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CASE REPORTS

ROSAI DORFMAN DISEASE

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Summary:

Mr. Shahinoor an 18 year old ,ale got himself admitted at DMCH in July,2007 with the complaints of bilateral neck swelling and fever for 1 month. The enlarged lymph nodes were clustered in cervical regions involving both anterior and posterior chains and largest one measuring 5 cm×2.5 cm.He was otherwise healthy on examination. Full blood count showed neutrophil leukocytosis and raised ESR.Sputum for AFB was found negative and xray chest was normal. FNA of lymph node showed non specific lymphadenitis with reactive hyperplasis. Lymph node biopsy was done and histopathology revealed Rosai Dorfman Disease, a very rare yet fascinating disorder also called Sinus Histiocytosis with Massive Lymphadenopathy.It is a benign proliferative disorder of the histiocytes. He was not given any tretament and is under follow up.

Introduction:

It is a very rare disorder. Less than 1000 cases reported in literature[1]. RDD originally described as Sinus Histiocytosis with Massive Lymphadenopathy, presents in its most typical form as massive painless bilateral cervical lymphnode enlargement in the neck, associated with fever, leukocytosis, elevated ESR and polyclonal Hypergammaglobulinaemia. It may occur at any age but mostly seen in young adults and children with aslight predilection for males (58%) and for inviduals of African descent[2,3]. Although an etiology is unknown, the disease is thought to be a disorder of immune regulation or response to a presumed infectious agents (HHV-6/EBV) with its major manifestation in lymphnodes with resultant proliferation of sinusoidal histiocytes[4]. Most efforts to identify a pathogen has culminated in indeterminate or negative results[5,6]. Approximately 25% to 40% of SHML cases described to date present in extra nodal organs or tissues , the most common are eye and ocular adnexa(esp. Orbit), head neck region[6], upper respiratory tract, skin and subcutaneous tissue[4,5], skeletal system and CNS[2,3]. Organs that are almost always spared are lung, spleen , bone marrow(the latter exclusive of focal involvement)[7,8]. Diseases that may be associated with RDD are amyloidosis, AIHA, HIV, Lymphoma etc[9-11].

Case history:

An 18 year old male presented with the complaints of bilateral neck swelling and fever for 1 month. He first noticed a swelling in the right side of neck and few days later similar swelling in the left side also.these were painless and were slowly increasing in size. It wa associated with high grade fever (max temp. 103 °F), intermittent in nature with chills and rigor which subside without much sweating and without the help of any drug. He gave history of dry cough in first 15 days of the illnes but later there was no cough. He gave no history haemoptysis, chest pain or dyspnoea. There was no history of pruritus or rash. However , he gave hiistory of sore throat about 1 week preceeding this episode of illness.

He was moderately anaemic, cervical lymph nodes were found to be hugely enlarged, sub mental 1, submandibular 2 , anterior cervical bilateral 2 in number 2 cm×2cm, posterior cervical bilateral 2 in number 5cm×2.5 cm . supraclavicular, epitrochlear, axillary or inguinal lymph nodes were not palpable. Lymph nodes were non tender, rubbery, matted but not fixed with underlyning structure or overlying skin and having no discharging sinus. There were no sign of bleeding or gum hypertrophy or bone pain. No hepatosplenomegaly or ascites found. Initial clinical diagnosis was lymphoma.

