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Multiple primary thyroid cancer in combination with malignant paraganglioma of the neck complicated by acute cerebrovascular event in the postoperative period: Clinical case

Actuality: Paraganglioma originates from the nerve ganglia along a.carotis, the ganglion of n.vagus, and the nerve plexuses around the sigmoid sinus, and has a rich tumor vasculature. Paraganglioma accounts for 0.8% of all CNS tumors and occurs most often at 40-60 years. Chemodectoma is located in the common carotid artery bifurcation zone and accounts for 2/3 of all glomus tumors.

Purpose: The article describes a clinical case of multiple primary thyroid cancer in combination with malignant paraganglioma of the neck complicated by acute cerebrovascular event (ACE) in the postoperative period treated at the Head and Neck Tumor Department of the Kazakh Institute of Oncology and Radiology.

Results: The presented clinical case demonstrates the results of the treatment of multiple primary cancer complicated by an ACE in the postoperative period. The qualification of doctors, adequate diagnostics contributed to choosing the right ACE treatment tactics taking into account all the patient-specific features, the tumor localization, and possible postoperative complications.

Conclusion: The presented clinical case confirms the available data on the necessity of all diagnostic procedures and their effectiveness in the assessment of the prevalence of the process and the involvement of the adjacent anatomical structures in the suspected chemodectoma to avoid postoperative consequences that can lead to disability and fatal outcome. A wrong choice of the volume of surgical intervention can result in severe postoperative complications. Timely diagnosis and knowledge of the clinical course of the ACE helped restore the patient's general condition and stop signs of cerebral ischemia. Successful recovery of a patient depends on the qualifications of the doctors and the prevalence of the tumor process. Adequate symptomatic therapy has a huge impact on the course of a complicated postoperative period.

Keywords: clinical case, malignant paraganglioma, chemodectoma, nerve ganglia, multiple primary cancer.

Introduction: Nowadays, paraganglioma (PG) remains quite a rare tumor and accounts for 0.016% of all malignant neoplasms of the head and neck in Kazakhstan. According to various sources, from 2 to 8 cases per 1 million people per year are registered in the world. The peak of occurrence is at the age of 40-60 years. According to Matiakin et al., 5-year survival after surgical treatment is 92-98% with carotid and vagal PG and 50-60% with atypical PG [1, 2]. After non-radical surgery, the patients with PG die from the generalization of the process mainly in the first three years; less often, they survive five years [2, 3].

Most authors note the predominance of right-sided carotid PG of the neck area [4, 5]. Its features include a tight fit to blood vessels and an expansive growth. The tumor only compresses the main vessels not invading the vessels of the neck. During growth, the tumor also compresses nearby organs (lateral wall of the pharynx, trachea, thyroid gland) and comes into contact with the glossopharyngeal nerves, the internal jugular vein.

The classifications of carotid PG clinical variants were developed, given the varied topographic and anatomical contacts between the tumor and the carot-

id arteries. Three types are distinguished based on the carotid PG relation to carotid arteries: 1) the encapsulated tumor is located in the bifurcation of the carotid arteries and does not germinate the walls of the carotid artery; 2) the tumors sprout only the external carotid artery (ECA); 3) the tumor germinates the internal carotid artery (ICA) [5]. There are other types and several anatomical options distinguished based on a retrospective assessment of contact between the tumor and the main vessels of the neck. The consideration of these types and variants is important for surgical intervention. They are: 1) the tumor has no close contact with the carotid arteries (51.5%); 2) the tumor partially surrounds the ICA and is adherent to its wall (30.5%); 3) the tumor circularly overgrows the ICA and/or OCA (18%) [5]. The classification by Athanasian [4] which is popular in Soviet and post-Soviet medicine distinguishes four options (Figure 1): I – the tumor pushes apart the ECA and ICA (40%), II – the tumor wraps around the ECA as a cuff (15%), III – the tumor wraps around the ICA (5%), IV – the tumor covers the OCA bifurcation and its both branches (40%).

