Coexistent primary lymphoma of the thyroid and cerebral aneurysm

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ABSTRACT

A rare case of primary lymphoma of the thyroid is reported in a 52-year-old woman with a previous history of hypothyroidism due to Hashimoto's thyroiditis, and rapid development of an anteromedial cervical tumor with symptoms of extrinsic compression over the upper airways and the esophagus. Contrasted computed tomography images and upper digestive endoscopy confirmed the compressive mass effects. The primary B-cell CD20+ lymphoma of the thyroid was diagnosed by thick-needle biopsy with histological and immunohistochemical evaluation. Incidental images of the head and neck revealed a cerebral aneurysm. Based on the diagnosis, the patient successfully underwent chemotherapy and radiation therapy with control of the lymphoma and is under surveillance in the Oncology and Neurosurgery outpatient care center. Primary lymphoma of the thyroid can present as a painless anterior and medial mass on the neck, leading to diagnosis challenges. The casual or causal relationship between lymphomas and cerebral aneurysms remains unclear.

Key words. Lymphoma; thyroid; Hashimoto's thyroiditis; cerebral aneurysm

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RESUMO

Linfoma primário de tiróide coexistente com aneurisma cerebral

Relata-se um raro caso de linfoma primário de tiroide em uma mulher de 52 anos com hipotiroidismo associado à tiroidite crônica de Hashimoto. Houve rápido crescimento de um tumor cervical antero-medial, com sintomas de compressão nas vias aéreas superiores e no esôfago. Imagens de tomografia computadorizada com contraste e de endoscopia digestiva alta confirmaram os efeitos compressivos. O linfoma de células B CD20+ primário de tiróide foi diagnosticado por punção aspirativa com agulha grossa e exame histológico

e imunoistoquímico. Imagens incidentais do pescoço e da cabeça revelaram um aneurisma cerebral. Com base no diagnóstico, a paciente se submeteu com sucesso a quimioterapia e radioterapia e houve controle do linfoma. A paciente continua em acompanhamento nos ambulatórios de Oncologia e de Neurocirugia. O linfoma primário de tiroide pode apresentar-se como uma massa indolor na região cervical anterior e média, causando dificuldades de diagnóstico. A relação, causal ou casual, entre linfomas e aneurismas cerebrais não está bem definida.

Palavras chave. *Linfoma de tiróide; tiroidite de Hashimoto; aneurisma cerebral*

INTRODUCTION

Primary lymphoma of the thyroid is a rare condition among tumors of the gland,[1-3] but it should be included in the differential diagnosis of anteromedial cervical masses. Clinical features of the disease are not specific, but this tumor evolves with compressive symptoms. It is worth mentioning the concomitance of primary lymphoma of the thyroid with hypothyroidism.[1,4] Several primary lymphomas have been described in the thyroid gland, including Hodgkin's and non-Hodgkin's lymphoma – B-cell, T cell, MALT, and Burkitt.[1-3,5-7]Radiation therapy and R-CHOP chemotherapy (rituximab, cyclophosphamide, adriamycin, vincristine, prednisolone) have been the first choice to treat thyroid lymphoma.[4]

The incidence of central nervous system (CNS) aneurysms is 1-7%, based on angiography and autopsy data; and the 1% prevalence of incidentally found aneurysms is increasing.[6,8] According to the literature, concomitant CNS lymphoma and aneurysms are exceedingly rare;[6,8] moreover, a similar association has not been described with primary lymphoma of the thyroid.

Our purpose is to report the very rare occurrence of a primary non-Hodgkin lymphoma (NHL) of the thyroid, coexistent with a cerebral aneurysm incidentally detected. Based on literature data, this association is not entirely clear.

CASE REPORT

A 52-year-old woman with previous diagnosis of Hashimoto's thyroiditis was referred to our hospital because she had presented with a non-productive cough, dysphonia and dysphagia for 15 days. Moreover, she had noticed the growth of an anteromedial cervical mass for 3 months. Physical examination revealed breathlessness and intense laryngeal stridor; additionally, a huge mass of hard consistence was palpated on thyroid topography. Soon after admission, she suddenly evolved with accentuated hypoxia and consequent cardiac arrest, which was immediately reverted with routine resuscitation maneuvers.

