CASE REPORTS

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Paraganglioma of the thyroid gland: A case report

Paragangliom štitaste žlijezde

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Abstract

Introduction. Thyroid paraganglioma is a very rare malignant neuroendocrine tumor. Immunohistochemical features of thyroid paraganglioma are helpful for the diagnosis. **Case report.** A 69-year-old female came to hospital with the presence of a growing thyroid nodule of the left lobe. Ultrasonic neck examination showed 5 cm hypoechoic nodule in the left thyroid lobe. Thyroid scintigraphy showed a big cold nodule in the left lobe. Computed tomography (CT) scan showed left lobe thyroid tumor with tracheal deviation on the right site. Extended total thyroidectomy was done. Intraoperative consultation with the pathologist confirmed thyroid cancer. The pathologist diagnosed thyroid paraganglioma on the base of immuohistochemical investigation. This thyroid paraganglioma was positive for neuron-specific enolase, chomogranin A, synaptophysin, and S-100 protein highlighted the sustentacular cells. Tumor cells were negative for thyroglobulin, epithelial membrane antigen, cytokeratin, calcitonin, and carcinoembryonic. After the surgery the patient was treated with chemotherapy, peptide receptor radionuclide therapy, and permanent TSH suppressive therapy. The patient was followed with measurements of thyroid hormone and serum neuron–specific enolase, chromogranin A level, every 6 months. Gastroscopy, colonoscopy, chest and abdomen CT scan as well as further tests (chest x-ray, ultrasound of the neck, and whole body octreotide scintigraphy) were done. No primary neuroendocrine tumor in digestive sistem or in the chest was found. After more than 3 years the patient has no evidence of the recurrent disease. **Conclusion.** Radical resection of thyroid paraganglioma, followed by chemotherapy and peptide receptor radionuclide therapy, should be considered the treatment of choice in patients with thyroid gland paraganglioma.

Key words:
neuroendocrine tumors; thyroid gland; paraganglioma; diagnosis; surgical procedures, operative; drug therapy.

Apstrakt

Uvod. Tiroidni paragangliom je rijedak maligni neuroendokrini tumor. Imunihistohemijske odlike ovog tumora bitne su za dijagnozu. **Prikaz bolesnika.** Bolesnica, stara 69 godina, javila se ljekaru zbog progresivno rastućeg čvora u lijevom režnju štitaste žlijezde. Ultrazvučni nalaz je ukazao na čvor veličine 5 cm u lijevom režnju, hipoehogene strukture sa mikrokalcifikatima. Scintigrafski nalaz ukazao je na hladan čvor u lijevom režnju. Kompjuterizovana tomografija pokazala je tumor lijevog režnja štitaste žlijezde koji je potiskivao dušnik u desnu stranu. Urađena je totalna tireoidektomija. „Intraoperativna konsultacija“ sa patologom ukazala je na karcinom lijevog režnja štitaste žlijezde. Na osnovu imunohistohemijskih pretraga preparata, patolog je postavio dijagnozu tireoidnog paraganglioma. Tumorske ćelije bile su pozitivne na neuron-specifičnu enolazu, hromogranin, sinaptofizin i S-100 protein, a negativne na tireoglobulin, kalcitonin, epitelni membranski antigen, citokeratin i karcinoembriogeni antigen. Nakon hirurškog liječenja sprovedena je hemioterapija, trajna tireostimulišući hormon (TSH) supresivna terapija i protein usmjerena radioterapija. Bolesnica je kontrolisana svakih 6 mjeseci, uz određivanje nivoa TSH, serumske neuron specifične enolaze i hromogranina A. Urađene su i gastroskopija, pankolonoskopija, kompjuterizovana tomografija grudnog koša i abdomena, scintigrafija cijelog tijela oktreotidom, i nijedan nalaz nije ukazao na postojanje primarnog neuroendokrinog tumora digestivnog trakta ili grudnog koša. Nakon više od tri godine kod bolesnice nema znakova postojanja recidiva bolesti. **Zaključak.** Totalna tireoidektomija sa postoperativnom hemioterapijom i ciljanom peptid-receptor radionuklidnom terapijom jeste metoda izbora u liječenju bolesnika sa tireoidnim paragangliomom.

Ključne reči:
neuroendokrini tumori; tireoidna žlezda; paragangliom; dijagnoza; hirurgija, operativne procedure; lečenje lekovima.

