Asymptomatic flow of Rosai-Dorfman disease

Nesimptomatični tok bolesti Rosai-Dorfman

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Abstract

Introduction. Sinus histiocytosis with massive lymphadenopathy is a rare benign self-limiting disease of unknown etiology. The salivary gland involvement, indicating the extranodal character of the disease, often presents a diagnostic dilemma requiring immunohistochemical staining of surgically removed tumor to confirm the diagnosis. Case report. We report a 43-year-old man presented with an asymptomatic mass in the left mandibular angle. On physical examination, the lesion was described as a painless, mobile, firm-elastic consistency nodule, which measured 4 × 3 cm in diameter, with normal overlying skin. A mass with the same characteristics, dimensions 2 × 2 cm, was also noted in the right parotid region. No other changes in regional lymph nodes were detected. On macroscopic examination the lesion was firm, multilobulated, yellowish and rounded, while on microscopic examination the lesion was composed almost entirely of polygonal histiocytes with abundant cytoplasm, emperipolesis, plasma cells arranged in sheets, and lymphocytes scattered or within clusters. The observed histiocytes were found to be CD68 and S100 protein positive.

Conclusion. Rosai-Dorfman disease is a benign and frequently overlooked clinical and pathological entity that may be misinterpreted as a neoplastic disease.

Keywords: histiocytosis, sinus; diagnosis, differential; immunohistochemistry; treatment outcome.

Introduction

Rosai-Dorfman disease (RDD) which is widely recognized as a sinus histiocytosis with massive lymphadenopathy (SHML) is a benign self-limiting disease, originally described by Juan Rosai and Ronald F. Dorfman in 1969. The disease was initially reported as a bilateral cervical lymph nodes enlargement, usually less than 5 cm, with relatively infrequent involvement of other groups of nodes. All the patients had typical histopathological findings of polygonal histiocytes with abundant cytoplasm, emperipolesis, plasma cells arranged in sheets, and lymphocytes scattered or within clusters. Typically, the histiocytes in RDD are positive for S-100 protein as well as CD68 and CD163 proteins. Moreover,
histiocytes are negative for CD1a, CD34, CD15, CD30, CD3, CD20, keratin, EMA, SMA, desmin and HMB45. Other clinical features commonly include fever, malaise and weight loss, frequently accompanied with elevated sedimentation rate (ESR) as well as hypergammaglobulinemia. Of note is that salivary gland involvement, indicating the disease extranodal character, frequently poses a diagnostic dilemma necessitating immunohistochemically staining to separate it from malignant neoplasms.

**Case report**

We reported a 43-year-old man, presented with an asymptomatic mass in the left mandibular angle of one year history. There was no history of fever, pain, respiratory tract infections or any other symptoms related to ear, nose or throat. There was also no family history of tuberculosis. On physical examination, the lesion was described as a painless, firm-elastic consistency nodule, which measured 4 × 3 cm in diameter that was freely mobile with normal overlying skin.

On further inspection, the right parotid gland region showed oval, painless mobile mass of soft consistency, measuring 2 × 2 cm and no other changes in regional lymph nodes (Figure 1). Intraoral examination revealed no significant findings.

Ultrasound examination revealed oval hypoechogenic mass in the left parotid area, at the largest site measuring 28.2 mm (Figure 2A). In the right parotid region the lesion measured 24.4 mm (Figure 2B). The results of standard biochemical analysis of blood including: glycemia, urea, creatinine, heaptogram, lactate dehydrogenase (LDH), creatine phosphokinase (CPK), transaminases, electrolytes as well as peripheral, blood smear were normal.

After routine medical consultation we decided to surgically remove tumor which was grossly multilobulated and partly surrounded by adipose tissue. On the macroscopic examination we found a homogenous, yellowish tumor, dimension 6 × 4 × 3 cm.

On light microscopic examination, the sections were stained with hematoxylin-eosin, and a lymph node with an infiltrate consisting of many histiocytic cells admixed with lymphocytes in salivary gland parenchyma was observed.

Immunohistochemical staining was performed on formalin-fixed paraffin-embedded tissue sections using the Dako-autostainer link 48 (Dako, Ontario, Canada) and the color was developed by EnVision Flex Target Retrieval Solutions (Dako, Burlington) using diaminobezidine (DAB) as the chromogen. The following antibodies were applied: anti-CD1a (O10, Predilute, DAKO, Carpinteria, CA, USA), anti-S-100 (S-100, Predilute, DAKO, Glostrup, Denmark), anti...
CD68 (PG-M1, Predilute, DAKO, Glostrup, Denmark), anti-CD3 (polyclonal rabit, Predilute, DAKO, Carpinteria, CA, USA), anti-CD30 (Ber-HL, Predilute, DAKO, Glostrup, Denmark), anti-CD34 (QBEnd 10, Predilute, DAKO, Glostrup, Denmark), anti-CD20 (L26, Predilute, DAKO, Glostrup, Denmark), anti-Ki67 (MiB-1, Predilute, DAKO, Glostrup, Denmark), anti-CKHMW (34BE12, 1:50, DAKO, Carpinteria, CA, USA), anti-CD23 (MHM6, 1:50, DAKO, Glostrup, Denmark), anti-EMA (E29, Predilute, DAKO, Glostrup, Denmark) and anti-CD138 (MI15, Predilute, DAKO, Glostrup, Denmark).

