Case Report

A Case Report of Thyroid Plasmacytoma and Literature Update

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Abstract

Plasmacytomas of the thyroid gland are rare, whether or not they arise as solitary (primary) lesions or secondary to systemic multiple myeloma. Here, we present the case of a 71-year-old female presenting with goiter and Hashimoto's thyroiditis, in whom the subsequent histopathological diagnosis of plasmacytoma was a surprise. In presenting this case, we summarize the last 25 years of literature on thyroid plasmacytoma and review the salient clinicopathological characteristics, differential diagnoses, management, and outcomes of this rare condition.

Keywords: Extramedullary, pathology, plasmacytoma, thyroid

Introduction

Plasmacytoma can occur in the thyroid gland either as primary lesions (solitary extramedullary plasmacytoma [EMP]) or secondary to systemic spread of multiple myeloma.[1] Differentiating between primary and secondary plasmacytoma is essential, because their clinical behavior and subsequent management are markedly different. Here, we describe a case of a thyroid plasmacytoma arising in a background of Hashimoto's thyroiditis. In doing so, we take the opportunity to emphasize the importance of clinical follow-up and review the last 25 years of literature on thyroid plasmacytoma including their clinicopathological features, important differential diagnoses, and outcomes.

Case Presentation

A 71-year-old female with a medical history of hypertension and diabetes presented with a massive goiter. Thyroid function tests on presentation revealed a thyroid-stimulating hormone (TSH) of 5.51 μIU/L (0.27–4.2), free T3 of 3.67 pmol/L (2.8–7), free T4 of 9.98 pmol/L (12–22), thyroid peroxidase antibody of 319 IU/mL (0–34), and thyroid thyroglobulin antibody of 683 IU/mL (0–115). A thyroid ultrasound showed enlarged (right lobe: 6.9 cm × 3.0 cm × 2.7 cm; left lobe: 7.4 cm × 3.1 cm × 3.8 cm; isthmus unremarkable) heterogeneous lobes bilaterally with prominent vasculature and microcalcifications, but no focal lesions. Scintigraphy was normal with homogeneous 1.7% Tc99m uptake. The laboratory and imaging findings were entirely consistent with autoimmune (Hashimoto's) thyroiditis. She underwent elective thyroidectomy 1 year later. The patient gave consent before surgery. The case is reported according to the regulations of Research Committee of the Biomedical Ethics Unit, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia. At that time, her TSH had risen to 11.0 μIU/L (0.27–4.2), but her free T4 levels were static at 9.84 pmol/L (12–22). Her operation was unremarkable, and she was discharged without any hoarseness of voice, but with low calcium level (1.95 mmol/L [2.12–2.52]) and hypoalbuminemia (25 g/L [40.2–47.6]). An intraoperative frozen section revealed chronic thyroiditis with a prominent plasma cell component.

On macroscopic pathological examination, the left lobe measured 9 cm × 6 cm × 3.5 cm and the right lobe measured 10 cm × 6 cm × 3.5 cm, both with prominent capsular blood vessels, gray-yellow in color, and firm in consistency [Figure 1a and b]. Microscopic examination [Figure 1c and d] revealed a diffuse, mature plasma cell infiltrate separated by fibrous septa. Occasional binucleation and mitotic figures

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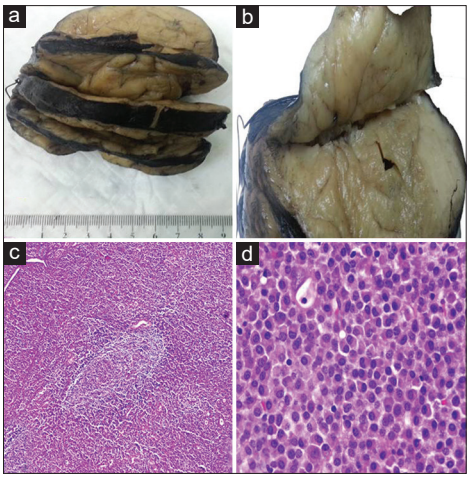

Figure 1: Gross and microscopic appearance, (a) The left lobe is shown and measures 9 cm. (b) The cut surface is gray-yellow in color. (c) Diffuse infiltration with mature plasma cell infiltrate separated by fibrous septa along with focal lymphoid follicle formation and germinal center (H and E 40×). (d) Sheet of diffuse mature plasma (H and E 200×)