Routine laboratory data and respective controls during hospitalization are shown in table 1; serum levels of thyroid stimulating hormone, free thyroxin, antithyroglobulin, and antithyroid peroxidase were unremarkable.

An ultrasound scan of the thyroid showed a diffusely heterogeneous gland with some nodules in the right lobe. Images of the cervical region obtained using contrast computed tomography showed a poorly delimited mass (70 x 58 x 60mm) in the anteromedial region of the neck (figures 1 A and B). A large aneurysm was seen in the left

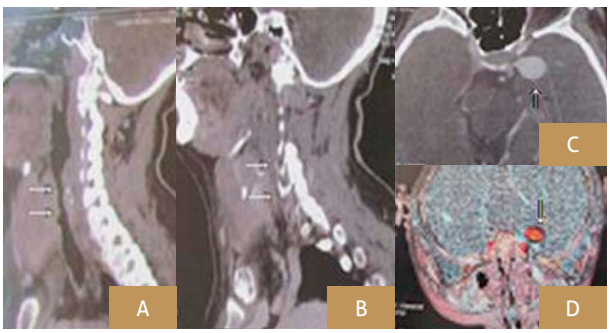

Figure 1. (Contrast tomography scan of the cervical region) A and B: presence of a heterogeneous poorly-delimited mass on the anterior and medial portions of the neck, compressing the pharyngeal and hypopharyngeal regions (arrows); B and C: incidental aneurysm found in the left posterior communicating artery measuring 22 x 20mm (arrows)

Table 1. Laboratory data of a woman with primary thyroid lymphoma and cerebral aneurysm

PARAMETERS (NORMAL RANGE)	DAY 1	DAY 3	DAY 5	DAY 8
Erythrocytes (4.4-6.0 x 10^{12}/mm^3)	3.24	3.59	3.72	3.76
Hemoglobin (11.1-16.1 g/dl)	**10.1**	**11.0**	11.3	11.5
Hematocrit (39-53 %)	**29.8**	**32.7**	**34.1**	**34.4**
Leukocytes (4.0-11.0 x 10^3/mm^3)	**20.1**	**17.8**	**15.1**	**13.7**
Platelets (150-450 x 10^3/mm^3)	**492**	430	358	354
Erythrosedimentation rate (≤ 15 mm/h)	ND*	**79**	**69**	**50**
C-Reactive protein (< 0.100 mg/dl)	**7.57**	**3.88**	**2.76**	ND
Sodium (135-145 mmol/l)	**126**	**126**	**124**	**129**
Potassium (3.5-5.2 mmol/l)	**3.3**	4.2	3.9	3.8
Calcium (1.16-1.32 mmol/l)	1.25	ND	1.20	ND
Urea (10-50 mg/dl)	**53.3**	**54.3**	**57.8**	**53.7**
Creatinine (0.7-1.3 mg/dl)	**1.4**	1.3	1.0	0.9
Glucose (70-100 mg/dl)	**111**	98	ND	ND
Aspartate transaminase (≤ 39 IU/l)	24.7	31.4	32.5	22.5
Alanine transaminase (≤ 32 IU/l)	22.6	22.1	24.7	ND
Gama-Glutamyl transferaseT (≤ 55 IU/l)	**287**	**338**	ND	25.1

