Case Report

Solitary Extramedullary Plasmacytoma of the Thyroid Gland in a Patient With Subclinical Hyperthyroidism

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ABSTRACT

Objective: Solitary extramedullary plasmacytoma (SEP) of the thyroid is rare, and its clinical and pathologic features are not entirely understood. Generally, patients with SEP of the thyroid also present with Hashimoto thyroiditis. We report, for the first time, a case of SEP of the thyroid in a patient with subclinical hyperthyroidism.

Methods: A 46-year-old woman presented to the emergency department with symptoms consistent with a panic attack. Following a physical examination, neck ultrasonography, and laboratory tests, we determined that the patient was hyperthyroid and possessed a toxic multinodular goiter. The patient elected to undergo a total thyroidectomy to treat the subclinical hyperthyroidism and to remove the nodules.

Results: SEP diagnosis requires consideration of the systemic spread of multiple myeloma and a combination of immunohistochemical examination, imaging, and other laboratory tests. Upon further examination, we confirmed SEP through the following criteria: the absence of kidney failure or hypercalcemia, a biopsy demonstrating plasma cell histology, a lack of bone or tissue involvement, and low serum myeloma protein concentration. The immunophenotype of the tumor cells further confirmed SEP diagnosis, with positivity for CD138, CD79a, and lambda light chain antibodies and no reactivity toward cyclin D1.

Conclusion: This case fulfilled the criteria for SEP, and we were able to rule out multiple myeloma. Currently, no standard treatment exists for SEP. Yet, the prognosis remains encouraging. Going forward, SEP of the thyroid should be considered in the differential diagnosis of a patient with subclinical hyperthyroidism and a toxic multinodular goiter.

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Introduction

Thyroid nodules are common occurrences, with palpable nodules afflicting 2% to 6% of the population.[1] However, ultrasonography uncovers thyroid nodules in 19% to 35% of the population.[1] While the majority of thyroid nodules are benign, 2 to 3 of every 30 nodules are cancerous.[2] The differential diagnosis of thyroid nodules commonly involves differentiated thyroid cancers, medullary thyroid cancers, and anaplastic thyroid cancer.[2] Less common diagnoses include lymphomas and metastatic lesions, with solitary plasmacytomas being even rarer.

Solitary plasmacytomas are characterized by a local accumulation of monoclonal plasma cells located in either bone or, less frequently, soft tissue.[3-5] A plasma cell neoplasm in soft tissue is known as a solitary extramedullary plasmacytoma (SEP) and accounts for less than 5% of all plasma cell neoplasms.[6,7] Other plasma cell neoplasms include multiple myeloma, solitary plasmacytoma of bone, monoclonal immunoglobulin deposition disease, and monoclonal gammopathy of undetermined significance.[8] The main diagnostic challenge is to distinguish SEP from the systemic spread of multiple myeloma.

Around 80% of SEPs are located in the upper respiratory tract and the oral cavity.[9] This makes the involvement of the thyroid gland by a SEP a rare event, and up until 2015, less than 80 cases of SEP in the thyroid had been reported in the literature.[8,10] In this report, we discuss the differential diagnosis of SEP of the thyroid as well as the clinical features of the case.

