CASE REPORT

Sonographic Manifestation of Thyroid’s Rosai-Dorfman Disease

Wen Wu Ling¹, Parajuly Shyam Sundar¹, Yan Luo¹, Yong Jiang², Di Ming Cai¹*

¹Department of Sonography, and ²Department of Pathology, West China Medical School of Sichuan University, Chengdu 610041, Sichuan, China

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Rosai-Dorfman disease (RDD) is a rare and benign histiocytic proliferative disorder of unknown etiology. It can affect all age groups, particularly young adults. The typical clinical manifestation is painless, bilateral, massive cervical lymphadenopathy with or without extra nodal involvement, along with fever, weight loss, and night sweats. However, thyroid involvement is very uncommon. The ultrasonographic manifestations of RDD are rarely reported. A case of RDD involving the thyroid that was recorded in our hospital PACS system during 2002–2010 is reported here, which was initially misdiagnosed as non-Hodgkin’s lymphoma (NHL). In our case, ultrasonography revealed diffuse enlargement of whole thyroid glands with heterogeneous hypoechogenicity. Areas of linear hyperechogenicity were noted on the sonograms with multiple enlarged nodes over the cervical, supravacuicular, and submandibular areas. Though not specific, in order to avoid unnecessary surgery or a total thyroidectomy, ultrasonography and ultrasonography-guided core needle biopsy should be performed to establish an accurate diagnosis.

Introduction

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a rare benign disease with a self-limiting clinical course [1]. The typical manifestation include painless, bilateral, massive cervical lymphadenopathy that may be accompanied by fever, weight loss, night sweats, and leukocytosis with neutrophilia in the clinical examination [2]. More than 90% of the patients suffer from painless lymphadenopathy over the neck and paratracheal area [3]. Most commonly, RDD affects young males, with a peak age around 20 years, with unknown etiology. Thyroid involvement in RDD has rarely been reported in the literature [4]. Herein, we report a case of RDD involving the thyroid and cervical nodes.
Case report

A 51-year-old married Chinese woman, with a history of enlargement of the right lobe of thyroid for 8 months, complained of migratory pain and enlargement of a left neck mass for 6 months. Clinical and physical examination revealed cardiopalmus, high-grade fever, insomnia, sweats, and weight loss. No signs of dyspnea or dysphagia were noted. The patient had a history of hypertension, but this condition was under control. There was no history of rashes, bleeding manifestations, contact with animals, or high-risk sexual behavior. No significant family history was noted.

Physical examination showed a regular pulse of about 80 beats/minute and a respiratory rate of about 20 breaths/minute. Multiple nodules or lumps of various sizes were palpable over the bilateral neck, supraclavicular, and submandibular areas. The lumps were movable, firm, and demonstrated haphalgesia. The thyroid glands were enlarged, firm, and demonstrated haphalgesia. The systemic skin appeared normal.

Laboratory test results were as follows: red blood cell count, 5.40 × 10¹² cells/L; mean corpuscular volume (MCV), 75.0 fl; mean corpuscular hemoglobin (MCH), 24.3 pg; total leukocyte count, 15.30 × 10⁹ cells/L (84.9% neutrophils and 9.3% lymphocytes); platelet count, 434 × 10⁹/L; total protein, 93.4 g/L; globulin, 49.6 g/L; and A/G, 0.88. All other blood examinations were normal. Ultrasonography revealed diffuse enlargement of the thyroid glands with heterogeneous hypoechogenicity. Areas of linear hyperechogenicity were noted on the sonograms (Fig. 1) with multiple enlarged nodes over the cervical, supraclavicular, and submandibular areas (Fig. 2). The maximum diameter of the lymph nodes was approximately 3.6 cm. Based on the diagnosis of non-Hodgkin’s lymphoma (NHL) based on the results of the sonograms, the patient underwent a total thyroidectomy and lymph node dissection. During surgery, multiple enlarged nodes and abnormal thyroid tissue were found. The excised thyroid specimen was grayish in color. Surgical histopathology of the thyroid and lymph nodes revealed sinus histiocytosis with massive lymphadenopathy (Figs. 3 and 4) along with Hashimoto’s thyroiditis. The immunohistochemical stains were positive for S-100 protein (Fig. 5) and CD68 antigens.