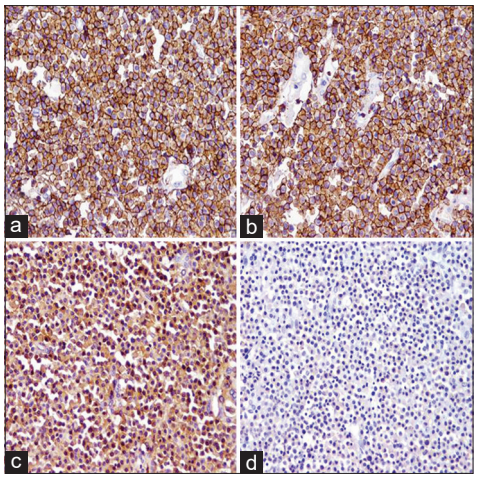

Figure 2: Immunohistochemistry, (a) Tumor cells show positive membranous reaction to CD45 (leukocyte common antigen). (b) Tumor cells show positive membranous reaction to CD38. (c) Tumor cells show positive cytoplasmic membranous reaction to kappa. (d) Tumor cells show negative reaction to lambda. Original magnification is 100×. DAB (3,3'-diaminobenzidine) was used as chromogen and hematoxylin as the counter stain

were visible, along with focal lymphoid follicle formation and germinal centers. Residual thyroid follicles were present with oncocytic follicular lining. On immunohistochemical testing, the lesion was positive for antibodies targeting kappa light chain, CD38, and CD45, but negative for lambda light chain, CD138, thyroglobulin, CD20, synaptophysin, chromogranin, NSE, CD30, calcitonin, and Bcl-2 [Figure 2a-d]. There was no evidence of follicular or papillary carcinoma. These histological features were consistent with EMP in a background of focal Hashimoto's thyroiditis. A thorough neck examination and serum and protein electrophoresis were recommended to rule out neck extension and multiple myeloma, respectively. Unfortunately, the patient moved shortly after the operation and was lost to follow-up.

Discussion

Here, we report a case of plasmacytoma of the thyroid, which, to the best of our knowledge, is only the second to be reported in a Saudi Arabian individual.[2] Plasmacytoma of the thyroid can be either primary or secondary to systemic spread of multiple myeloma. Primary EMPs fall into the spectrum of plasma cell neoplasms, but account for only 3%–5% of total,[3] usually arising in the head and neck region (80%–90%),[4] but rarely at other sites. This includes the thyroid where, since first being described by Voegt in 1938,[5] only a few cases have been described. Although the exact incidence of thyroid EMP is difficult to establish due to its rarity, early large attempts to quantify thyroid EMP revealed seven thyroid cases in 272 (3%) EMPs,[6] and conversely, Hazard and Schildecker found only two EMPs in 14,000 thyroid operations.[7] In their effort to summarize the literature on thyroid plasma cell neoplasms in 1994, Kovacs *et al*.[1] collated 50 cases of solitary EMP of the thyroid and 16 cases of thyroid involvement with systemic multiple myeloma. In a similar effort, but including the Japanese literature, Ohshima *et al*.[8] identified 34 cases of solitary thyroid EMP in the Western literature and further 32 cases in the Japanese literature. Since then, further 19 cases of solitary EMP of the thyroid [Table 1] and 11 cases of thyroid EMP with multiple myeloma [Table 2] have been reported as case reports in the English literature.

Similar to Kovacs *et al*.,[1] we found that there was a female predominance of primary EMP of the thyroid (63% vs. 61% in Kovacs *et al*.) and average age of presentation in the sixth to seventh decade (58 [±14] vs. 63.6 years in Kovacs *et al*.).