Abbreviation: SEP, solitary extramedullary plasmacytoma.
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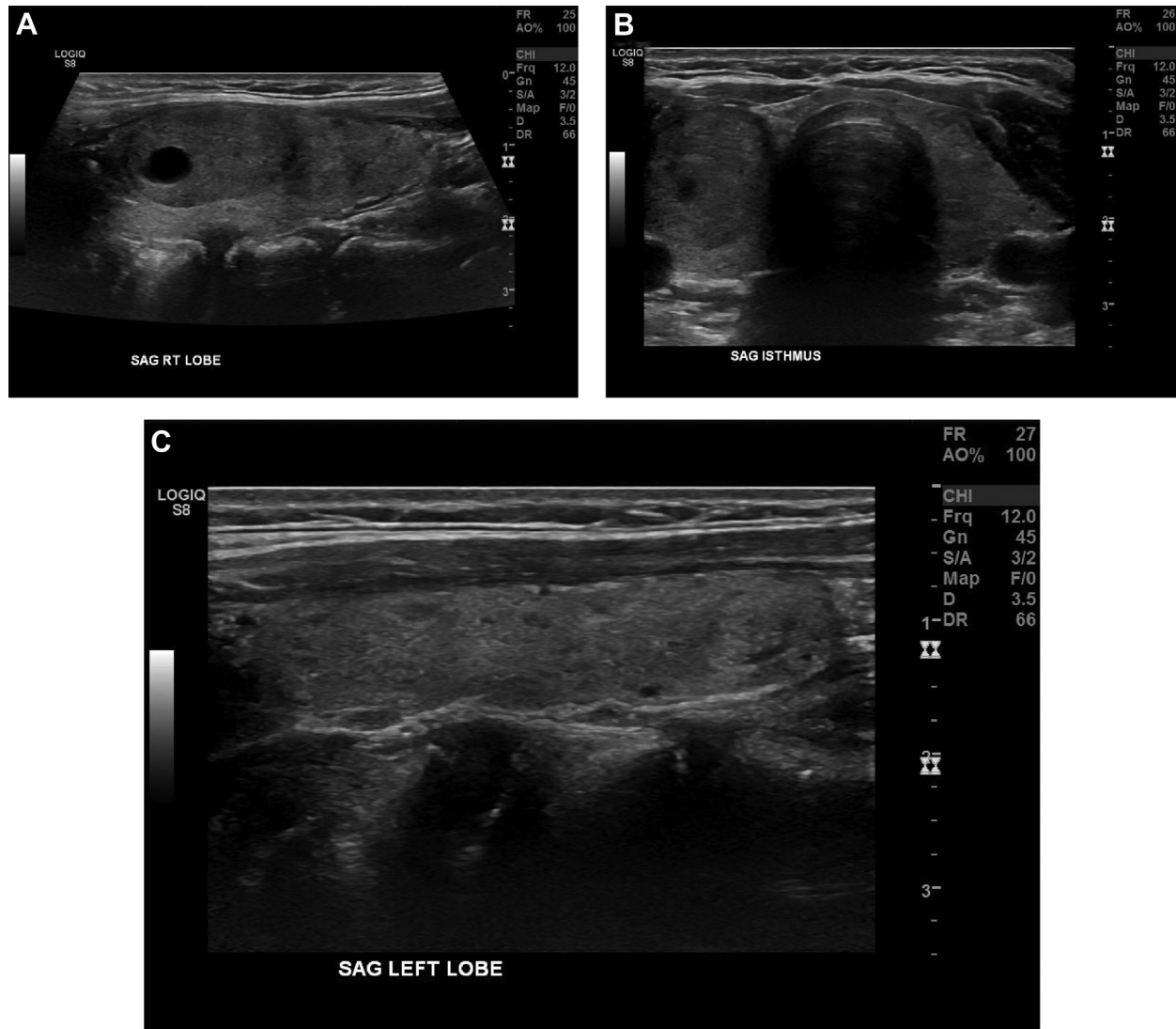
Fig. 1. Ultrasound images of the thyroid. *A*, Sagittal view of the right lobe. *B*, Sagittal view of the isthmus. *C*, Sagittal view of the left lobe.

Case Report

A 46-year-old woman presented to the emergency department with complaints of anxiety, dizziness, weight loss, and decreased appetite. The patient denied compressive symptoms. Originally believed to be a panic attack, the patient was started on escitalopram and lorazepam. Further workup was consistent with subclinical hyperthyroidism, and the patient was prescribed methimazole (10 mg, 3 times a day) and noted improved symptoms. The patient denied a family history of thyroid disease or personal history of exposure to ionizing radiation.

A physical examination revealed a dominant 3-cm, right, nontender, upper-pole nodule with no tracheal shift and without lymphadenopathy. Laboratory tests measured 0.98 ng/dL of thyroxine (reference: 0.76-1.46 ng/dL), 3.29 pg/mL of triiodothyronine (reference: 2.18-3.98 pg/mL), and 0.06 μIU/mL of thyrotropin (reference: 0.31-4.60 μIU/mL), which were consistent with subclinical hyperthyroidism. Thyroglobulin antibody levels were high, at 32.6 IU/mL (reference: 0.0-30.0 IU/mL), while the patient was negative for thyroid peroxidase antibodies, thyroid-stimulating immunoglobulin, and thyrotropin-binding inhibitory immunoglobulin.