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Introduction

Thyroid paraganglioma is a rare malignant tumor, arising from the neural crest-derived paraganglia of the autonomic nervous sistem [1]. Extra-adrenal paraganglia which are histochemically non-chromaffin, are related to the parasympathetic system and are located primarily in the head and neck region, the superior mediastinum and retroperitoneum [2, 3]. There are 25-case reports on this tumor described in the literature [4]. Paragangliomas of the head and neck region account for 0.012% of all head and neck tumors. They are malignant in 4–16% cases [5]. The carotid body and glomus jugulare account for more than 80% of the cases. In the head and neck region, paraganglia are presented as paired orbital, jugulotympanic, and very rare in the laryngs, trachea and the thyroid [6]. It is typically presented with fast tumor growth progression and presented neck tumor. The neuroendocrine lesions of the thyroid are few and include C-cells lesions (C-cell hyperplasia and medullary carcinoma), mixed C-cell and follicular-derived tumors, paraganglioma, intrathyroid adenoma, and metastasis to the thyroid from neuroendocrine carcinoma arising elsewhere.

Thyroid paraganglioma arise from inferior laryngeal paraganglia, which can be found within the thyroid capsule [7].

All reported cases of paraganglioma of the thyroid occurred in women, and manifesteted as a solitary nodus, and ranged in size from 1.5 to 10 cm [8]. They can be confined to the thyroid or in some cases can exhibit infiltration into surrounding tissue.

Surgical treatment is the basic treatment for thyroid paraganglioma. Additional treatment includes thyroid stimulating hormone (TSH) suppressive therapy by L-thyroxine, chemotherapy, and peptide receptor radionuclide therapy. Although debates on radicalism of surgical treatment have lasted to this day, total thyroidectomy is the most widely accepted surgical treatment.

We reported a patient surgically treated for thyroid paraganglioma.

Case report

A 69-year-old female was sent to the Department for Endocrine Surgery, Clinical Center of Montenegro due to neck tumor. Although the patient knew about the nodule in the left lobe for 1 year, over the last month she noticed painless growth of a nodule. Inspection of the neck showed neck deformity on the left side, and palpatory 5 cm wide fixed painless tumor of the left thyroid lobe. There was no evidence of cervical lymph nodes enlargement. Laryngoscopy showed left laryngeal nerve pulsy. We evaluated a nodule by fine-needle aspiration (FNA) of the thyroid as follows: THY 5, malignant tumor.

Ultrasonography examination of the neck showed hypoechoic heterogeneous 5 cm large and irregular contour nodule, with calcification in the central part. There was no enlargement of the cervical lymph nodes. Chest X-ray showed no metastases. There was a normal thyroid hormone and calcitonin level. Thyroid scintigraphy showed a cold nodule in the left lobe. CT scan showed a left thyroid lobe tumor, 5 cm wide, no tracheal infiltration (Figure 1).

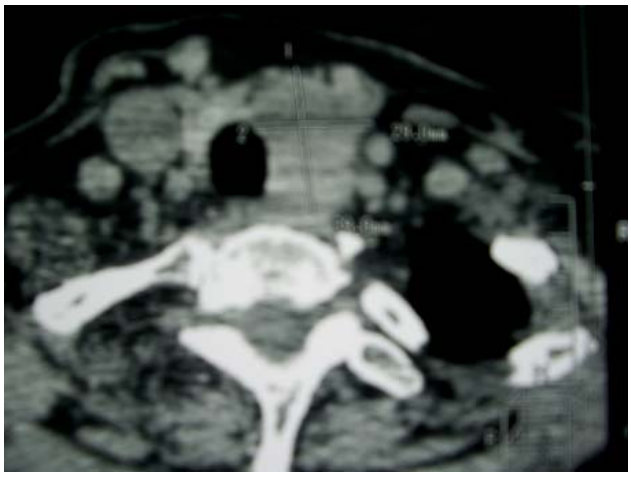

Fig. 1 – Computed tomography scan of thyroid paraganglioma.

During the surgery a left thyroid lobe tumor was found, infiltrating strap muscles on the front left neck side. The tumor also infiltrated the left jugular vein and the front part of the trachea. Extended total thyroidectomy with tangential tumor resection from trachea was performed (Figure 2).