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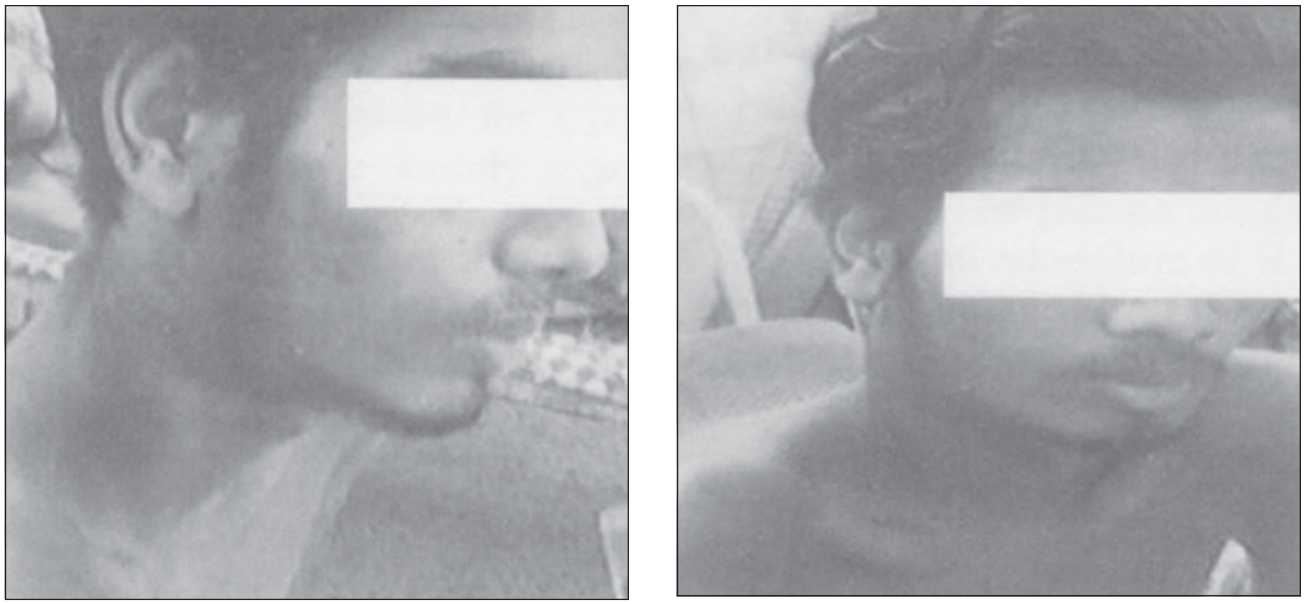

Fig.-1: *Cervical lymphadenopathy.*

CBC showed anaemia with Meutrophil leukocytosis, ESR 121 mm 1st hour, X ray chest P/A view normal study, MT negative and USG whole abdomen showed normal study. FNA of lymph node was done and non specific lymphadenitis was found with reactive hyperplasis of lymphnode.

Left anterior cervical node was excised and biopsy was done. Histopathology revealed:

1. Sinuses are broad and prominent.
2. 2. Proliferation of Histiocyte and emperipolesis present.
3. 3.No malignancy seen.
4. So the comment was Rosai Dorfman Disease.

Final diagnosis was Rosai Dorfman Disease.

Discussion :

In Rosai Dorfman Disease., grossly enlarged nodes are matted together by prominent perinodal fibrosis, therir cut surface varies from grey to golden yellow depending upon the amount of fat present. Microscopically there us pronounced dilatation of the lymph sinuses resulting in partial or complete architectural effacement. These sinuses are occupied by lymphocytes, plasma cells and by numerous cells of histiocytic appearance with a large vesicula nucleus and abundant clear cytoplasm that may contain large number of neutral lipids. Many of these histiocytes have within their cytoplasm intact lymphocuyes, a feature that has been designated as "**Emperipolesis"** or lymphocytophagocytosis[15]. Although not specific, this is a constant feature of RDD and is therefore of great diagnostic significance. Neutrophils exixted in all cases to form microabscesses.