Neck ultrasonography confirmed an enlarged, multinodular thyroid gland with heterogeneous echogenicity and multiple hypoechoic zones. The largest nodule was a 2.3 × 1.3 × 1.8 cm hypoechoic right upper-pole nodule (Fig. 1A). There were 3 additional smaller nodules that were midgland of the right lobe (0.9 cm), in the lower pole of the left lobe (1.1 cm), and midgland of the left lobe (1.3 cm), respectively. The isthmus measured 2 mm in thickness, with no evidence of nodules (Figure 1B). The ultrasound confirmed no regional lymphadenopathy. Options for further evaluation as well as treatment plans were discussed with the patient. The patient chose to forego additional workup and nonoperative management and opted to undergo total thyroidectomy for subclinical hyperthyroidism and the nodules. The surgery was uneventful. The patient's voice was at baseline at her first postoperative visit. The patient's calcium and parathyroid hormone levels were normal at 9.2 mg/dL (reference: 8.6-10.2 mg/dL) and 36 pg/mL (14-64 pg/mL), respectively.

Pathologic examination revealed lymphocytic thyroiditis with adenomatous nodules. There were 3 foci of microscopic papillary cancer, with the largest being 8 mm in the right lobe. Of note, there was an 8-mm nodule of plasma cells in the left lobe. This was an incidental finding because this typically would not be biopsied. The
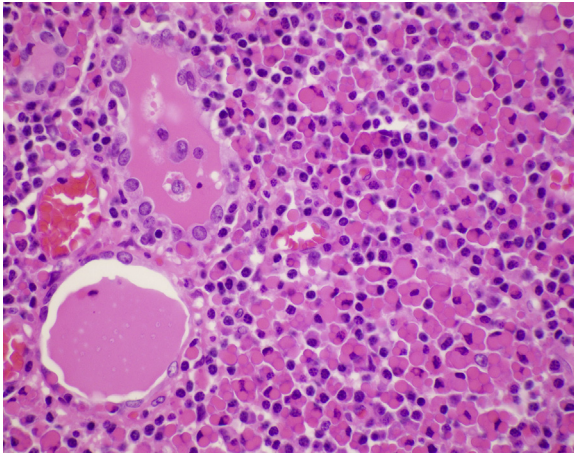
Fig. 2. Immunohistochemistry and microscopic examination of the thyroid. Numerous plasma cells are interspersed among thyroid follicles. Many of the plasma cells contain prominent cytoplasmic Russell bodies. The plasma cells were CD138$^+$, CD79a$^+$, and lambda-restricted. Hematoxylin and eosin, Magnification: x600.

preoperative ultrasound imaging of the left lobe did not reveal the 8-mm nodule (Figure 1*C*).

Immunohistochemistry and microscopic examination of the thyroid demonstrated a well-circumscribed nodule composed of mature-appearing plasma cells with Russell bodies (Mott cells) and scattered lymphocytes in the background (Figure 2). Immunostaining was performed for CD3, CD5, CD10, CD20, CD79a, CD138, Bcl-2, Bcl-6, cyclin D1, and Ki-67 in addition to kappa and lambda light chains. The tumor cells were positive for CD138, CD79a, and lambda light chain antibodies, with no immunoreactivity toward cyclin D1. This suggested extramedullary plasmacytoma.

Postoperatively, the patient was referred to oncology, where workup was performed. Laboratory evaluation involved workup for multiple myeloma, which included serum and urine immunofixation, a complete blood count, serum protein electrophoresis, a 24-hour urine protein test, and a β2-microglobulin tumor marker test.[11] Imaging included a positron emission tomography-computed tomography scan.

No evidence of lytic bone lesions or malignant disease appeared in the positron emission tomography-computed tomography scan, and the marrow tracer activity was in the physiologic range. The complete blood count was normal, including a white blood cell count of 6300/μL (reference: 3800-11 800/μL) and hemoglobin of 12.7 g/dL (reference: 11.1-15.3 g/dL). Serum immunofixation and a urine immunofixation test revealed no monoclonal proteins. Serum protein electrophoresis confirmed a normal electrophoretic pattern of total protein, 6.4 g/dL (reference: 6.1-8.1 g/dL); albumin, 4.1 g/dL (reference: 3.8-4.6 g/dL); α1-globulin, 0.2 g/dL (reference: 0.2-0.3 g/dL); α2-globulin, 0.6 g/dL (reference: 0.5-0.9 g/dL); β1-globulin, 0.4 g/dL (reference: 0.4-0.6 g/dL); β2-globulin, 0.3 g/dL (reference: 0.2-0.5 g/dL); and γ-globulin, 0.9 g/dL (reference: 0.8-1.7 g/dL). In addition, urine protein levels were normal. A serum free kappa light chain level of 10.5 mg/L (reference: 3.3-19.4 mg/L), lambda light chain level of 8.6 mg/L (reference: 5.7-26.3 mg/L), and β2-microglobulin level of 1.56 mg/L (reference: ≤2.51 mg/L) were all in the physiologic range.