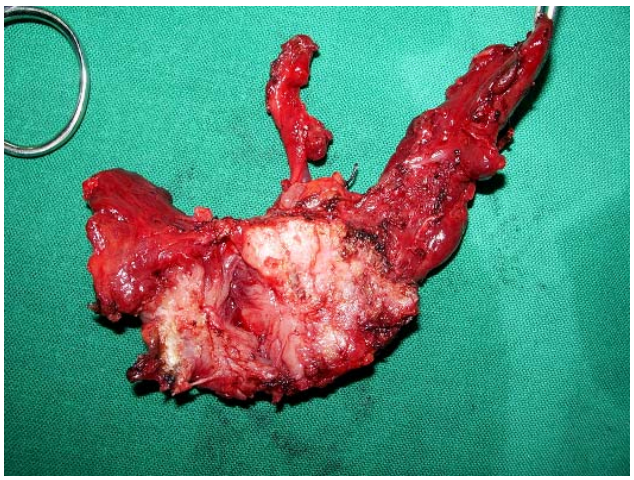

Fig. 2 – Thyroid paraganglioma – total thyroidectomy.

The entire thyroid gland was removed with the left strap muscles, left jugular vein. Debulking was very difficult, due to the presence of a firm neoplasm that spread beyond the gland capsule with infiltration into surrounding tissues. A central neck dissection was made and one lymph node with metastatic disease was found. There was no evidence of postoperative hypoparathyroidism, or respiratory insufficiency. The first postoperative day the patient was treated at Intensive Care Unit, and the following 5 days at the Department for Endocrine Surgery. The following day the patient went home in good condition.

The pathologist diagnosed an invasive neuroendocrine carcinoma of the thyroid. Convencional histology was per-

formed on formalin-fixed and paraffin-embedded tissue blocks, 4 micrometer sections were cut, deparaffinized in xylene and stained with haematoxylin and oesin (H&E). Light microscopy of this tumor revealed the hallmark nesting growth pattern with chief and sustentacular cells seen in thyroid paraganglioma arrising in sites other than the thyroid (Figure 3) There were prominent vascularity and thin fibrous

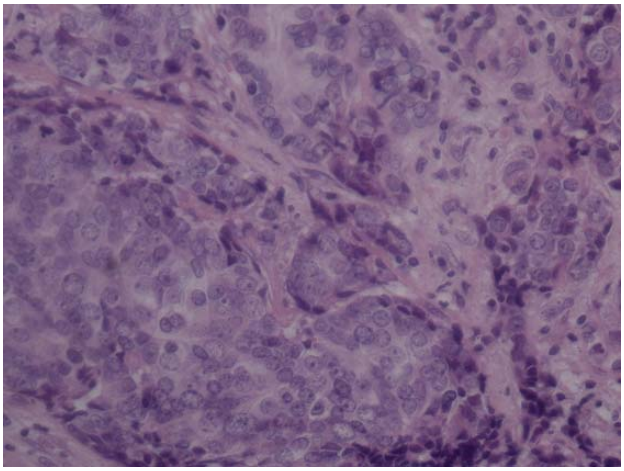

Fig. 3 – Cellular detail showing nests of tumor cells embraced by sustentacular cells (H&E, 40 ×).

septa separating nests of tumor cells. Some cells also exhibited isolated bizarre cells and mitoses, by examining well-fixed histological section. In 2 cervical lymphonode we found metastases of this tumor. This thyroid paraganglioma was positive for neuron-specific enolase, chromogranin A, synaptophysin, and S-100 protein highlights the sustentacular cell (Figure 4). Ki 67 was expressed in 25% of tumor cells. Tumor cells were negative for thyroglobulin, epithelial membrane antigen, cytokeratin, calcitonin, and carcinoembryonic antigen (CEA). These immunohistochemical features of thyroid paraganglioma were helpful for differentiating it from medullary carcinoma.

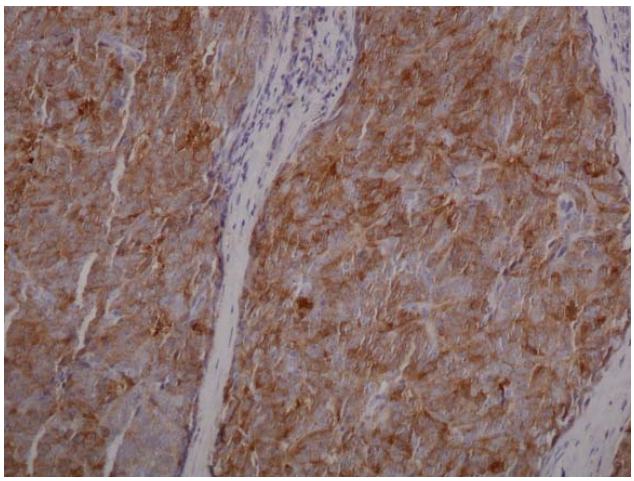

Fig. 4 – Tumor cells evident by chromogranin A immunostaining (20 ×).