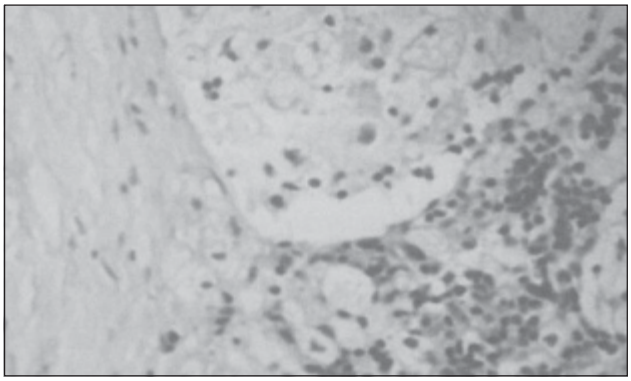

Fig.-2: *Histopathology of Rosai Dorfman Disease.*

Ultrastructuarally, the histiocytes located in the sinus have extensive pseudopodia and lack Birbeck's granule; viral particles or other evidence of infection and consistently lacking. The sinus histiocytes are strongly reactive for S-100 protein but negative for CD1a. Their immunohistochemical profile suggests that they are monocytes that have recently been recruited from circulation. The plasma cells show a polyclonal pattern of immunoglobin expression. The lymphocytes are an admixture of B & T cells. The histopathologic features of RDD in extranodal sites are similar to the nodal disease except for the fact that fibrosis thends to be more pronounced and lymphocytophagcoytosis less conspicuous.

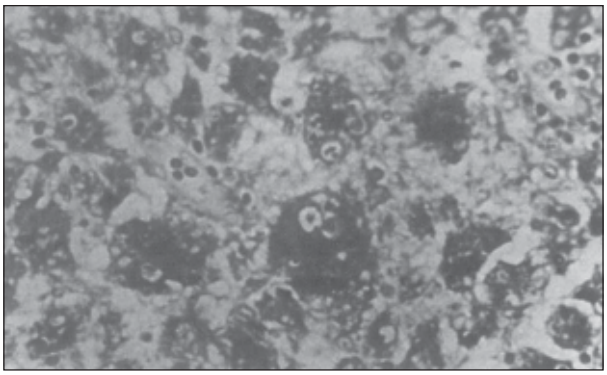

Fig.-3: *RDD, soft tissue, the very large RDD cells have emperipolesis of leukocytes, the phenotype was CD68+ve and CD1-ve, (Fascin immunostain, original magnificationx125)*

The etiology of RDD remains unknown, the two most likely possibilities are being infection by a virus or some other micro organism and the manifestation of a subtle undefined immunologic defect. It has been suggested that stimulation of monocytes-macrophage via M-CSF leading to immune suppressive macrophages ay be the main pathogenic mechanism of RDD.The differential diagnoses for RDD includes nos specific sinus hyperplasia (in which cells lack emperipolesis and are non-reactive to S-100), LCH (positive for both S-100 and CD1a)[16] leprosy and metastatic malignant melanoma.

RDD is considered to be benign. In approximately 50% of the patients, the disease resolves without appreciable sequelae, one third have residual asymptotic adenopathy and 17% have persistent symptomatology after 5 to 10 years. Regression is usually heralded by diminution of extranodal disease.[12], Review of the literature on treatment strategies of RDD, concluded that clinical observation without treatment is advisable when possible. Surgical debulking may be necessary in the presence of vital organ compression. Chemotherapy is in general ineffective, while radiotherapy has shown limited efficacy, reserved for cord compression or acute respiratory distress. Others have also advocated the use of long term prenisolone[13], steroid therapy resulted in reduction of lymphadenopathy and associated fevers[12]. Suggested chemotherapy protocols are combinations of vinca alkaloid, alkylating agents and steroids. But in general the outcome is inferior to that of Lymphoma or LCH[17]. Patients given antibiotics or anti-tuberculosis drugs showed no response[12].

Of 9 patients treated with radiotherapy 3 achieved complete remission, 3 had persistent SHML and 3 died of disease. Of 12 patients, 10 showed no response while 2 others achieved complete and durable remission with methotrexate and 6-mercaptopurine. Surgery and radiation therapy employed in 8 patients led to complete remission in 1 case and partial responses in 6 cases. High-dose interferon- was given to 1 patient with longterm remission[12].

Conclusion :

Much of what is known of SHML today was pioneered by two pathologists,Juan Rosai and ronald Dorfman. Since its initial description in 1969, SHML remains a disorder defined primarily by its histopathologic features.due to its rarity , neithet community based nor systematic treatment studie have been undertaken. Although a few hundred publications related to SHML can be found in the literature, many are single case reports with small series of patients.

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