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. 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 prominent vasculature and microcalcifications, but no focal lesions. This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

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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. 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, usually arising in the head and neck region (80%-90%), but rarely at other sites. This includes the thyroid where, since first being described by Voegt in 1938, 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, and conversely, Hazard and Schildecker found only two EMPs in 14,000 thyroid operations. In their effort to summarize the literature on thyroid plasma cell neoplasms in 1994, Kovacs et al. 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. 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 in case reports in the English literature.

Similar to Kovacs et al., 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, 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), lymphoplasmacytic lymphoma, large B cell lymphoma with plasm/oimmunoblastic differentiation, medullary carcinoma, and plasma cell granuloma, 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,
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.\textsuperscript{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.[13] 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. 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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