

Case Report

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Primitive Seminoma of the Thyroid Gland: A Novel Situation, an Exceptional Primitive Location

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Abstract

The thyroid gland is exceptionally a metastatic site. Thyroid metastasis from a testicular seminoma is even more exceptional. We report the case of a patient with an atypical 8-cm thyroid nodule showing the histology and the immunoprofile of a pure seminoma. No testicular or extra-testicular tumor was discovered. To our knowledge, this situation has never been described. After surgery, the patient underwent chemotherapy and remains disease-free four years later.

Keywords: Thyroid; Tracheal compression; Intrathyroid metastasis

Patient and Methods

A 46-year-old male patient without any previous relevant medical history was referred to our institution in February 2008 for a left cervical mass increasing in volume over the past three months. The patient reported no other accompanying symptom. The clinical examination found an 8-cm nodule of the left thyroid lobe, mobile on swallowing, no vascular thrill, no cervical lymph node nor sign of thoracic extension. Under fiberoptic examination the vocal cords were mobile without any sign of hypopharyngeal or tracheal compression.

The initial imaging included a US scan of the neck and the thyroid gland and a neck and chest CT scan which described an 8×4×3 cm left thyroid lobe nodule (Figure 1A) without thoracic extension, compression of the neighboring organs or other sign of metastasis. The thyroid biological workup was normal (T4 11 pg/ml, TSH 3.33 μUI/ml, thyroglobulin 33.7 μg/ml, antithyroglobulin antibodies <10 UI/ml, thyrocalcitonin 2 ng/ml). Thyroid fine-needle aspiration suggested a non-epithelial tumor, compatible with a poorly-differentiated lymphoma.

In order to confirm the diagnosis, the patient was operated on for a left thyroid lobectomy. Locally dissection of the thyroid was difficult as

the tumor adhered to the surrounding tissues without invading them. This did not seem clinically compatible with a lymphoma. Nonetheless frozen section examination revealed a poorly-differentiated tumor resembling a lymphoma. Total thyroidectomy was therefore not achieved.

The microscopic examination demonstrated a neoplastic proliferation invading the thyroid parenchyma, composed of uniform, large cells with a clear cytoplasm, large, and irregular nucleus with one or two nucleoli. The tumor cells were arranged in sheets and clusters or cords separated by fine fibrous trabeculae associated with a lymphocytic infiltrate. Granulomas composed of histiocytes were also seen admixed with the lymphocytes. The immunohistochemical study was performed on representative 3-microns thick sections of formalin-fixed paraffin-embedded tissue using the automated immunostainer (Benchmark XT) from Ventana Medical Systems, Tucson, AZ, USA with UltraView Ventana detection system (Table 1). The resection margins were tumor-free.

A cytogenetic study revealed no isochromosom 12p, which is usually a cytogenetic marker of germ cell tumor.

Based on the morphology and the immunoprofile, a histological diagnosis of pure seminoma invading the thyroid gland was retained (Figure 2).

The patient was then transferred to the medical oncology unit at the Léon Bérard Center for further diagnostic investigations and therapeutic support. Testicular clinical and US examinations were normal. The complementary biological assessment did not find any

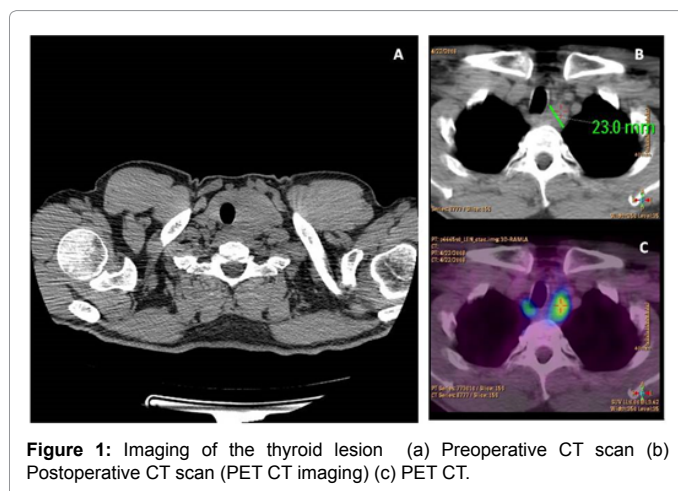


Figure 1: Imaging of the thyroid lesion (a) Preoperative CT scan (b) Postoperative CT scan (PET CT imaging) (c) PET CT.

