

Plasmacytoma of the Thyroid Gland: Case Report and Review of the Literature

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Abstract. Primary plasmacytoma of the thyroid gland is a rare disease, and up-to-date, its clinical pathological features are not fully understood. A case of a Plasmacytoma of the thyroid gland which is the first reported case in the Kingdom of Saudi Arabia has been detected. The present case is an extramedullary, non-mucosal plasmacytoma of the thyroid gland in a 57-years-old male who was presented with a large diffuse thyroid swelling. Histopathological examination of the surgical specimen, along with immunohistochemical studies, confirmed the diagnosis of plasmacytoma. Hematological work up for multiple myeloma was negative.

Keywords: Plasmacytoma, Thyroid gland, Extramedullary, Immunohistochemistry, Hematological studies.

The Case

A 57-year-old male was presented to the outpatient clinic with a 9 months history of a progressively enlarging, painless, neck mass. The mass was associated with pressure symptoms, including change in voice, dyspnea, and dysphasia. The patient denied any history of weight loss.

Clinical examination revealed a firm nodular thyroid swelling with no associated cervical lymphadenopathy. Neck ultrasonography confirmed the enlargement of the thyroid gland.

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Fine needle aspirate (FNA) cytological preparation from the mass was consistent with follicular lesion, recommending a tissue biopsy to rule out malignancy.

Thyroid function test (TFT) showed high thyroid stimulating hormone (TSH) level of 10.89 mU/L (range: 0.27-4.2 mU/L) and low FT4 of 8.93 pmol/L (range: 12-22 pmol/L) and normal FT3 level. Thyroglobulin antibodies titer was highly positive, 7215 IU/ml (normal 0-60 IU/ml).

Computed tomography scan (CT-scan) of the neck showed diffusely enlarged thyroid gland, especially the right lobe, which appeared heterogeneous in the post-contrast study. The enlarged gland compressed the trachea as well as the esophagus, but there was no evidence of invasion to the adjacent structures, or to the lymph nodes with an observation that malignancy could not be excluded. There was no retrosternal extension.

CT-scan abdomen was also requested and showed prominent left lobe and caudate lobe modularity, suggesting liver cirrhosis. No focal masses or abdominal lymphadenopathy were found. A small gall bladder stone was noted.

Preoperative ear, nose, and throat (ENT) consultation and fibro-optic laryngoscope examination of the patient revealed normal mobile vocal cords. The patient was submitted to total thyroidectomy and no enlarged lymph nodes were noted intraoperatively.

The histopathological examination of the surgical specimen revealed an irregularly enlarged thyroid gland, soft to firm in consistency, and having an intact capsule. A cut surface of the gland showed effacement of the normal colloid appearance of the gland, and replacement by a gray white homogenous neoplastic growth.

Microscopic examination of histological sections revealed infiltration of the thyroid gland by diffuse sheets of neoplastic plasma cells with extensive stromal amyloid substance deposition (Fig. 1-5). The residual thyroid parenchyma showed dense lymphocytic infiltrated with lymphoid follicle formation and atrophy of follicular cells, suggestive to Hashimoto's thyroiditis. A panel of immunohistochemical antibodies was used including CD138, kappa and lambda chain and

immunoglobulin G (IgG). Neoplastic plasma cells showed light chain restriction on immunohistochemical staining (Kappa & IgG).

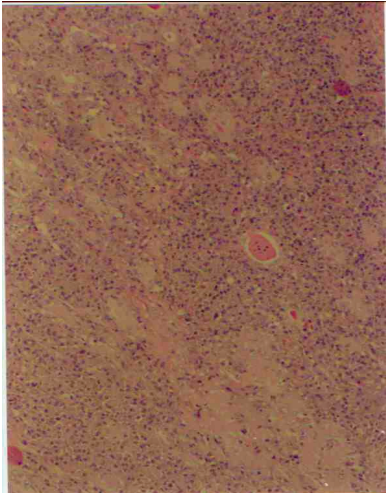


Fig. 1. Microscopic examination revealed infiltration of thyroid gland by diffuse sheets of neoplastic cells. (Hematoxylin and Eosin stain, X 200)