Figure 1 – Diagram of carotid paraganglioma growth variants by L.A. Athanasian [4]

Most popular out of modern diagnostic methods in neck PG are the highly informative non-invasive (ultrasound scanning with color Doppler mapping) and X-ray methods (computed tomography with dynamic contrast enhancement, spiral computed tomography, magnetic resonance imaging, angiography). There is a proposed algorithm for examining this group of patients [6]. Angiographic studies, including radionuclide angiography of carotid arteries with ^{99m}Tc pertechnetate, selective carotid angiography, and polypositional X-ray contrast angiography, are the most informative when examining a suspected neck PG. The literature provides detailed descriptions of the typical signs of angiographic semiotics and a characteristic symptom complex of morphological and functional angiographic signs [1, 7, 8]. Carotid angiography allows proper diagnostics of a carotid PG in 93.8% of cases [3].

Complete surgical excision of a carotid body tumor is the method of choice since the results of radiation and chemotherapy are not satisfactory [6, 9, 10].

The clinical case described is of interest for several reasons. First, it demonstrates the combination of a malignant extra-organic tumor of the neck area, in this case, a malignant paraganglioma, which accounts for only 0.8%, with differentiated thyroid cancer [1]. Secondly, in the complicated postoperative period, the patient experienced an *acute cerebrovascular event (ACE)*. *ACE often results in* the patient's disability, including permanent neurological disorders in 60% of patients; 20% of patients need constant care; about 35% die in the acute period of the disease [6, 7, 11]. In this case, the remission was achieved due to an adequately conducted combination therapy. Adequate rehabilitation helped the patient recover by 85%.

Patient's information: Patient A., year of birth 1982, appealed to the Center of Head and Neck Tumors of the Kazakh Institute of Oncology and Radiology (KazIOR) with a directional diagnosis of "thyroid cancer STI (T1N0M0), condition after surgical treatment, metastases to the lymph nodes of the neck on the right (?)" on 19.11.2018.

Clinical data:

Medical history: According to the patient, she was ill since 2015, when she detected a formation in the lower

third of the neck and got a feeling of discomfort in that area. In December 2017, she appealed to the Almaty Oncology Center (AOC), where they made a puncture from the formation of the thyroid gland. Cytological conclusion No. 18249-182-54: epithelial cells with severe hyperplasia. Observation in dynamics was recommended.

The formation was growing over time. The patient re-applied to the AOC, where she was further examined. Ultrasound of the thyroid gland as of 13.06.2018 showed two nodular formations of a cystic-solid nature sized 4.9x9.7 mm and 12.2x19.8 mm in the right lobe and two similar formations sized 8.4x15.9 mm and 11.8x15.5 mm in the left lobe. Surgical treatment was recommended.

On 21.06.2018, the patient underwent surgery at the AOC in the volume of "thyroidectomy, incisional biopsy of the tumor formation of the neck area on the right." The post-op histological conclusion No. 26929-55 of 30.06.2018: "1) a follicular adenoma is detected in the right lobe of the thyroid gland. 2) a follicular carcinoma with invasion into the capsule of formation is in the left lobe. IHC conclusion No. 604/18 as of 19.07.2018: «a minimally invasive variant of follicular carcinoma, G1 with the focus of invasion into the adjacent thyroid tissue in the left lobe of the thyroid gland. A follicular adenoma against the background of macro-microfollicular colloid goiter in the right lobe. Hyalinized fibrous tissue, no tumor elements were detected. Lymph nodes with reactive hyperplasia, no tumor elements detected."

The patient noted the progressive growth of the formation on the neck a month after surgery. The CT conclusion of 20.07.2018 (Figure 2): "On a series of CT scans in the projection of the submandibular region on the right, an additional formation is determined. It is sized 4.6x5.0x6.7 cm and has clear, uneven contours of an inhomogeneous structure due to areas of necrosis in the structure. This formation non-intensely accumulates contrast medium. The nearest vessels are pushed back; there is an invasion to the vessel wall of the common carotid artery (CCA), its branches. In the analysis of bone structures, lytic destruction of the corner of the lower jaw on the right is determined, sized 3.5 x 4.0 cm, with a tissue component in the structure, and perifocal infiltration (metastases)."