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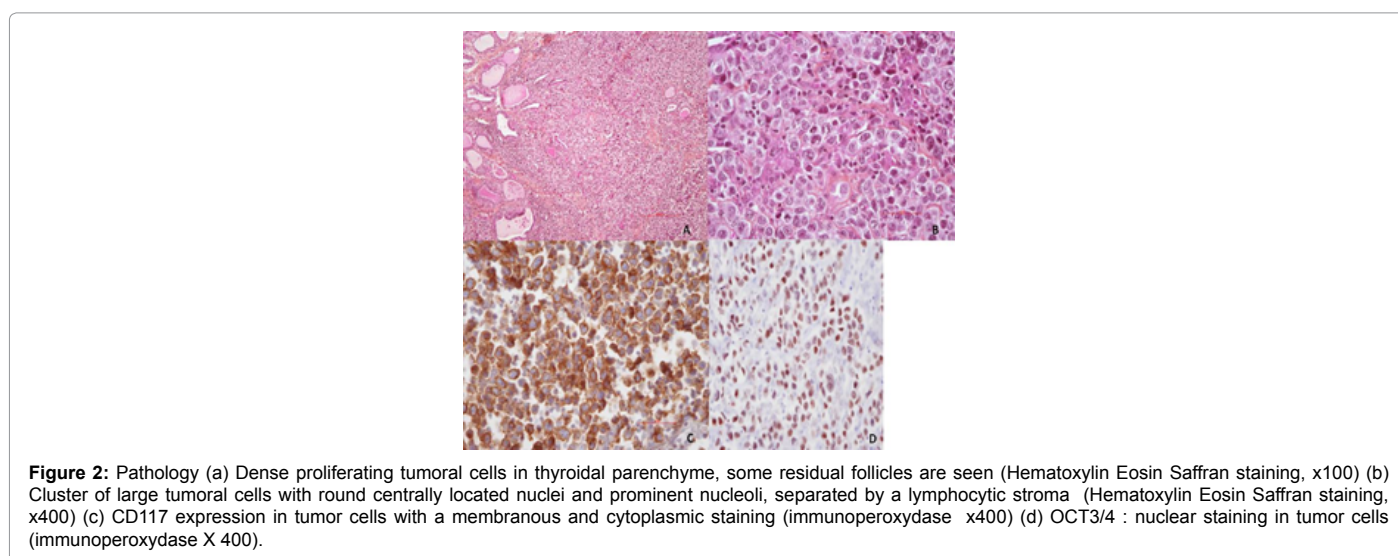
Received November 04, 2013; **Accepted** February 27, 2014; **Published** February 28, 2014

Citation: Buiret G, Fléchon A, Devouassoux-Shisheboran M, Plouin-Gaudon I, Ambrun A (2014) Primitive Seminoma of the Thyroid Gland: A Novel Situation, an Exceptional Primitive Location. *Thyroid Disorders Ther* 3: 144. doi:10.4172/2167-7948.1000144