*ND: not done. Abnormal data are shown in bold

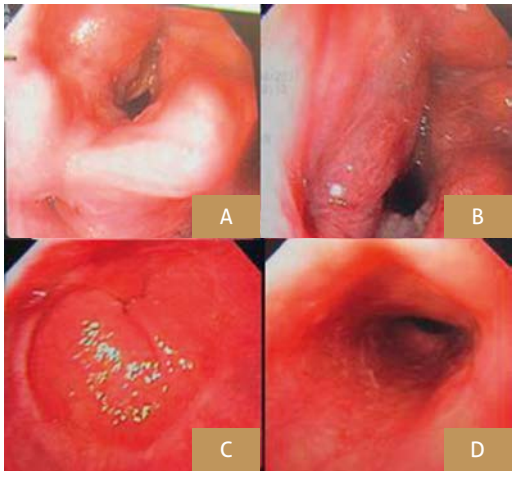

Figure 2. Upper digestive endoscopy features of extrinsic compression exerted by the thyroid mass over the upper airways (A and B), and the cervical esophagus (C and D)

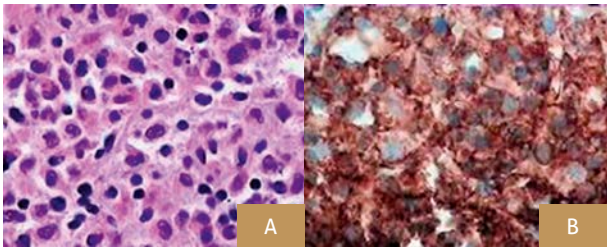

Figure 3. (Photomicrography images of thyroid mass sample) A: monotonous proliferation of atypical lymphoid cells of intermediate and large size, with hyperchromatic nuclei of variable size and a necrotic background, consistent with a high grade B-cell lymphoma (HE x400); B: positive CD-20 marker, counterstained by Harris hematoxylin solution, revealing blue nuclei surrounded by brown stained membranes (Immunohistochemistry x 400)

posterior communicating artery (figures 1 C and D). Upper digestive endoscopy imaging showed conspicuous compressive effects caused by the neck mass (figure 2).

Findings from fine needle aspiration biopsy (FNAB) were inconclusive, but core needle biopsy (CNB) yielded data consistent with high grade B-cell CD20+ lymphoma (figure 3). In addition to routine histopathological evaluation, tumor samples were assessed by immunohistochemistry, cytochemistry, and fluorescence in-situ hybridization (FISH). Positive findings included antigens Ki-67 MIB1 (80%), CD20 L26, and CD45RB PD7/26/16&2B11, whereas antigens CD3 SP7, and cytokeratins 40, 48, 50, and 50,6 kDa AE1/AE3 were negative. FISH analysis of MYC aberrations was not conclusive.

The patient underwent a tracheostomy and was treated with chemotherapy (R-CHOP) and radiation therapy. After clinical improvement, she was referred to an outpatient oncology care center and for neurosurgery evaluation concerning the management of her asymptomatic aneurysm.

DISCUSSION

Accurate physical examination, laboratory investigation, and imaging evaluation of the head, thorax and abdomen helped establish the diagnosis of primary thyroid lymphoma.[1-3] This very rare malignancy is a lymphomatous condition affecting the gland without contiguous spread or metastasis from lymphoma of another place in the body at diagnosis.[3]

Primary thyroid lymphoma usually affects women between 50 and 80 years with previous history of Hashimoto's thyroiditis; it accounts for 0.6 to 8% of all thyroid malignancies.[1-4,9-11] The most frequent subtype of this thyroid tumor is large B-cell diffuse lymphoma.[1-3,9,10] The 52-year-old female patient described here had hypothyroidism due to a previous Hashimoto's thyroiditis.[4,6,11] Lymphoid tissue is nearly absent in normal thyroid, but intense lymphocyte infiltration often develops in patients with autoimmune thyroiditis, contributing to diagnosis challenges.[1-3,6,7,10,12]

This middle-aged woman had typical features of an anterior cervical mass with accentuated increase of volume in a short span of time.[1] Her fast-growing tumor was associated with symptoms indicative of upper airway and esophageal obstruction, as frequently described in this setting.[1,2,4,11] Systemic symptoms classically related to lymphomas, including fever, night sweats and weight loss are absent in nearly 90% of cases.[6,10] Our patient presented with fever and sweating, with leukocytosis and elevation of urea and creatinine serum levels during admission, but these changes were due to an urinary infection with *E. coli*, which was controlled by antibiotics.