Discussion

RDD was first described in 1969 by Rosai and Dorfman [1]. It is an uncommon disease that manifests along with non-Langerhans cell histiocytosis and has a benign and self-limiting clinical course, which includes two main forms. One form presents in the nodes, the other in the cutaneous tissue [5]. The extranodal form (which occurs in 43% of cases) present most commonly in the skin, upper respiratory tract, and bone, but it may also involve the head and neck regions, including the thyroids, kidneys, digestive

![Fig. 1 Sagittal sonogram of the right thyroid showing enlarged thyroid glands with heterogeneous hypoechogenicity and areas of linear hyperechogenicity.](image1)

![Fig. 2 Color Doppler sonogram of the left neck showing unremarkable flow to the enlarged cervical node with obscuration by a fatty hilum.](image2)

![Fig. 3 Photomicrograph showing the cytomorphological features of the excised cervical node. The lymphatic sinuses are significantly dilated, and a large number of histiocytes with large cytoplasm indicate lymphophagocytosis (HE, hematoxylin-eosin, 40× magnification).](image3)
tract, central nervous system, and other locations [4,6–9].

Thyroid involvement in RDD, as seen in our patient, has rarely been reported in China.

RDD, along with extranodal diseases, may affect all age groups, but it generally occurs in the first two decades of life and shows no differences among ethnic groups [2,4]. The etiology of the disease is uncertain, but some reports show that the disease may correlate with herpes virus hominis-6 and -8 (HHV-6 and -8), Epstein-Barr virus (EBV) infection, associate other immune diseases [10,11]. Clinically, RDD typically presents with painless, bilateral, massive cervical lymphadenopathy and is frequently associated with fever, weight loss, night sweats, and leukocytosis with predominant neutrophilia.

Making the correct diagnosis is very important because most cases of RDD are self-limiting and may not require invasive treatments [10].

The diagnosis of RDD is based on histopathology [2]. It is characterized by numerous large histiocytes with abundant cytoplasm and phagocytosed lymphocytes, which is known as emperipolesis. It is a nonspecific but suggestive feature of RDD [4]. In immunohistochemical studies, RDD patients are positive for S-100 protein and CD68 antigens and negative for CD1a antigens [2,4]. Some reports suggested that the positive expression of the S-100 protein in histiocytes can be used to establish a diagnosis of RDD [12].

The differential diagnosis includes many histiocytic disorders, such as Hodgkin’s disease, malignant histiocytosis, and lymphomas as well as Langerhans cell histiocytosis. RDD, when it presents with extranodal diseases, may be misdiagnosed as a malignant disease or metastatic lymphadenopathy [2,4,13]. The treatment of RDD includes various medicines or surgical excision, particularly when it affects important extra-nodal organs [4].

In our case, the patient presented with the typical clinical manifestations of high-grade fever, insomnia, sweats, weight loss, and haphalgesia. She also presented with bilateral enlarged nodes in the neck and painful enlargement of the thyroid glands. Laboratory tests showed leukocytosis with predominant neutrophilia. Thyroid function was also unremarkable. Preoperative ultrasonography of the thyroid and neck were indicated of lymphoma. Instead of ultrasonography-guided core needle biopsy, the patient underwent a total thyroidectomy with lymph node excision, which was an inadequate treatment in this case. Based on the sonographic diagnosis of lymphoma, the patient should have received ultrasonography-guided core needle biopsy. Ultrasound-guided intervention may have helped to establish the subtype of lymphoma [14,15].

RDD rarely involves the thyroid. According to the cases presented by Lee et al [13], RDD with thyroid involvement has only been reported in female patients (mean age: 56 years), which is significantly different from nodal RDD that is predominantly seen in young males. However, Lee’s report was similar to the patient reported above in this case. In addition, autoimmune thyroiditis is frequently associated with RDD and thyroid involvement, which raises the suspicion that both entities might share a common pathogenesis. Thyroid involvement in RDD is commonly misdiagnosed as thyroid malignancy with lymph node metastasis, which may lead to unnecessary operations and postoperative complications. The ultrasonographic manifestations of RDD are rarely reported. In our case, ultrasonography revealed enlargement of the thyroid glands with heterogeneous hypoechogenicity. Areas of linear hyperechogenicity were noted on the sonograms with multiple enlarged nodes over the cervical, supraclavicular, and submandibular areas. She was initially diagnosed with NHL. Although lymphoma commonly presents with the of a single lobe, heterogeneous parenchymal hypoechogenicity may be accompanied by multiple enlarged lymph nodes. Hence, differential diagnosis is still a challenge [16]. The clinical presentations might be helpful for making a preoperative differential diagnosis, while thyroid function tests, ultrasonography, thyroid isotope scan, and fine needle aspiration are less useful [13]. Histopathological examination and immunohistochemical stains are the gold standard for the diagnosis of RDD. Preoperative diagnosis is very helpful, which may prevent an unnecessary thyroidectomy and postoperative complications [4,13].

In conclusion, thyroid involvement in RDD is extremely rare. In order to avoid unnecessary surgery or a total thyroidectomy, ultrasonography and ultrasonography-guided
core needle biopsy should be performed in order to establish an accurate diagnosis.

References