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Antibodies	Clone	Dilution	Results in tumor
AE1/AE3	AE1/AE3 (Dako)	1/50	Cytoplasmic, dot staining
KL1	KL1 (Beckman Coulter)	1/50	Cytoplasmic, dot staining
EMA	E29 (Dako)	1/200	Negative
TTF-1	8G7G3 (Invitrogen)	1/50	Negative
Thyroglobulin	G9 (Dako)	1/2000	Negative
CD3	Polyclonal (Dako)	1/50	Positive in lymphocytes
CD20	L26 (Dako)	1/200	Positive in few lymphocytes
S100 protein	Polyclonal (Dako)	1/700	Negative
HMB-45	HMB45 (Dako)	1/100	Negative
Melan-A	A103 (Dako)	1/50	Negative
CD117	CKIT (Dako)	1/300	Membranous and cytoplasmic staining of tumor cells
OCT3/4	MRG1.1 (Cliniscience)	1/20	Nuclear staining in tumor cells
CD30	BerH2 (Dako)	1/20	Negative
HCG	Polyclonal (Dako)	1/600	Negative
AFP (alpha foeto protein)	Polyclonal (Dako)	1/2000	Negative

Table 1: Immunohistochemical study of the thyroid tumor.



elevation of serum tumor markers (AFP 4 ng/ml (N<10), total HCG <2UI/l). A PET CT (Figures 1B and 1C) revealed a 2-cm intensely uptaking mass located on the posterior side of the trachea and a less intense 11-mm node in the left cervical lymph node level IV. No other isotopic fixation was seen.

The diagnosis of a primary pure seminomatous tumor of the thyroid gland was retained with a local relapse and a nodal invasion.

In order to complete the treatment, the patient received four five-day cycles of bleomycin -toposid - cisplatin with intervals of three weeks [1]. Germinal tumor markers (hCG, AFP, LDH), PET CTs and CT scans remained normal and after a four-year follow-up, the patient is well and tumor-free.

Discussion

Intrathyroid metastases are rare. Calzolari et al. [2] found 25 cases of intrathyroid metastasis among 17122 thyroidectomies (0.15%) of which 22 had a history of previously treated cancer. The thyroidectomy therefore led to the seeking of the primitive cancer in three patients. According to Ishikawa et al. [3], four patients out of 970 thyroidectomies (i.e. 0.4%) had an intrathyroid metastasis, all of them with a past history of cancer. Papi et al. [4] described 36 cases of intrathyroid metastasis in a series of 27962 thyroidectomies (0.13%). Finally, in the series of 1016 patients operated on for thyroid cancer, Wood et al. [5] reported 15 cases of intrathyroid metastasis

(1.4%). Overall the majority of reported cases were metastases of renal carcinoma. Nevertheless intrathyroid metastases may be underestimated and seem more frequently reported in autopsy series of patients who died of cancer (1.2 to 25%) than in living cancerous patients [2,6-8]. In the series of Shimaoka et al. [8], out of 5668 autopsies of patients who died of cancer, 302 (5.3%) had an intrathyroid metastasis and only three were patients with a primary testicular cancer (1% of cases of the intrathyroid metastases).

The misdiagnosis of lymphoma after the frozen section examination is explained by the fact that seminoma is a proliferation of isolated cells over a lymphoid infiltrating reaction, resembling a poorly-differentiated lymphoma.

Treatment of a unique metastasis inside the thyroid gland must be aggressive (total thyroidectomy, radiotherapy, chemotherapy as it can be potentially curative [5]. However overall and progression-free survivals remain poor, 31% and 18% respectively at five years in the series of Calzolari et al. [2], depending on the type of primitive carcinoma.

Metastases of testicular seminoma are most often located in retroperitoneal lymph nodes. Only two cases of such intrathyroid metastasis have been reported [9,10]. Here, the situation is different: the patient had never been diagnosed beforehand nor even treated for a seminoma. Moreover, although the first hypothesis was a thyroid metastasis of testicular or extra-testicular seminoma, the initial

complete workup did not find any primitive cancer. A primitive seminoma of the thyroid gland can therefore be proposed. Germinative tumors develop on the midline (central nervous system, mediastinum and retroperitoneal). The thyroid gland, being located on the midline, an aberrant migration of germ cells within the gland can be hypothesized. Another hypothesis may be a metastatic thyroid tumor from a burned-out seminoma, a spontaneously and completely regressed testicular tumor with no treatment [11].

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