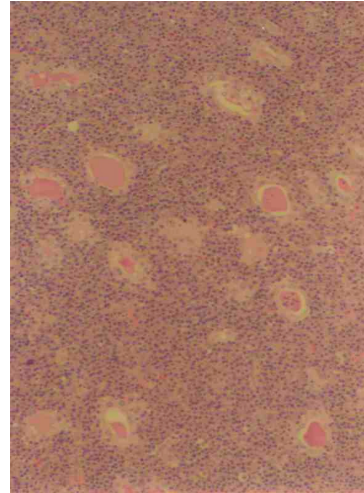


Fig. 2. Microscopic examination revealed infiltration of thyroid gland by diffuse sheets of neoplastic cells. (H&E, X100)

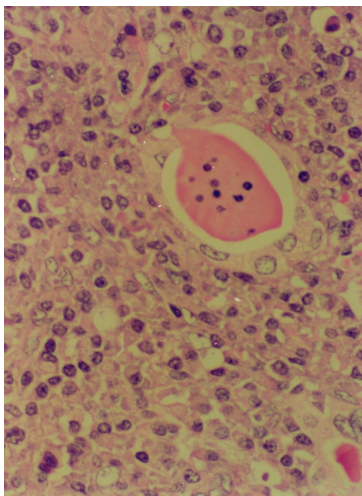


Fig. 3. High power view of the same case. The neoplastic plasma cells showed pleomorphism and hyperchromatism. Tumor cells are entangling thyroid follicles that are lined by atrophic follicular cells. (H&E, X400)

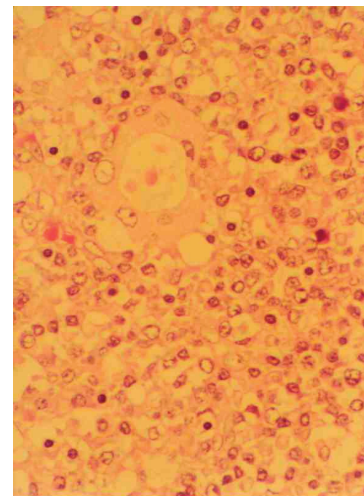


Fig. 4. High power view of the previous figure. Note, intact thyroid follicles with absence of lymphoepithelial lesions. (H&E, X400)

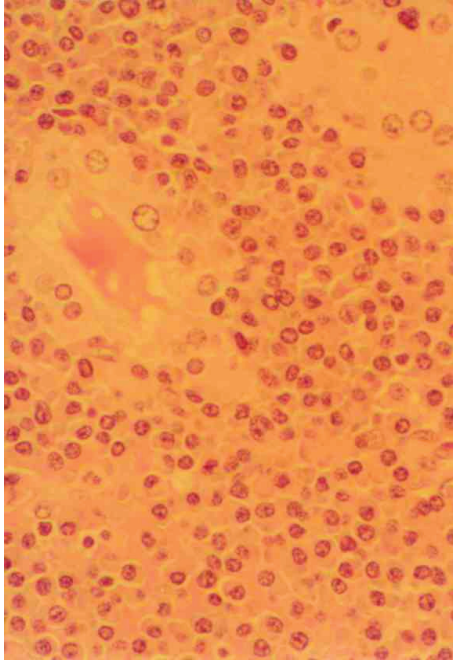


Fig. 5. High power view of the previous figure demonstrating atypical plasma cells, showing pleomorphism, hyperchromatism, binucleate and multinucleate forms. (H&E, X400)

The microscopic slides of the above case were reviewed by different groups of surgical pathologists that confirmed the diagnoses of plasmacytoma in a background of Hashimoto's thyroiditis. Electron microscopic examination confirmed the plasma cells nature of the neoplastic cells. Bone marrow examination was negative for neoplastic cell infiltrate. Urine protein electrophoresis, as well as Bence Jones protein measurements was also negative.

Skeletal survey showed spondylitic changes in C3-4 & C5-6 and lumbosacral region with some osteophytes formation anteriorly. The rest of the survey was normal.