Figure 2 – Patient A., year of birth 1982: Head and neck CT of 20.07.2018.
 CT picture of the metastatic formation of the submandibular region on the right with the invasion of the wall of the common carotid artery

The conclusion of angiography of the aortic arch performed at the Mediterra Private Medical Center on 08.08.2018: "thoracic aorta and arch branches are without angiographic signs of damage. On the right: brachiocephalic trunk, CCA, subclavian artery, vertebral artery are patent. Multiple pathological branches depart from the ECC, leading to the formation of a rounded shape, with the accumulation of contrast medium in the venous phase and pronounced reflux into the external and internal jugular veins. Conclusion: angiographic signs of a chemodectoma are observed on the right."

The conclusion of angiography from the branches of the aortic arch on 10.09.2018 showed "the presence of a rounded hypervascular formation in the projection of the ECC of a rounded shape, with early venous reflux. The source is the afferent arteries of the ECC on the right. Then, X-ray endovascular occlusion of the glomus formation of the neck area on the right was performed using emboloid 500-700. Control angiography revealed a decrease in arteriovenous reflux to 90%, complete patency of the main arteries."

The postoperative period was uneventful.

The patient was referred to KazIOR for surgical treatment. The available coverglass preparations and units were reviewed at KazIOR. The conclusion of the revision of prepared preparations (27 pcs.) No. 26920-55/18: "There is a minimally invasive variant of follicular carcinoma, G1 (ICD – Ocode 8335/3) with foci of invasion into the adja-

cent thyroid tissue in the left lobe of the thyroid gland. There is a follicular adenoma in the right lobe of the thyroid gland. Hyalinized fibrous tissue, no tumor elements detected." The case was discussed at a meeting of a multidisciplinary group (MDG). Based on the CTs of the tumor invasion into the neck arteria walls and its branches, surgical treatment under the supervision of vascular surgeons was recommended.

The timeline for this clinical case is provided in Figure 3.

Diagnostics:

General condition at admission: "The patient's condition at admission – relatively satisfactory. Consciousness – clear. The position – active. The build – normal. Visible skin and mucous membranes – pale pink. Subcutaneous fat and muscle system developed evenly. Osteoarticular apparatus – without deformation. The chest is of the right shape. Vesicular breathing, no wheezing is heard in the lungs. The heart boundaries – normal. Heart tones – muffled, rhythmic. AT – 120/80 mm Hg, HR – 72 bpm. The abdomen – soft and painless at palpation. The liver and spleen – not enlarged. Kidney percussion – negative on both sides. Stool and diuresis – regular. Locally: the face is asymmetric due to a tumor formation in the projection of the lower jaw on the right, of a dense consistency, motionless, painful, 5.0 × 3.0 cm in size. In the upper back of the neck to the right, there is a tumor conglomerate of dense consistency of up to 7.0 cm in diameter."

Figure 3 – Timeline of medical care case

Tests at admission:

Before surgery, the patient underwent a duplex neck scan to assess the main vessels' condition and a CT of the neck to assess the process spread.

Series of CTs as of 26.10.2018 showed the condition after thyroid gland surgery: "In the soft tissues of the neck on the left, in the projection of the bifurcation of the CCA, an additional formation sized 6.7x5.3x4.9 cm is visualized. It has uneven, fairly clear contours and contacts the adjacent CCA with its wide base below and above the bifurcation. A pathological structural reconstruction of the alveolar bone and the branch of the lower jaw on the right is visualized. It is 3.8 cm long and has lytic destruction foci. The teeth roots are in the area of bone changes. There is a soft tissue component sized 3.6x3.3x2.7 cm, which extends to the zygomatic region. Single lymph nodes of the mental region on the right are enlarged up to 1.4 cm in diameter, the lymph nodes of the soft tissues of the neck on the left are enlarged up to 1.6 cm in diameter. This formation accumulates contrast intensively and inhomogeneously. In a limited area, the lumen of the CCA, ECA, and ICA passes through the thickness of the formation" (Figure 4).

