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Research Paper

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KEYWORDS : Rosai Dorfman Disease, Emperipolesis, Massive Lymphadenopathy, S-100.

Rosai Dorfman Disease

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ABSTRACT

19 year old male patient presented with complaint of bilateral swelling in submandibular region for last 6 months associated with pain,anorexia and weakness.CBC and ESR were normal.CXR was normal.We diagnosed case by FNAC and confirmatory diagnosis could be put forwarded by histopathological examination and immunohistochemistry.

INTRODUCTION :

Rosai-Dorfman disease (RDD) is a rare histiocytic disorder initially described as a separate entity in 1969 by Rosai and Dorfman under the term sinus histiocytosis with massive lymphadenopathy (SHML) (20). The causes of RDD are not fully understood and treatment strategies can be different according to severity or vital organ involvement.

CASE HISTORY:

19 year old male patient presented with history of swelling in bilateral submandibular region for last 6 months associated with pain.He was also complaining of anorexia and weakness.CBC and ESR were normal.CXR was normal.On examination, Multiple submandibular lymph nodes, which were 2–3 cm in diameter, non-tender, movable, firm, discrete and free from superficial and deep structures were present.FNAC was done which showed numerous large histiocytes with abundant pale cytoplasm and phagocytosed lymphocytes (Emperipolesis)(FIGURE-1) in background of lymphocytes and plasma cells,multinucleated histiocytic giant cells and eosinophils..Biopsy was done and sent for histopathological examination.Grossly specimen was greyish white firm tissue measuring 3.2.1cm.On cut section it was homogenous white in appearance.Histopathology showed dilatation of lymph sinuses with effacement of follicles.There was proliferation of sinus histiocytes,lymphocytes and plasma cells within cytoplasm(Emperipolesis).(FIGURE 2).Biopsy was sent for immunohistochemistry and it was positive for S-100(FIGURE-3).Patient responded well to steroid treatment.

DISCUSSION:

Although RDD may occur in any age group, it is most frequently seen in children and young adults (11). Patients presenting with isolated intracranial disease tend to be older (5). The disease is more common in males and in individuals of African descent (14). RDD has been reported following bone marrow transplant for precursor-B acute lymphoblastic leukemia (2) and concurrently or after Hodgkin's and non-Hodgkin's lymphoma (15). A cytokine-mediated migration of monocytes may be involved in histiocytes accumulation and activation. This functional activation could be triggered by different stimuli due to the coexistence of RDD and autoimmune diseases, hematological malignancies and post-infectious conditions. In fact, many viruses like Herpesvirus 6 (HHV-6) (16) and Epstein-Barr virus (EBV) (21) have been implicated as potential causative agents however, there is no strong evidence for this at the moment. FNAC is a useful and reliable tool for the diagnosis of RDD, and as such, biopsy is avoidable.(4,6,13)Cytology usually reveals numerous large histiocytes with abundant pale cytoplasm and phagocytosed lymphocytes (Emperipolesis). In Emperipolesis, the lymphocytes are not attacked by enzymes and appear intact within the histiocytes (in contrast to phagocytosis). The phenomenon of emperipolesis is highly useful for the diagnosis of RDD using FNAC. Histopathologically, lymph nodes show pericapsular fibrosis and dilated sinuses, heavily infiltrated with large histiocytes, lymphocytes and plasma cells. The presence of emperipolesis, or the engulfment of lymphocytes and erythrocytes by histiocytes that express S-100, is considered diagnostic of RDD although not uniquely. Apart from S-100 antigen positivity, immunohistochemical stains of RDD cells are also positive for CD68, CD163, α1-antichymotrypsin, α1-antitrypsin, fascin and HAM-56 while CD1a is typically negative (11). RDD lesions have a moderate expression of IL-6, which could be related to the associated polyclonal plasmacytosis and hypergammaglobulinemia. Furthermore, the lesions tend to express strongly IL-1β and TNF-α. Systemic symptoms in RDD may be related to enhanced production of these cytokines. The most frequent clinical presentation of RDD is a massive bilateral and painless cervical lymphadenopathy with fever, night sweats and weight loss. Mediastinal, inguinal and retroperitoneal nodes may also be involved. Extranodal involvement by RDD has been documented in 43% of cases with the most frequent sites being skin, soft tissue, upper respiratory tract, multifocal bone, eye and retro-orbital tissue with lymphadenopathy or as an isolated initial manifestation of disease (8). Other reported sites include urogenital tract, breast, gastrointestinal tract, liver, pancreas and lungs. Head and neck involvement has been reported in 22% of cases, most commonly the nasal cavity followed by the parotid gland (11). Intracranial RDD usually occurs without extracranial lymphadenopathy, and most intracranial lesions are attached to the dura with only few extending intraparenchymally. CNS disease can present clinically and radiologically as meningioma, but the presence of emperipolesis in the CSF is usually diagnostic of Rosai-Dorfman disease (12). More recently, RDD cases presenting with initial spine, kidney, thyroid, isolated mediastinal and unifocal skeletal involvement have been reported(1,10,17,19). Histologically, the disease must be differentiated from Langerhans cell histiocytosis (LCH), infectious and lymphoproliferative disorders (5), as well as sinus hyperplasia. S-100 positivity can usually distinguish between the latter condition and RDD, whereas in both conditions the histiocytes have a strong macrophage antigen expression (7) .Laboratory features in RDD are often non-specific. Leukocytosis, elevated sedimentation rate and polyclonal gammopathy have been reported in most patients. Normochromic normocytic and autoimmune hemolytic anemia and elevated serum ferritin have also been described (3,8). Skeletal lesions of RDD are typically osteolytic and can be confused radiographically with LCH (8). Fludeoxyglucose F-18 positron emission tomography (PET) scan was found to be sensitive indicator for early prediction of treatment response in patients with systemic RDD (18). The clinical course of RDD is unpredictable with episodes of exacerbation and remissions that could last many years. The disease is often self-limiting with a very good outcome, nevertheless 5-11% of patients die from their disease. RDD patients can be subdivided into three categories: 1) patients with only lymph nodes that enlarge suddenly with spontaneous regression and without any further recurrences; 2) patients with immunologic abnormalities at presentation who have a more widespread nodal disease and a higher fatality rate (8,9); 3) patients with several extranodal site involvement, multinodal disease and a protracted clinical course with multiple relapses and remissions for years. In these cases, the severity of disease depends on the type and number of extranodal sites (14). Treatment depends upon the individual patient and is planned after thorough testing to determine the extent of disease. Ideal treatment, however, has not been established, and there is no ongoing clinical trial. It is believed that