The patient was referred to the oncology and radiotherapy services who advised no further treatment. The patient did well for one year follow-up after surgery with no evidence of recurrence.

Literature Review

Plasma cell dyscrasias (monoclonal gammopathies) are a group of disorders that are characterized by expansion of a single clone of immunoglobulin-secreting plasma cells, with resultant increase in serum levels of single complete or partial immunoglobulin. The homogenous immunoglobulin identified in the blood is often referred to as an “M” component^[1]. Plasma cell dyscrasias are further subdivided into six major variants^[1,2]; multiple myeloma, localized plasmacytoma, lymphoplasmacytic lymphoma, heavy-chain disease, primary or immunocyte-associated amyloidosis, monoclonal gammopathy of undetermined significance.

Localized plasmacytoma are further sub-classified into two groups; a) solitary skeletal plasmacytoma, mainly affecting bones of spine, pelvis, and femur, which it can evolve into multiple myeloma, and b) extramedullary plasmacytoma (EMP) that involves soft tissues, and this is our concern in this review^[1-4].

EMP represents less than 5% of all plasma cell neoplasms. It affects males 2-3 times more than females and typically occurs in between the 4th and 7th decades of life. The most common location of EMP is upper respiratory tract and oral cavity. Although, it may involve many sites in the head and neck, including minor salivary gland, parotid gland, tongue, temporal bone, and thyroid gland. EMP has been also reported outside head and neck including, pleura, mediastinum, spermatic cord, ovary, intestine, kidneys, pancreas, breast, and skin^[4-6].

Thyroid gland is one of the rarest sites to be affected by EMP. Approximately 50 cases of solitary thyroid plasmacytoma have been reported in the literature^[7-9]. However, it is not uncommon for multiple myeloma to involve the thyroid gland.

Most of the symptomatology of EMP is related to their specific location in the head and neck. In Kapadia *et al.* series^[8]; 80% of head and neck solitary plasmacytoma presented with a mass, 35% complained

airway compression, and 12%-26% reported to have cervical lymph nodes metastasis at initial presentation.

On the other hand, EMP of the thyroid usually presents with painless, firm, non-tender, mobile, multinodular or diffuse thyroid mass with no associated cervical lymphadenopathy (usually misinterpreted as goiter). Rapidly growing thyroid mass that brought the patient to seek medical advice is reported in some series^[7-9].

Patients usually are euthyroid or hypothyroid. The antithyroid antibodies may be elevated^[7-9]. Immunohistochemical staining can demonstrate monoclonal plasma cells for kappa or lambda immunoglobulin chains^[10]. Primary plasmacytoma of the thyroid, like malignant lymphoma, is often accompanied by evidence of autoimmune thyroiditis in the residual portion of the gland^[11].

The gold standard diagnostic test for thyroid solitary plasmacytoma is a histological examination of tissue biopsy, since there are very few reports about diagnosing of these cases by FNA cytology examination. Saad *et al.*^[12], diagnosed plasmacytoma of larynx by FNA cytology. Another unique study in Sao Paulo, Brazil^[13] (University of Sao Paulo Medical School) reported a case of a solitary plasmacytoma of the thyroid in a 58-years-old man who was presented with an 8 m history of rapidly enlarging, non-tender neck mass, was diagnosed as multinodular goiter by ultrasound scanning. FNA cytology showed numerous atypical plasma cells consistent with plasmacytoma. A cytoplasmic analysis of the aspirate revealed monoclonal kappa positive cells. Urine protein electrophoresis and Bence Jones proteins were negative. The patient was euthyroid and the antithyroid antibodies were positive in very high titers (4500 U/L). The patient was subjected to near total thyroidectomy and resection of 8 lymph nodes. Histopathological examination proved malignant plasmacytoma in a background of chronic lymphocytic thyroiditis. The patient received a full course of external beam radiotherapy, and it was mentioned that the patient was doing well 6 yrs after surgery.

