare disease. Our first case can easily be misdiagnosed as tuberculosis or lymphoma and the second can be mistaken for mycosis fungoides (Cutaneous T cell lymphoma). Background knowledge and high index of suspicion is required to diagnose this rare disorder with a variable but relatively benign prognosis.

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