et al. [1] have shown that, on pre- and post-treatment evaluation of the lymph nodes, infiltration of Ki67- and CD3-positive, CD8-positive, granzyme B-positive T cells increases. It has been observed that, in patients with Hodgkin lymphoma who are treated with lenalidomide and who develop TFR, cytokines (particularly interleukin [IL]-6, IL7, APRIL, BAFF/BLyS) are released because of B cell activation, and levels of free light chains increase distinctively; these changes are reflected in the clinical properties. Likewise, it has been shown that when the TFR subsides, cytokines and light chain levels decrease to normal levels [5]. Therefore, for patients who develop TFR, it is suggested that dexamethasone be used, as it provides distinctive improvement by especially inhibiting CD40 regulation [1]. The mechanism through which the R-HCVAD treatment leads to TFR is not known, but one of the above-listed mechanisms may play a role.

Yusuf Kayar¹, Nuket Bayram Kayar²

¹Bezmialem Vakif University, Department of Internal Medicine, ²Bagcılar Education & Research Hospital, Department of Family Medicine, Istanbul, Turkey

Correspondence to: Yusuf Kayar
Bezmialem Vakif University, Department of Internal Medicine, Vatan Street, Fatih, Istanbul 34093, Turkey
E-mail: ykayar@yahoo.com

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Extramedullary plasmacytoma of the thyroid: report of a rare case

TO THE EDITOR: Extramedullary or extra-osseous plasmacytomas (EMP/EOP) are localized plasma cell neoplasms that arise in tissues other than bone. EMP comprises 3–5% of all plasma cell neoplasms. The upper respiratory tract and the oral cavity are the most common sites for EMP [1], and the thyroid gland is one of the rare sites for this neoplasm. Here, we report a case of EMP of the thyroid in a 53-year-old male who presented to the surgery outpatient department (OPD) with a left-sided thyroid swelling of six months duration.

CASE
A 53-year-old male patient presented to the surgery OPD with history of swelling of the left side of his neck for the last six months. The swelling had gradually increased to its present size over this time period and was not associated with pain, changes in his voice, or difficulty in breathing. A well-healed scar was present on the front of the patient’s neck, as he had undergone surgery four years earlier for which no further details were available. The patient had not received any post-operative chemotherapy or radiotherapy. On examination, a soft, non-tender swelling measuring 8×10 cm was noted on the front of the neck toward the left side that moved with deglutition but not with protrusion of the tongue. The cervical lymph nodes were not enlarged. There were no signs of pressure effects on the trachea, larynx, esophagus, or major veins of the thorax, and no sign of hypothyroidism or hyperthyroidism.

All routine investigations, including complete blood count, liver function test and renal function test, were within normal limits. A thyroid profile showed slightly increased thyroid-stimulating hormone levels (TSH, 5.92 mIU/mL; normal range, 0.5–5.0 mIU/mL) and slightly decreased T4 levels (3.65 μ/dL; normal range, 4.5–12.6 μ/dL). Contrast-enhanced computed tomography of the neck and chest showed a well-defined mass lesion of 6×6×10 cm in the region of the left lobe of the thyroid gland extending up to the hyoid bone. Inferiorly, the mass extended 2 cm above the level of the aortic arch. Ultrasoundography of the abdomen showed fatty liver with an enlarged prostate, and no enlarged lymph nodes or hepatosplenomegaly were observed. Fine-needle aspiration cytology of the swollen area was performed, revealing a dispersed population of atypical plasma cells along with a few benign follicular epithelial cells that were infiltrated by lymphocytes. The possibility of plasmacytoma of the thyroid in a background of thyroiditis was suggested. Following a cytology report, an extensive workup for multiple myeloma (MM) was performed, which showed normal bone marrow, and radiographs of the skull, chest, spine, and pelvis did not show any abnormalities. Serum protein...
Electrophoresis showed normal levels of serum proteins with a very low serum M protein level of 0.25 g/dL. Other values were as follows: serum total protein 6.90 g/dL, albumin 4.41 g/dL, alpha 1 globulin 0.35 g/dL, alpha 2 globulin 0.77 g/dL, and gamma globulin 0.82 g/dL with an A:G ratio of 1.77. The serum kappa-free light chain level was increased (24.07 mg/L; normal range, 3.30–19.40 mg/L), while the level of lambda free light chain and the kappa/lambda ratio were within normal limits (19.06 mg/L and 1.26, respectively). Serum β2 microglobulin and calcium levels were within the normal ranges. The patient was prepared for surgery, and a total thyroidectomy was performed. Intraoperatively, there was a 10×8 cm swelling on the left lobe of the thyroid with a shift of the trachea to the right side without any infiltration of the adjacent structures or capsule, and there was no lymphadenopathy. Gross examination of the specimen showed a globular soft piece of tissue measuring 8.5×6×5 cm. The external surface was nodular with an adherent capsule and showed prominent blood vessels. The cut section of the specimen was gray, firm, and fleshy.