Bourtsos *et al.*^[14] reported a different aspiration cytology finding of a case; a thyroid plasmacytoma that was initially misinterpreted as medullary carcinoma due to presence of a background of amyloid substance in the aspirate, together with the clinical impression of a thyroid mass suspected malignant. Bourtsos *et al.*^[14] suggested that EMP

should be considered in the differential diagnosis of a neck mass that yields cells associated with amyloid or amyloid-like material.

One of the most challenging issues in the diagnosis of solitary thyroid plasmacytoma is to rule out the possibility of disseminated multiple myeloma. Evidence of normal bone marrow on histological examination, absence of lytic bone lesions on skeletal survey, together with low paraprotein levels is confirmatory of solitary thyroid plasmacytoma^[15,16]. However, previous studies reported that up to 25% of patients with a solitary plasmacytoma may have elevated levels of “M” proteins in the blood or urine, and that these high levels should raise the suspicion of disseminated process^[17,18]. Rubin *et al.*^[17] reported a case of EMP of the thyroid and reviewed 40 similar cases reported in the literature. They found that 43% of patients presented with regional lymphadenopathy that had no effect on the prognosis, serum monoclonal antibodies were noted in 33% of patients, while urine paraprotein was found in 11% of the cases. Thyroid scanning revealed a cold nodule in majority of the cases. TFT revealed that 50% of tested patients were hypothyroid, whereas the rest were euthyroid. Bone marrow examination was normal in all patients, and interestingly, concurrent chronic lymphocytic thyroiditis, which is Hashimoto’s thyroiditis, was detected in 63% of patients, suggesting an autoimmune association. In addition, Rubin described resolving of serum monoclonal gammopathy following surgery, and irradiation of the primary tumor site of their reported case with EMP of the thyroid. Rubin suggested that the diagnosis of EMP should be considered in patients presenting with obstructive thyromegaly associated with autoimmune thyroiditis.

EMP can be classified into 3 stages^[2,18,19]:

- Stage I: localized to the primary site.
- Stage II: presence of local extension or lymph nodes involvement.
- Stage III: disseminated or metastatic disease.

Although the prognosis for disseminated EMP of the head and neck is better than multiple myeloma, the treatment of EMP is still controversial. Some authors advocated radiotherapy alone; others advocated surgery alone while few advocated combined approach^[20-22].

Galieni *et al.*^[2] conducted a retrospective analysis of 46 patients with a diagnosis of EMP established in four Italian institutions, between

August 1970 and June 1993. They concluded a favorable prognosis of EMP, and the completed remission can be achieved by radiotherapy in almost all cases, denoting the particular sensitivity of plasmacytoma to irradiation. Surgical removal can be as a sole treatment if the mass is small and respectable. Treatment with chemotherapy was found to have no effect on the course of EMP, except in a case of disseminated disease. In addition, they claimed that single and selected cases of disease diffusion, particularly those with rapid soft tissue involvement, could benefit from intensive treatment followed by autologous bone marrow transplantation.

Alexiou *et al.*^[22] reviewed more than 400 publications found in the literature between 1905 and 1997. They concluded that surgery alone could give the best results in cases of EMP of upper aerodigestive tract, when resectability is complete. However, if complete surgical tumor resection is incomplete or impossible and/or lymph nodes are involved; then combined approach is recommended^[22,23].

In spite of the results of these retrospective studies, it's concluded that these results should be confirmed in randomized large series trials and comparing different treatment modalities.

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حالة بلازماسيتوما في الغدة الدرقية مع مراجعة الدوريات في هذا المرض النادر

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المستخلص. هذه حالة بلازماسيتوما توجد فقط بالغدة الدرقية وهو مرض نادر الحدوث، وهو من الناحية الإكلينيكية المرضية غير مفهوم، هذه حالة بعيدة عن النخاع وجدت فقط بالغدة الدرقية لمريض ذكر عمره ٥٧ عامًا والذي حضر بتضخم متجانس بالغدة الدرقية، وقد أثبت الفحص التشريحي للغدة بعد العملية مع فحص الخلايا المناعية الكيميائية تشخيص بلازماسيتوما، كما أثبتت الفحوصات الأخرى عدم وجود مرض الميلوما المتعددة.