The postoperative course was uneventful, and the patient was disease-free 9 months later.

Discussion

SEP of the thyroid remains a rare occurrence with plasmacytoma, comprising only 2 of every 14 000 thyroid operations.[12]

However, SEP exhibits some distinguishing features. In patients with SEP of the head and neck, 80% present with a soft tissue mass, and 43% of patients with SEP of the thyroid present with regional lymphadenopathy.[13,14] Up to 35% of patients with SEP of the head and neck present with airway compression.[13] Men and women are afflicted equally by SEP of the thyroid, with a mean age of incidence of 58.5 years.[14] While Hashimoto thyroiditis is seen anywhere from 63% to 82% in patients with SEP of the thyroid; we believe that this is the first case of SEP of the thyroid in a patient with subclinical hyperthyroidism.[14,15]

While SEP contains some distinguishing features, the workup should mainly focus on ruling out multiple myeloma. Multiple myeloma can involve the thyroid in the late stages of the disease.[16] In 80% of cases, SEP of the head and neck was the primary tumor, while in 20% of cases, it was part of the systemic dissemination of multiple myeloma.[13] Therefore, the diagnosis of SEP requires an extensive examination to determine if there are plasma cell tumors at other sites.

There are 5 diagnostic criteria to confirm an extramedullary plasmacytoma: 1) biopsy of tissue showing plasma cell histology, 2) bone marrow plasma cell infiltration not exceeding 5% of all nucleated cells, 3) absence of osteolytic bone or other tissue involvement, 4) absence of hypercalcemia or kidney failure, and 5) low serum myeloma protein concentration, if present.[9] The immunophenotype includes the expression of CD138, kappa or lambda monotypia, and the absence of cyclin D1.[8,17] Through immunohistochemistry, imaging, and laboratory tests, we were able to investigate if the neoplasm existed as an extramedullary component of multiple myeloma or as a solitary manifestation. The absence of bone lesions, hypercalcemia, and kidney failure as well as the lack of a monoclonal component, presence of CD138, and lambda light chain predominance, fulfilled the diagnostic criteria for SEP and ruled out multiple myeloma.

The prognosis for SEP remains favorable. In a review of 50 cases, for the 40 patients with follow-up data, the 5-year survival rate for SEP of the thyroid was 73%, with 10% of patients dying of other causes.[15] Long term follow-up is recommended because progression to multiple myeloma occurs in 12% of patients with SEP.[5]

A preferred treatment modality for SEP does not exist, with current therapeutic options consisting of surgery, radiation, or a combined approach.[7,10,11] Radiation therapy exists as the most common form of therapy for SEP.[6] Generally, SEP responds well to radiation therapy, with a recommended average dose of 46 Gy.[9] For cases of SEP in the upper aerodigestive tract, when resectability is good, surgery provides the best treatment.[18] If complete surgical resection is unlikely, then a combined approach of surgery and radiation is recommended.[18] Specifically for SEP of the thyroid, surgery serves as the most common form of therapy.[14,15] In a population of patients with SEP of the thyroid where 98% were treated with surgery, 55% of them were additionally treated with local radiation.[15] No difference in outcomes between surgery, radiation, or a combined approach has been observed for SEP of the thyroid.[15]

Conclusion

The connection between subclinical hyperthyroidism and risk for thyroid plasmacytoma is not well established, and this case reports, for the first time, an instance of SEP of the thyroid in a patient with hyperthyroidism. The diagnosis must rule out multiple myeloma because thyroid involvement may represent disseminated disease. Going forward, plasmacytoma of the thyroid should be considered in the differential diagnosis in patients with subclinical hyperthyroidism and toxic multinodular goiter.

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