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70% to 80% of patients have spontaneous improvement of symptoms without treatment, although they may have alternating episodes of worsening and relieving of symptoms for a long period of time. Some patients with severe or persistent disease or cases where organ function is threatened (such as breathing obstruction or kidney failure) may require treatment with surgery, steroids, and/or chemotherapy. Rarely radiation therapy may be used. Chemotherapy may include vinblastine, 6-MP, methotrexate, thalidomide, or Gleevec. The ultimate goal of an overall treatment plan, of course, is to use as little treatment as possible to keep the disease under control and preserve quality of life.Rosai-Dorfman does not usually threaten life or organ function. It is believed that 5% to 10% of patients have progressive disease that may damage tissue. However, for most patients, the disease is self-limited, and the outcome is good.

FIGURE-3 S 100 POSITIVITY

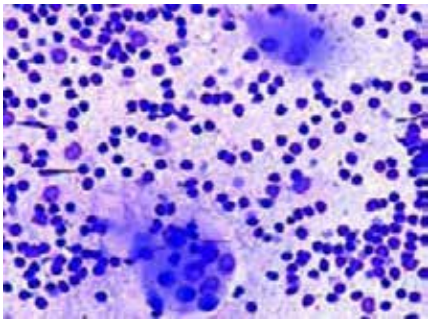

FIGURE-1 FNAC

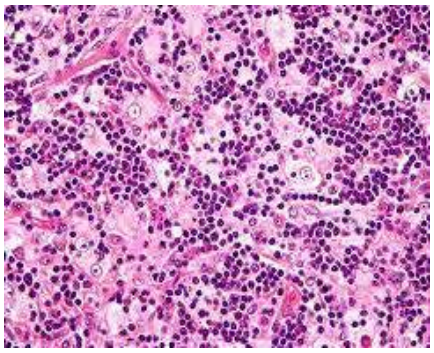

FIGURE-2 HISTOPATHOLOGY

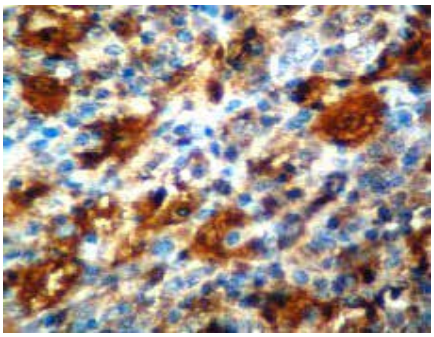

FIGURE-3 S 100 POSITIVITY

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