The conclusion of BCA duplex scanning with color mapping, angio-spectral analysis of 21.11.2018: "ICA and ECA pass through the formation, stenotic compression by formation, budding of the ICA and ECA is possible."

Therapy: Conducted surgical treatment: Surgical treatment in the below volume was performed together with a vascular surgeon: "The removal of a neck tumor on the right with resection of the CCA, the lower jaw from the 4th teeth up to the right corner of the lower jaw." The surgical report of 22.11.2018: "Intraoperatively, during the examination, a tumor conglomerate was discovered on the right, in the middle and the upper third of the neck. It was sized 6.0 x 5.0 cm and wrapped around and invaded the CCA. The CCA was destroyed when trying to mobilize the tumor from the CCA and was fixed with a vascular clamp. Then, an attempt was made to mobilize the ICA (diameter – 0.3 mm), which was also wrapped around with the tumor. It was decided to resect the CCA and ICA. They were fixed with a vascular clamp and resected. The tumor was removed as a single unit. Later, the lower jaw fragment was removed in aseptic conditions. The lower jaw body was sewed with a Gigli saw in the projection of the

4th teeth on the right within the healthy tissue. The lower jaw body was exposed up to the right corner of the lower

jaw and removed as a single unit. Layered closure of the wound was conducted."

Figure 4 – Patient A., year of birth 1982: Head and neck CT of 26.10.2018. Homostructural solid formation of the neck on the right. A destructive process in the lower jaw on the right. Metastases (?)

On Day 1 after surgery, the patient developed acute brain stroke symptoms due to the CCA ligation. A series of brain MRIs of 23.11.2018 provided the images of the sub- and supratentorial brain divisions in the sagittal, axial, and coronary planes. The patients developed cytotoxic edema of the cortex and subcortical white matter of the right frontal, parietal and temporal lobes, with the limitation of diffusion to the DWI and hemorrhagic impregnation areas. The middle structures shifted to the left by 0.6 cm; the right lateral ventricle and the

third ventricle were compressed. The IV ventricle was unchanged. The corpus callosum was developed correctly. The Turkish saddle was of the usual form; the pituitary was homogeneous. The craniocervical transition was without abnormalities. The tonsils of the cerebellum were located above the Chamberlain line. Conclusion: MR showed a picture of acute ischemic infarction in the right cerebral hemisphere (pool of the right middle cerebral artery), with hemorrhagic impregnation. Condition after ligation of the right ICA (Figure 5).

Figure 5 – Patient A., year of birth 1982: MRI of the brain as of 23.11.2018. MR-picture of acute ischemic infarction in the right cerebral hemisphere (pool of the right middle cerebral artery), with hemorrhagic impregnation. Condition after ligation of the right internal carotid artery

A tracheostomy was performed on 23.11.2018 since the patient was administered the mechanical ventilation. The

thoracic organs condition was monitored. X-ray of 26.11.2018 showed hypostatic changes in the lungs (Figure 6).

Figure 6 – Patient A., year of birth 1982: Thoracic organs X-ray of 26.11.2018. Picture of hypostatic changes in the lungs

By the decision of the daily board of doctors, the patient remained in the intensive care unit from 23.11.2018 to 29.11.2018. MRI made to assess the brain condition showed positive dynamics. On 27.11.2018, MRI showed acute ischemic infarction in the right cerebral hemisphere, with hem-

orrhagic soaking and a positive tendency. No MTS in the brain observed (Figure 7).

Thoracic organs X-ray of 28.11.2018 showed hypostatic changes in the lungs, with a stable x-ray picture over time (Figure 8).

Figure 7 – Patient A., year of birth 1982: MRI of the brain as of 27.11.2018. MR picture of acute ischemic infarction in the right cerebral hemisphere, with hemorrhagic impregnation, with a tendency to positive dynamics.