Previous diagnosis of hypothyroidism and nodular goiter of probable immunologic origin have been reported in 27% to 100% of cases, suggesting the strong association between primary thyroid lymphoma and chronic lymphocytic thyroiditis.[1,4,6,11] It is estimated that primary thyroid lymphoma evolves from Hashimoto's thyroiditis in 5% of cases.[10] Moreover, the longstanding course of this thyroiditis may increase the risk of lymphoma by 50-60 times.[1,3,11]

FNAB is the first choice for investigation of suspected thyroid malignancies,[11] but the procedure has limitations,[1,4,6] as observed in the present case. Core needle biopsy (CNB) was later performed to clarify previous inconclusive data,[1,10,13] and the findings characterized the diagnosis of a high grade B-cell CD20+ lymphoma. The tumor was successfully treated through association of R-CHOP with radiation therapy.[11]

An additional concern in the present case study refers to the coexistence of a cerebral aneurysm. The association of cerebral aneurysms with primary lymphomas of the central nervous system in the absence of phakomatoses or radiotherapy is exceedingly rare and may be merely casual.[7] These aneurysms are scarcely described in patients with CNS lymphomas, including their various subtypes – large B-cell, T-cell, Burkitt, and MALT.[5,8] It is relevant to note that malignant cells are not invariably detected infiltrating the walls of the aneurysm.[15]

The etiopathogenesis of these aneurysms remains elusive, mainly due to the low number of published cases, and it might include tumor arterial embolism, tumor infiltration of vessel walls, arterial recanalization, and ballooning of the vessel walls by hemodynamic stress.[5,15] Statistical data from five reports about cerebral aneurysms associated with primary CNS lymphoma were compared with the findings of this primary thyroid lymphoma (Table 2). Four of the patients (80%) had lymphoma of B-Cell lineage, and three were men (60%). The mean age of the patients was 63.4 (± 5.32) years, with median age of 65 (56 to 69) years. Aneurysms were found at the middle cerebral artery (60%), anterior cerebral artery, and anterior and posterior communicating arteries.[5,8,14-16]

Three (60%) aneurysms were resected, and respective histopathology studies revealed lymphomatous cells invading the vessel walls in two of them, while tumor embolus was detected in the remaining case. Patients with Hashimoto's thyroiditis should be monitored for detection of primary thyroid lymphoma.[11] Although this condition is a rare hypothesis, it can severely affect the patient's quality of life. Circulating lymphomatous cells could invade the vessel walls,[5,15] but the relationship between lymphoma and cerebral aneurysm is unclear.[8]

The authors believe that case reports can enhance the suspicion index about rare conditions, which could be underdiagnosed, misdiagnosed or scarcely described.

Table 2. Data of five patients with primary central nervous system lymphomas and cerebral aneurysms, compared with data of a patient with primary thyroid lymphoma and cerebral aneurysm

REFERENCES	GENDER-AGE	LYMPHOMA	ANEURYSM SITE	HISTOLOGY OF ANEURYSM
Roitberg et al[4]	M*/ 65 years	B-cell	ACA#	Tumor cells in the wall
Suslu et al[7]	F†/ 67 years	B-cell	MCA§	ND∞
Anda et al[14]	F/ 69 years	B-cell	MCA	Tumor embolus
Hasegawa et al[15]	M/ 60 years	MALT‡	MCA	Tumor cells in the wall
Terasaki et al[16]	M/56 years	T-cell	AComA˅, PComA˟	ND
**Santos VM et al	F/ 52 years	B-cell	PComA	ND

*M: male; †F: female; ‡MALT: mucosa-associated lymphoid tissue; #ACA: anterior cerebral artery; §MCA: middle cerebral artery; ˅AComA: anterior communicating artery; ˟PComA: posterior communicating artery; ∞ND: not done. **Primary thyroid lymphoma coexistent with cerebral aneurysm

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