Open Access Case Report

Journal of Renal Endocrinology

J Renal Endocrinol 2019;5:e10.

http://www.jrenendo.com

Nickan Research Institute

Rosai-Dorfman disease; a case report and review of the literature

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Abstract

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy (SHML) is a rare idiopathic and benign disorder. We report a case of a previously healthy 44-year-old female patient who first presented with painless enlargement of the submandibular and parotid glands. She, later on, experienced multiple recurrences. The diagnosis of RDD in this patient was confirmed with pathology examinations and immunohistochemistry evaluations.

Citation: Hassanzadeh S, Nasri P, Khosravifarsani M. Rosai-Dorfman disease; a case report and review of the literature. J Renal Endocrinol. 2019;5:e10.

Introduction

Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy (SHML) is a rare benign disorder that was first described by Destombes in 1965, and then Rosai and Dorfman reported the first clinical series of RDD in 1969. RDD is typically characterized by high proliferation of the non-Langerhans sinus histiocyte cells within the lymphatic system (1).

Although RDD usually involves the lymph nodes, extra-nodal involvement occurs in 40% of the patients involving different organs such as the skin, soft tissues, eyes, bones, nasal sinuses, central nervous system, salivary glands, kidneys, respiratory tract, liver, breast, and gastrointestinal tract (1, 2).

The causes and underlying pathogenesis of RDD are still unclear. Additionally, it does not have any standardized treatment approaches (1). The prevalence of the RDD has been reported to be around one case per 200 000 individuals. Although RDD may occur at any age, it is mostly seen in pediatrics and young adults and is more common in male individuals compared to females (1, 3).

The signs and symptoms of RDD include painful and massive bilateral cervical lymphadenopathies that may be associated with other nonspecific signs and symptoms such as fever, malaise, night sweats, weight loss, normocytic anemia, hemolytic anemia, neutrophilia, elevated erythrocyte sedimentation rate (ESR) level, and polyclonal gammopathy. In addition, the lymph nodes of the mediastinum, inguinal, and retroperitoneum areas may be involved (1,4).

Although the clinical characteristics of RDD are not predictable, it is associated with slow progression and low mortality. Approximately 20% of the cases spontaneously regress with monitoring and follow-up; However, some cases experience occurrences of exacerbation and remission (1,2). Herein, we present a case of RDD in the head and neck that was diagnosed after multiple biopsies.

Case Presentation

A previously healthy 44-year-old female presented to the ear, nose, and throat (ENT) clinic with a three-month history of painless enlargement of the parotid gland and submandibular lymph nodes.

She denied experiencing any other symptoms including nonspecific symptoms such as fever, weight loss, or malaise. Moreover, her past medical, social, and family histories were unremarkable. Consequently, bilateral functional endoscopic sinus surgery (FESS) and right nasal mass excision were performed. The specimen reports of the nasal cavity and parotid mass revealed chronic sinusitis in the maxillary and ethmoid sinuses. In addition, there were granulomatous inflammations in the nasal cavity, parotid gland, cheek mass, and the maxillary and ethmoid sinuses. Acid-fast staining (AFS) and periodic acid-Schiff (PAS) staining were negative for mycobacteria and fungus, respectively. The pathological impression was

Received: 16 October 2019, Accepted: 2 December 2019, ePublished: 23 December 2019

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Implication for health policy/practice/research/ medical education

The prognosis of RDD is not exactly clear. Outcomes are usually favorable, particularly in cases with nodal and cutaneous involvement, and are mostly self-limited.

granulomatous inflammation of the sinonasal cavity. Her laboratory tests are demonstrated in Table 1.