**Fig. 1.** Extramedullary plasmacytoma: gross-cut section of a specimen appears gray, firm, and fleshy.

**Fig. 2.** Microscopy of extramedullary plasmacytoma of the thyroid. (A) Sheets of plasma cells infiltrating the thyroid parenchyma with few entrapped atrophic thyroid follicles (H&E, ×100). (B) Sheets of plasma cells with some binucleated forms (H&E, ×400). (C) Many lymphoid follicles with germinal centers (H&E, ×100). (D) CD138-positive tumor cells on immunohistochemistry.
in appearance (Fig. 1). Microscopically, multiple sections taken from the tumor showed sheets of plasma cells infiltrating the thyroid parenchyma with few entrapped atrophic thyroid follicles (Fig. 2A). These cells have eccentric, round nuclei with abundant eosinophilic cytoplasm. Sporadic binucleated and multinucleated plasma cells were also observed (Fig. 2B). Many lymphoid follicles with germinal centers were also present (Fig. 2C). Thus, a diagnosis of EMP in a background of Hashimoto’s thyroiditis was made. Immunohistochemistry (IHC) showed CD138-positive tumor cells while CD20 was negative, thus clinching the diagnosis of EMP (Fig. 2D). IHC for kappa light chain showed strong cytoplasmic positivity in the tumor cells while that of the lambda light chain was negative (Fig. 3). The patient is undergoing regular follow-up and has been asymptomatic for the past eight months.

**DISCUSSION**

Plasma cell neoplasms consist of monoclonal gammopathy of undetermined significance (MGUS), plasma cell myeloma, plasmacytoma, immunoglobulin deposition disorders, and osteosclerotic myeloma (POEMS syndrome) [1]. Plasmacytomas are further divided into solitary plasmacytoma of the bone (SPB) and EMP that involve the soft tissue without any signs of systemic spread [1]. In contrast to SPB, which frequently converts into MM, EMP remains localized [2]. EMP is extremely rare and comprises 3–5% of all plasma cell neoplasms. It occurs more commonly in men (M:F=2–3:1) at 40–70 years of age, with the median age at diagnosis being 55 years [1, 3]. The head and neck regions are the most common site for EMP (80–90%), and about 0.4% of all head and neck cancers is the result of EMP [4]. EMP has also been reported in other locations, such as the breast, pancreas, ovary, kidney, spermatic cord, pleura, mediastinum, etc. [3]. The thyroid gland is a very unusual site for EMP. Wiltshaw [5] reported 7 cases of EMP of the thyroid out of 272 cases of EMP, while Hazard and Schildecker [6] reported EMP in only two cases out of 14,000 thyroid operations. Macpherson et al. [7] found only one case of EMP out of 870 thyroid tumors, while Aozasa et al. [8] reported EMP of the thyroid in 6 out of 62 cases. Galieni et al. [9] reported only one case out of 46 cases of EMP. As the current case, EMP of the thyroid in a background of lymphocytic thyroiditis has also been reported by other authors [3, 8, 10].