Gastroscopy, colonoscopy, chest and abdomen CT scan as well as further tests (chest x-ray, ultrasound of the neck, and whole body octreotide scintigraphy) were done with no primary neuroendocrine tumor found in the digestive system or in the chest.

One month after the surgery the wound was healing well, with no evidence of local recurrence. There was no evidence of hypoparathyroidism or laryngeal nerve palsy. The patient continued on L-thyroxin suppressive therapy with TSH level 0.05 mU/L.

Two months after the surgery the patient had 6 courses of chemotherapy. One year later, octreoscan body scintigraphy showed normal finding, and tumor marker finding with low chomogranin A serum level. One year after the surgery the patient had peptide receptor radionuclide therapy. There was no evidence of local recurrent disease on body octeoscan scintigraphy.

The patient was regularly controlled for 3 years with no evidence of local recurrent disease.

Discussion

Medullary carcinoma is a typical neuroendocrine tumor of the thyroid gland. Other neuroendocrine lesions of the thyroid are C-cell hyperplasia, intrathyroidal nodules and tumors that display neuroendocrine features including hyalinizing trabecular neoplasms, insular carcinoma, true paraganglioma, parathyroid lesions, and tumors metastatic to the thyroid [9]. All the 25 reported cases of paraganglioma of the thyroid occurred in women, manifested as a solitary node [10]. They can be confined to the thyroid or some cases can exhibit infiltration into surrounding tissue. Most thyroid paraganglioma are confined within the thyroid capsule, but in 3 cases the neoplasm was locally invasive and infiltrated through the tracheal wall [11]. Also, in the presented case the tumor spread beyond the thyroid capsule with infiltration of the left laryngeal recurrent nerve, and strap muscule. Light microscopy revealed the hallmark nesting (Zellballen) growth pattern with chief and sustentacular cells seen in paraganglioma arising in sites other than the thyroid [12]. Paraganglioma stains positive for chomogranin A, synaptophysin and S-100 protein. Not surprisingly, the diagnosis of thyroid paraganglioma is rarely established preoperatively by FNA biopsy or intraoperatively by frozen section. The histopathological features usually suggest medullary carcinoma [13]. This is due to the clustering of cells with granular cytoplasm and a richly vascularized stroma. In contrast of medullary carcinoma, paraganglioma tends to exibit S-100 protein staning in sustentacular cells composed at the periphery of the cell nest and they lack staining for cytokeratin, CEA and calcitonin. Our paraganglioma stained positive for neuron-specific enolase, chromogranin A, sinaptophysin, and S-100 protein. Differential diagnosis includes 2 main entites, namely hyalinizing trabecular adenoma of thyroid and medullary carcinoma [14]. Tumor cells of medullary carcinoma also can express a variety of other hormons besides calcitonin, such as corticotropin, melatonin-stimulating hormone, serotonin and gas-

trin [15]. The gold standard for the diagnosis of medullary carcinoma is immunostaining for calcitonin [16]. Medullary carcinoma also stains positive for CEA.

About 6% of patients with thyroid cancer present with life-threatening tumor invasion of the trachea. After the complete tumor resection, 5-year and 10-year survival rates of 40–75% can be achieved [17]. An incomplete tumor resection has a negative effect on the prognosis. A tangential tumor resection (shaving) is indicated if no transmural invasion of trachea occurrs.

The aim of enlarged surgical treatment in thyroid carcinomas is to guarantee respiratory and alimentary functions as well as symptomatic benefits, to obtain local control of the disease and recovery of the adjuvant therapeutic options, such as metabolic and conventional radiation [18].

Conclusion

Malignant thyroid paraganglioma is a rare tumor. The pathologist can diagnose thyroid paraganglioma by examining well-fixed histological section with immunohistochemical investigation of chromogranin A, neurone-specific enolase, and protein S-100. Thyroid paraganglioma tumor cells are negative for thyroglobulin, and calcitonin. This tumor usually invades the thyroid capsule. Invasive tumor presents a delicate surgical problem because of radical surgical eradication. The prognosis of thyroid paragangliloma appears to be favourable, provided that surgical excision is complete. Total thyroidectomy, followed by chemotherapy and peptide related radiotherapy should be considered the treatment of choice.

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