One year later, she returned presenting with a mass recurrence and a lump in the right side of her face as well as nasal discharge (Figure 1). Therefore, spiral computed tomography (CT) scan of the paranasal sinuses without contrast was performed. The report showed evidence of thickened and soap bubble appearance in the wall of paranasal sinuses in the left and right maxillary sinuses. There were also opacities in the total space of the right maxillary and most of the left maxillary sinuses, and in the left nasal cavity and right frontal sinus (Figure 2). The patient underwent bilateral FESS once more. The pathology evaluation reported granulomatous inflammation with negative AFS and no fungal elements. Her polymerase chain reaction (PCR) test showed no evidence of mycobacterium genome. Therefore, she did not receive any particular medication.

She was again referred to the ENT clinic after a year due to a complaint of a left submandibular mass. Subsequently, neck mass resection and bilateral FESS were performed. Fine needle aspiration of the submandibular lymph node was done which reported no presence of malignant cells. The pathology evaluation revealed mild chronic sialadenitis in the submandibular gland, chronic sinusitis in the sinonasal cavity, and SHML in submandibular and cervical lymph nodes that were consistent with RDD. In addition, immunohistochemistry evaluation showed

Table 1. Laboratory tests of the patient

Laboratory test	Result
WBC (×10³/µ)	7.36
RBC (×10³/µ)	4.49
Hemoglobin (g/dL)	9.2
Hematocrit (%)	31.2
MCV (FL)	69.4
Platelet (×10³/µ)	537
Neutrophil (%)	75.8
Lymphocyte (%)	18.1
ESR 1 h (mm)	89
CRP	2+
BUN (mg/dL)	8
Creatinine (mg/dL)	0.73
Cholesterol (mg/dL)	191
Triglycerides (mg/dL)	79
HDL-c (mg/dL)	32
LDL-c (mg/dL)	143
Calciume total (mg/dL)	9.9
Phosphorus (mg/dL)	3.5
AST (U/L)	20
ALT (U/L)	8
Alkaline phosphatase (U/L)	332
LDH (U/L)	257
Albumin (gr/dL)	3.74
HBS AG	Non-reactive
Anti-HIV	Non-reactive
HCV Ab	Non-reactive

Abbreviations: WBC: White blood cell, RBC: Red blood cell, MCV: Mean corpuscular volume, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, BUN: Blood urea nitrogen, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, HBS Ag: hepatitis B surface antigen, HCV-Ab: Hepatitis C virus antibody.

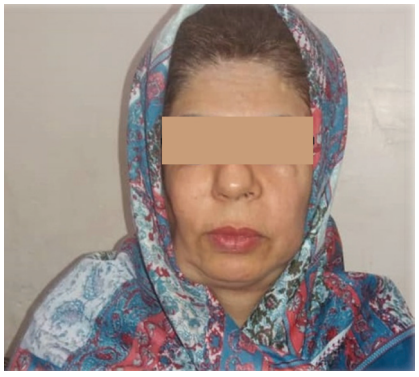

Figure 1. An image of the patient presenting with lumps in her submandibular and parotid glands.

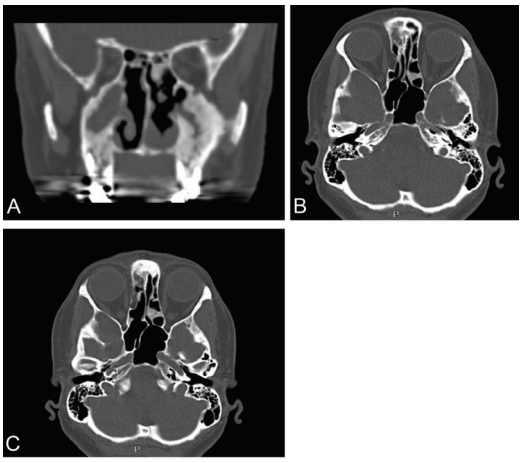

Figure 2. Computed tomography scan of the paranasal sinuses (A. Coronal cut, B. Sagittal cut).

positive CD20, CD3, CD68, S100 which confirmed the diagnosis. Furthermore, serum protein electrophoresis revealed hypergammaglobulinemia (Figure 3).