Immunohistochemical assessment revealed follicular dendritic cells (CD23 positive), rare plasmocytes (CD138 positive), epithelial cells of salivary ducts and plasmocytes (EMA positive), basal cells (CKHMW positive), rare lymphocytes, epitheloid histiocytes and germinal centre of lymph follicles that were slight Ki67 positive, histiocytes CD68 positive (Figure 4A) and S-100 protein positive (Figure 4B). The Mantle zone of lymph follicles was also CD20 positive. In addition, numerous T-lymphocytes were CD3 positive, endothelial cells were also CD34 positive and staining for CD1a and CD30 was completely negative.

The postoperative course of the presented patient was uneventful, the patient subjectively felt good, and occasional control visits were advised to him (Figure 5).

**Discussion**

The patient presented with an asymptomatic mass in the left mandibular angle of one year history and no other exceptional clinical findings. What made this case somewhat unusual was the fact that the patient was 43-year-old male (an atypical age group) and the salivary gland involvement thus presenting us a challenge to separate it from other malignant neoplasms. However, further microscopical finding as well as immunohistochemical assessment confirmed the disease.

Rosai-Dorfman disease is a benign clinical entity which is characterized by over-production and accumulation of a specific type of white blood cell (histiocyte) in the lymph nodes of the body, most often those of the neck (cervical). Literature reviews reported till 2004 show about 600 cases of RDD of which 81% were diagnosed in the first and second decades 4.

The etiology of the disease is not known and the pathogenesis is speculated to have been related to an unidentified infectious agent or an altered immune response 5. The course of the disease spans over a few to many years, characterized by episodes of waxing and waning in the size of lesion before it undergoes complete resolution.

Microscopically, the lesions have sheets of polygonal histiocytes with abundant cytoplasm, emperipolesis, plasma cells, and lymphocytes scattered and within clusters.

The most common clinical presentation of the disease is painless and bilateral cervical lymphadenopathy (87.3% of cases), affecting one or all cervical ganglion chains. The initial stages are characterized by lymph nodes which are isolated, mobile, and small, but during disease progression they become adherent and form a 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 involvement 6, 7. Rarely the extranodal disease may be the initial and the only manifestation of the disease what was our case 8.

The cause of the disease has not yet been established, but two theories exist. In the first theory, SHML is caused by a specific infectious process based on the generally infectious process seen at the onset of the disease (localized
lymphadenopathy, fever, leukocytosis with neutrophilia, increased ESR, and hypergammaglobulinemia), which tends to spontaneously regress after some time. In the second theory, the disease is attributed to an abnormal immunologic response, because depression of immunologic cells can be observed. However, in our case, no laboratory evidence points to an etiologic agent.

The patients with extranodal disease confined to head and neck regions. Nodal involvement was not observed, although nodal involvement may have occurred during an earlier phase. Fever occurs in up to 30% of cases but was absent in our patient. In 85% of cases, patients with RDD are in good general health without significant symptoms of the disease.

Identification of SHML at an extranodal site (salivary gland) without associated lymphadenopathy raises the suspicion of other diagnoses including Langerhan’s cell histiocytosis, Kuttner’s tumor, malignant histiocytosis, Hodgkin’s disease, and metastatic carcinoma.

Large histiocytes with intracytoplasmic lymphocytes are also cytological features of other diseases. Lack of eosinophils is substantial in differentiating SHML from Langerhan’s cell histiocytosis, malignant histiocytosis and T-cell lymphomas. The absence of necrosis and mitotic activity is also important in differential diagnosis from Hodgkin’s disease, which is characterized by classical Reed–Sternberg (RS) cells seen in the background consisting of neutrophils, lymphocytes, plasma cells and eosinophils. Though a large number of foamy macrophages can mimic mononuclear variants of RS cells, eosinophils and lymphophagocytosis are not seen.

Immunohistochemical stains help a lot in diagnosing SHML since SHML histiocytes are strongly positive for CD68, negative for CD1a and variably positive for S-100 protein. On the other hand, Langerhans cell histiocytosis is positive for both S-100 protein and CD1a, and the cells of Langerhan’s cell histiocytosis ultrastructurally reveal characteristic rod-shaped Birbeck granules.

Conclusion

Sinus histiocytosis with massive lymphadenopathy (SHML) is a benign disease usually characterized by spontaneous or steroid induced diminution of all clinical symptoms. It is an often overlooked clinical and pathological entity that may be misinterpreted as a neoplastic disease.

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REFERENCES


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