Figure 8 – Patient A., year of birth 1982: Thoracic organs X-ray of 28.11.2018. Picture of hypostatic changes in the lungs. Stable X-ray picture over time

Due to a relatively positive dynamics (the reduction of bias of median structures up to 0.8 cm; previous data – 1.0 cm), the board of doctors decided to transfer the patient from the intensive care unit to a specialized department to continue antibiotic and antifungal therapy. The patient was activated. The postoperative wound in the submandibular region on the right was healed by primary intention. The patient was discharged after 18 days of stay in the Head and Neck Tumor Department of KazIOR in a satisfactory condition. The discharge diagnosis based on the postoperative histological conclusion No. 0.65997-07 of 22.11.2018: "Primary multiple metachronous cr: thyroid gland cr StI (T1N0M0). Condition after thyroidectomy. Malignant paraganglioma of the neck area on the right with the invasion of the lower jaw on the right StIII (T3N0M0). Condition after surgical treatment." Such a histological picture is observed when a malignant paraganglioma invades the lower jaw. A course of radiation therapy was recommended, given the postoperative histological conclusion.

Starting from 18.02.2019, the patient received external-beam radiotherapy on the lymph node region of the neck and the bed of the formation in the lower jaw, SBD 2 Gy, 5 fractions per week, to TBD 40 Gy. The outcome was satisfactory. The patient developed a standard radiation reaction, RTOG degree 1.

On a follow-up examination one year later, a series of CTs on 31.10.2019 have shown the condition after surgical treatment for thyroid gland cancer, after a combination treatment for malignant paraganglioma of the neck on the right. A formation sized 2.5×1.6×3.2 cm was detected in the soft tissues of the neck on the right against the background of moderately pronounced cicatricial changes, with clear even contours, increased density, without perifocal infiltration of adjacent tissues. There is a local accumulation of liquid sized 0.9 x 0.6 cm along the lower contour of the formation. No contrast accumulation detected. On the edge of the resection of the lower jaw alveolar bone, there is a visible tissue component sized 0.9 x 0.8 cm on the right, which intensely and homogenous-

ly accumulates the contrast medium. Conclusion: the formation of the soft tissues of the neck on the right. MTS lesion of the lower jaw alveolar bone on the right (Figure 9).

Figure 9 – Patient A., year of birth 1982: CT of the head and neck as of 31.10.2019.

The formation of the soft tissues of the neck on the right. MTS-lesion of the lower jaw alveolar bone on the right

Thoracic organs X-ray of 05.11.2019 showed no focal or infiltrative changes in the lungs (Figure 10).

The surgical report of 19.11.2019: "Removal of a recurrent tumor of the neck on the right with the ligation of the IJV on the right." The postoperative period was uneventful. Post-op histological conclusion No. O.060675-77 of 19.11.2019: "No tumor cells found in the surgical material." CT control at the follow-up examination on 04.02.2020: "Postoperative fibrotic changes in the soft tissue in the projection of the submandibular region on the right, without convincing CT signs of additional focal lesions at this level. Postoperative changes in the area of partial resection of the lower jaw on the right, without pronounced lytic destruction of the bone at this level. No signs of a relapse or MTS" (Figure 11).

Figure 10 – Patient A., year of birth 1982: Thoracic organs X-ray of 05.11.2019.

The absence of focal or infiltrative changes

Figure 11 – Patient A., year of birth 1982: Head and Neck CT of 04.02.2020:

No signs of a relapse or MTS

By the time of preparation of the article, the patient remained under the supervision of an oncologist and was undergoing rehabilitation.

Results and Discussion: The presented clinical case describes the treatment outcomes of multiple primary cancer and postoperative complications in the form of ACE. This clinical case demonstrates that conservative ACE therapy, including MRI-assisted control of cerebral ischemia, the thoracic organs X-ray, early activation of the patient, and the maintenance of stable homeostasis against adequate infusion therapy, allows achieving

a positive effect and the patient's recovery. The treatment tactics should be chosen individually, taking into account all the patient's features, the tumor localization, and possible postoperative complications. Up to date, we have achieved a stabilization of the primary process after the combination treatment. The patient is under dynamic supervision. She passes control examinations (head and neck CT, ultrasound of the thyroid gland) every six months, and undergoes rehabilitation to achieve complete recovery.

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