Plasma cells are an unusual finding in the thyroid, with the frozen section plasmacytosis raising early suspicion of an unusual entity in this case. The diffuse involvement of the thyroid with plasma cells, normal scintigraphy, and no evidence of a focal lesion are commonly reported,[1] so our case is not unusual in that regard. The morphological features and CD38 positivity with kappa light chain restriction made the diagnosis relatively straightforward. However, the diagnosis is not always straightforward. The main histopathological differential diagnoses are mucosa-associated lymphoid tissue (MALT) lymphoma (especially with marked plasma cell differentiation),[37,38] lymphoplasmacytic lymphoma, large B cell lymphoma with plasmo/immunoblastic differentiation, medullary carcinoma,[11,34] and plasma cell granuloma,[39] so both morphological and immunohistochemical features must be considered in addition to a high index of suspicion for EMP. Here, there was no CD20 positivity and lymphoepithelial complexes were absent, This ruled out MALT lymphoma. On the other hand, the relatively low proliferation rate and nuclear atypia did not suggest an aggressive B cell lymphoma. Calcitonin and neuroendocrine markers were negative, ruling out medullary carcinoma, and the kappa light chain restriction was inconsistent with plasma cell granuloma. However,

Table 1: Cases of solitary extramedullary plasmacytoma of the thyroid reported since 1994

Author and year	Reference	Sex	Age	Localized or systemic	Associated thyroid disease	Treatment	Outcome
Hassan *et al*., 2014	[9]	Male	53	Localized	Hashimoto's thyroiditis	Total thyroidectomy	NS
Mertens de Wilmars *et al*., 2015	[10]	Female	78	Localized	No	Radiotherapy	Disease-free at 17 months
Bhat *et al*., 2014	[11]	Male	60	Localized	Hashimoto's thyroiditis	Total thyroidectomy	NS
Lee *et al*., 2014	[12]	Female	56	Localized	Hashimoto's thyroiditis	Total thyroidectomy	NS
Ridal *et al*., 2012	[13]	Female	52	Localized	No	Left lobo-isthmectomy and completion right lobectomy and post-operative radiotherapy	Disease-free at 5 months
Yao *et al*., 2012	[14]	Female	45	Localized	Hashimoto's thyroiditis	Total thyroidectomy and neck lymph node dissection	NS
Puliga *et al*., 2011	[15]	Female	74	Localized	Multinodular goiter	Total thyroidectomy	Disease-free at 16 months
Patten *et al*., 2011	[16]	Female	54	Localized	Micropapillary carcinoma and Hashimoto's thyroiditis	Radiotherapy	Disease-free at 5 months
Shahani *et al*., 2011	[17]	Male	82	Localized	Previous DLBCL	Left lobectomy and radiotherapy	Disease-free at 26 months
Abdel Khalek *et al*., 2010	[18]	Female	60	Localized	No	Total thyroidectomy	NS
Fraser *et al*., 2010	[19]	Female	64	Localized	Hashimoto's thyroiditis	Total thyroidectomy	NS
Meccawy 2010	[2]	Male	57	Localized	Hashimoto's thyroiditis	Total thyroidectomy	Disease-free at 12 months
Avila *et al*., 2009	[20]	Female	40	Localized	No	Left lobectomy	Disease-free at 12 months
Ozkan *et al*., 2008	[21]	Male	57	Localized	No	NS	NS
Chaganti *et al*., 2007	[22]	Male	71	Localized	Hashimoto's thyroiditis	Right lobectomy	Disease-free at 24 months
Kuo *et al*., 2006	[23]	Female	19	Localized	No	Right lobectomy	Disease-free at 3 years
De Schrijver and Smeets 2004	[24]	Female	69	Localized	No	Total thyroidectomy	NS
Hasegawa *et al*., 1999	[25]	Female	61	Localized	Hashimoto's thyroiditis	Total thyroidectomy and post-operative radiotherapy	NS
Ohshima *et al*., 1994	[8]	Male	52	Localized	Hashimoto's thyroiditis	Right lobectomy	Disease-free at 3 years

DLBCL: Diffuse large B cell lymphoma, NS: Not stated

Table 2: Cases of thyroid involvement with multiple myeloma reported since 1994

Author and year	Reference	Sex	Age	Localized or systemic	Associated thyroid disease	Other comments
Sahu *et al*., 2019	[26]	Male	57	Systemic	No	
Gochhait *et al*., 2019	[27]	Male	57	Systemic	No	
Singh *et al*., 2017	[28]	Male	57	Systemic	No	Initially normal bone marrow
Park *et al*., 2010	[29]	Female	68	Systemic	No	
Ozdemir *et al*., 2009	[30]	Male	57	Systemic	No	Relapse site of multiple myeloma
Serefhanoglu *et al*., 2008	[31]	Female	76	Systemic	No	
Terrier *et al*., 2006	[32]	Female	78	Systemic	No	Relapse site of multiple myeloma, responded to thalidomide and dexamethasone
Wahner-Roedler *et al*., 2003	[33]	Female	87	Systemic	No	
Bourtsos *et al*., 2000	[34]	Male	73	Systemic	No	
Schiller *et al*., 1995	[35]	Male	68	Systemic	No	
Vailati *et al*., 1995	[36]	Female	55	Systemic	No	