Consequently, the patient was referred to our oncology clinic for treatment. Treatment was initiated with prednisolone. After four months, the patient complained of tumor growth; thus, thalidomide was added to her treatment. However, due to the lack of response to the mentioned treatments, etoposide was administered. As a result, the size of the tumor was reduced and the patient did not have any other complaints. However, the tumor recurred again after four months. Currently, the patient refuses any further treatments.

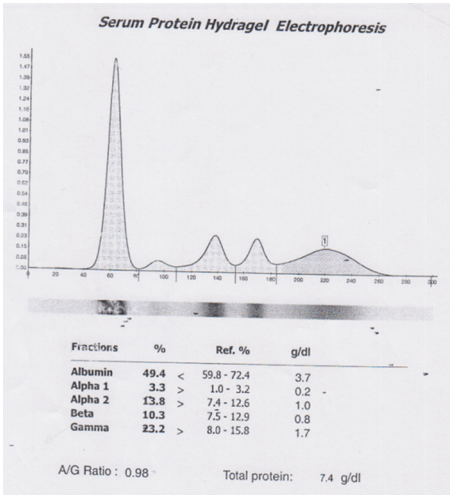

Figure 3. The serum protein electrophoresis result indicating hypergammaglobulinemia

Discussion

RDD is one of the non-Langerhans cell histiocytoses (non-LCH) diseases that are characterized by benign and distinctive infiltration of histiocytosis in the sinuses of the lymph nodes. Painless adenopathy and extra-nodular involvement are seen in 80% and 43% of the cases, respectively (2,5).

RDD is heterogeneous and may develop alone or along with other disorders such as autoimmune, hereditary, and malignant diseases and its prevalence is approximately 1 per 200 000 individuals (1, 3). The etiology of RDD is still unclear and probably varies over the phenotype spectrum of RDD (1).

Disorders such as immunodeficiency disorders, autoimmune diseases, or neoplastic processes have not yet been proven as the etiologies of RDD. In addition, molecular studies of RDD have not shown any evidence of clonal rearrangement, implying a reactive or non-neoplastic condition (1-3,6-9). However, there have been studies that suggested viral infections such as herpes viruses, Epstein-Barr virus, cytomegalovirus, and HIV as triggering factors, but no association has yet been proven (8,9).

Around 11% of RDD cases have involvement of the nasal cavity and paranasal sinuses which is more commonly seen in patients of Asian ancestry (2). The involvement of sinonasal presents with symptoms such as nasal obstruction, nasal dorsum deformity, epistaxis, facial asymmetry, and aural fullness (10).

Moreover, the involvement of the oral cavity may present with nodules in the hard and soft palate, swelling of the gingival and oral mucosa, thickened mucosa of the oropharynx, enlargement of the tongue and tonsils, or frequent episodes of tonsillitis (2). Involvement of the salivary and parotid glands, larynx, pharynx, thymus, bone, gastrointestinal, eye, skin, subcutaneous tissue, skeletal muscle, central nervous system, and the thyroid gland are among the other sites that might be involved and may cause mass-mediated symptoms (1, 9, 11, 12).

There are various treatment options for RDD such as surgical resection, systemic corticosteroids, chemotherapy, and radiotherapy. However, there is still no agreement on the therapy for RDD; therefore, the treatment is adjusted based on the patient's clinical presentations (1).

Conclusion

In summary, the prognosis of RDD is not exactly clear. Outcomes are usually favorable, particularly in cases with nodal and cutaneous involvement, and are mostly self-limited. However, some patients may have unpredictable clinical outcomes, with fluctuations of the remission and reactivation periods of the disease that may result in a long-term condition (1).

Conflicts of interest

The authors have no conflicts of interest to declare.

Authors' contribution

MRKF handling the patient. PN conducted the primary draft. SH conducted the secondary edit. All authors read and signed the final paper.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been observed by the authors. Permission for publication and informed consent regarding this case report has been obtained.

Funding/Support

None.

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