While rendering a diagnosis of EMP of the thyroid, it is essential to exclude the possibility of MM. A diagnosis of EMP of the thyroid is confirmed by a normal bone marrow examination, absence of osteolytic lesions on a bone survey and normal levels of serum proteins on electrophoresis. Specific diagnostic criteria for EMP have been established by Galieni et al. [9]: (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 hypercalcemia or renal failure, and (v) a low level of serum M protein, if present. Our case met all of these diagnostic criteria for EMP.

The treatment of EMP remains controversial; all three modalities, including radiotherapy alone, surgery alone, or a combined approach, are advocated by various authors [11]. Although EMP is very sensitive to radiotherapy and complete remission can be achieved by irradiation alone in most cases, surgery remains the treatment of choice if the tumor is resectable. A combined approach is advocated if surgical removal is not possible or is incomplete and if lymph node involvement is present. In the present case, since the tumor was limited to the left lobe of the thyroid gland with no extracapsular extension, surgical removal with close follow-up for recurrence was advocated. The patient has been followed up regularly in the surgical OPD for the last eight months and has remained asymptomatic to date. Long-term follow-up of EMP is advised, as around 20% cases of EMP may progress to MM [11].

EMP of the thyroid is a very rare entity, and its diagnosis is made only after ruling out the diagnosis of MM through...
appropriate investigations. The prognosis of localized plasmacytoma is favorable, but regular follow-up is essential as EMP may progress to MM in approximately 20% of cases.

Mohammad Jaseem Hassan1, Sabina Khan1, Mukta Pujani1, Sujata Jetley1, Prabhat Kumar Raina2, Rayees Ahmad2

Departments of 1Pathology, 2General Surgery, Hamdard Institute of Medical Sciences and Research (HIMSR), India

Correspondence to: Sujata Jetley
Department of Pathology, HIMSR, Jamia Hamdard, New Delhi 110062, India
E-mail: sujatajetley@gmail.com

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JAK2 V617F-positive polycythemia vera accompanied by renal artery stenosis

TO THE EDITOR: Polycythemia vera (PV) is a chronic myeloproliferative disorder with pancytosis that is unrelated to a secondary cause. Although the discovery of JAK2 V617F mutation in the pathogenetic mechanism of PV has made the diagnosis clearer and easier, until recently, diagnosis of PV involved excluding secondary causes of erythrocytosis in clinical practice. Among the secondary causes, smoking history, elevated erythropoietin (EPO) level, and hypoxemia measured by arterial blood gas analysis are well known and recognized as minor criteria for the diagnosis of PV. With the upfront evaluation of JAK2 mutation status in patients with erythrocytosis, clinicians are apt to be neglectful about the evaluation of these secondary causes. However, based on our case, evaluation of other causes is clinically significant.

CASE
A 30-year-old woman presented with headache, hypertension, and abnormal laboratory findings on routine health examination. Her initial blood pressure was 190/140 mmHg, and pulse rate was 84 beats/min. The laboratory testing yielded a white blood cell count of 22.5×109/L, hemoglobin at 22.5 g/dL, hematocrit level at 66.9%, and platelet count of 400.0×109/L. Physical examination revealed mild splenomegaly. She did not have hypoxemia and had never smoked. Sequentially performed bone marrow aspiration and biopsy revealed panmyelosis consistent with PV, and molecular testing revealed the presence of JAK2 V617F mutation. However, the consequently identified EPO level was elevated to 470 mIU/mL, and hypertension, which was initially considered to be caused by polycythemia, persisted after phlebotomy. For the exploration of secondary hypertension with an elevated EPO level, we performed CT angiography covering the adrenal glands and renal arteries and found irregular severe stenosis of the right renal artery and multifocal irregular stenosis of the left renal artery. Moreover, her right kidney was severely atrophied (Fig. 1). Anti-nuclear antibody (ANA), anti-neutrophil cytoplasmatic antibody (ANCA), C3, C4, and lipid profile were all within normal range. We continued with intermittent phlebotomy for the management of PV and decided to perform angioplasty of the narrowed renal artery (Fig. 2). Additionally, we prescribed the anti-platelet agent clopidogrel because the pa-