particular care must be taken when making a cytological diagnosis on fine needle aspirates, because the presence of mimicking nuclear atypia and amyloid, the stromal amyloid of medullary carcinoma and the light chain deposits of plasmacytoma being identical, can prompt a misdiagnosis of medullary carcinoma.[11,34] The distinction between EMP

and medullary thyroid carcinoma is important because the management is different. Medullary thyroid carcinoma is usually treated by thyroidectomy and neck dissection rather than thyroidectomy/radiotherapy alone. Further, follicular neoplasm of the Hürthle cell type shares prominent cytomorphological patterns with plasmacytoma including discohesive aggregates of tumor cells accompanied by dispersed single cells, tumor cells with abundant cytoplasm, eccentrically placed nuclei, and occasional multinucleation, so should be considered when examining cytological preparations.[12]

Regrettably in this case, the patient was lost to follow-up, and despite the clinical recommendation to screen for multiple myeloma, this could not be performed; about a third of upper respiratory tract EMP have systemic spread on further examination, and many of the case reports of thyroid EMP are subsequently found to have systemic involvement.[40] In their comprehensive analysis of outcomes of 46 EMP at different sites (albeit only one confined to the thyroid), Galeini *et al*.[41] established specific diagnostic criteria for primary (localized) EMP: (i) monoclonal plasma cell histology on tissue biopsy, (ii) plasma cells in the bone marrow representing <5% of all nucleated cells, (iii) absence of lytic skeletal lesions or other tissue involvement, (iv) a lack of hypocalcaemia or renal failure, and (v) a low level of serum M protein, if present. We were unable to establish whether this lesion was localized or part of a systemic manifestation of multiple myeloma. However, given that there was concomitant Hashimoto's thyroiditis, which to our knowledge has yet to be reported in 13 thyroid cases of multiple myeloma in Kovacs *et al*.[1] or in the further 11 multiple myeloma cases summarized in Table 2, it is much more likely that this case represents a primary EMP without systemic spread. Conversely, 36/44 (82%) of primary EMPs in Kovacs *et al*.[1] and 10/19 (53%) of primary EMPs summarized in Table 1 arose in a background of Hashimoto's thyroiditis, and further investigations are warranted to establish whether the autoimmune or chronic inflammatory process is causative for primary EMP as suggested for other lymphomas and papillary carcinoma.[1]

Although there is no major consensus on the optimal treatment for primary EMP, both surgery and radiotherapy alone or in combination have frequently been used to manage the disease; indeed, all the newly reviewed cases in Table 1 were successfully treated with either or both modalities. Accordingly, surgery in our case was appropriate in this case. Further systemic chemotherapy would have been warranted if the lesion had manifestations of systemic disease. Clinical outcomes for patients with localized disease are extremely good. In contrast to solitary plasmacytoma of the bone, which frequently converts into multiple myeloma, EMP remains localized, with 83% showing no evidence of disease after a mean follow-up of 56 months in Kovacs *et al*.[1] and only 3/50 patients progressing to multiple myeloma during follow-up. Likewise, when considering all EMPs, they have a favorable prognosis (15 years survival rate of 78%) when treated locally by irradiation and/or surgery.[41]

Of our 19 new cases summarized in Table 1, there were no recurrences or deaths from the disease, albeit with only short follow-up periods. By contrast, nearly half of all patients with plasmacytoma occurring in the context of multiple myeloma died of their disease with a mean survival of 9.7 ± 15.7 months and further 33% had persistent disease.[1]

In conclusion, primary and secondary plasmacytomas are rare thyroid neoplasms that are often unexpected, and in the case of primary plasmacytoma, are often associated with Hashimoto's thyroiditis. Clinical examination and imaging are generally unhelpful in diagnosis, and care must be taken with pathological assessment, particularly when interpreting cytology samples. Follow-up is essential, because primary and secondary lesions have markedly different management and outcomes. Finally, further research is required to establish the relationship between inflammatory thyroid disease and the development of primary EMP.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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