Case Report / Olgu Sunumu

Multiple primary malignant paraganglioma of the head and neck with lymph node metastasis

Lenf nodu metastazlı baş ve boynun çoklu primer malign paragangliyoması

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ABSTRACT

Paragangliomas of the head and neck are usually benign tumors. Malignant form is quite rare and criteria for malignancy are not clear. Clinical, biochemical and histological features of malignant forms are not sufficient to reliably distinguish them from benign tumors and malignancy is established only in the presence of distant metastasis. Herein, we report a patient with glomus jugulare on the right, glomus vagale and glomus caroticum tumors on the left side with cervical lymph node metastasis on the right side.

Keywords: Glomus caroticum; glomus jugulare; glomus vagale; malignant paraganglioma.

ÖZ

Baş ve boyun paragangliomaları genellikle benign tümörlerdir. Malign form son derece seyrek olup malignite kriterleri açık değildir. Malign formların klinik, biyokimyasal ve histolojik özellikleri onları benign formdan ayırt etmek için yeterli değildir ve malignite ancak uzak metastaz olduğunda saptanabilir. Bu yazıda sağ tarafta glomus jugulare, sol tarafta glomus vagale ve glomus karotikum tümörleri olup sağ tarafta boyun lenf nodu metastazı gösteren bir hasta sunuldu.

Anahtar Sözcükler: Glomus karotikum; glomus jugulare; glomus vagale; malign paraganglioma.

Paragangliomas of the head and neck are highly vascularized, locally invasive but usually benign tumors representing less than 0.5% of all head and neck tumors.[1,2] They originate from extra-adrenal neuro-endocrine cells distributed along the great vessels and nerves. Paragangliomas are mainly classified as sympathetic secretory (5%; predominantly thorax, abdomen pelvis) versus parasympathetic non-secretory (95%, predominantly head and neck) lesions.[1] Functioning tumors have clinical symptoms of paroxysmal hypertension, palpitation, headache, sweating due to secretion of catecholamines. Most of these are sporadic but they can also present as a part of familial syndrome. Bilateral or multifocal tumors are more frequent in syndromic forms. The malignant form is rare and corresponds to about 5-10% of head and neck paragangliomas. Small series or sporadic cases have been reported. Fifty-nine cases have

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been presented in a 10-year period collected by a national cancer data base study in the USA.[3] On the other hand, cellular criteria for malignancy are missing. Clinical, biochemical and histological features of malignant forms cannot be reliably distinguished from benign tumors and malignancy is established only in the presence of distant metastasis mainly to liver, lymph nodes, lung etc.[2-4] Metastatic growth is higher in extra-adrenal sympathetic paragangliomas than adrenal or parasympathetic paragangliomas.[5]

We report a patient with glomus jugulare on the right and glomus vagale and glomus caroticum tumors on the left side with cervical lymph node metastasis on the right side. Radiological investigation has ultimate importance in case of an uncommon clinical problem. The objective of this presentation is to review the literature on metastatic paraganglioma of the head and neck and to increase physician awareness of this rare condition outlining the follow-up and optimal management plan.

CASE REPORT

A 37-year-old female was admitted with the complaints of a mass on the left side of the neck, unilateral hearing loss, pulsatile tinnitus on the right ear, cough, hoarseness of voice, pharyngeal fullness and swallowing difficulty. Otoscopy revealed a normal eardrum on the left but a vascular mass in the right ear canal with purulent discharge. Audiometry demonstrated total hearing loss on the right ear. Physical examination of the neck demonstrated soft tissue at the carotid level on the left with some bruit and palpable thrill. Laryngoscopy showed right vocal cord paralysis. Twenty-four hour urinary metanephrine concentration was 671 μg/day (52-341 μg/day).

Tomography demonstrated glomus jugulare on the right, glomus vagale and glomus caroticum on the left and bilateral nodal metastasis (Figure 1a-c). Glomus jugulare was destroying the neighboring bony structures of the right temporal bone, filling the middle ear and external auditory canal, surrounding the carotid canal cranially and extending caudally to the neck through the jugular foramen with subdural extension. Internal and external carotid arteries of the left side were displaced with glomus caroticum at the carotid bifurcation. Tumor was surrounding both arteries. Glomus vagale tumor was located at the level of left jugular foramen enlarging the canal. T_1-weighed magnetic resonance imaging (MRI) with contrast enhancement at coronal cut demonstrated high signal intensity images on right temporal bone and at the level of carotid bifurcation and jugular foramen on the left side of the neck (Figure 2). Digital subtraction angiography confirmed glomus vagale and glomus caroticum on the left due to vascularity and localization of the masses (Figure 3). I-metaiodobenzylguanidine (MIBG) scintigraphy to demonstrate occult tumors revealed nothing particular other than three defined lesions.

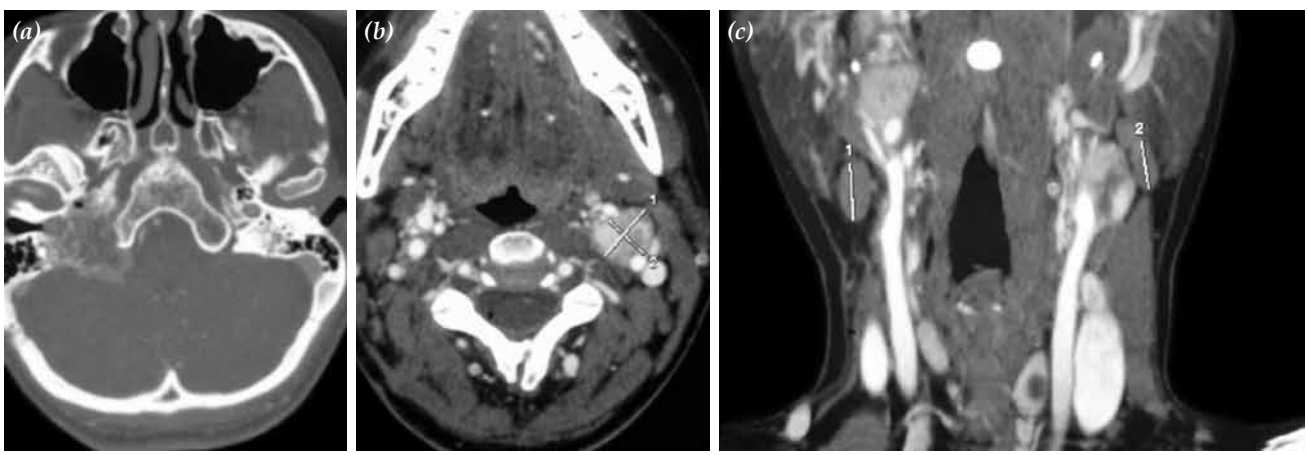

Figure 1. ***(a)*** *Glomus jugulare on the right side of the temporal bone, axial view.* ***(b)*** *Glomus caroticum located between carotid branches of the left common carotid (marked with line).* ***(c)*** *Coronal cut demonstrates glomus jugulare on the right, glomus caroticum on the left. Glomus vagale on the left side is superimposed by bony and vascular structures. Bilateral nodal metastasis is seen on both sides (marked with lines).*

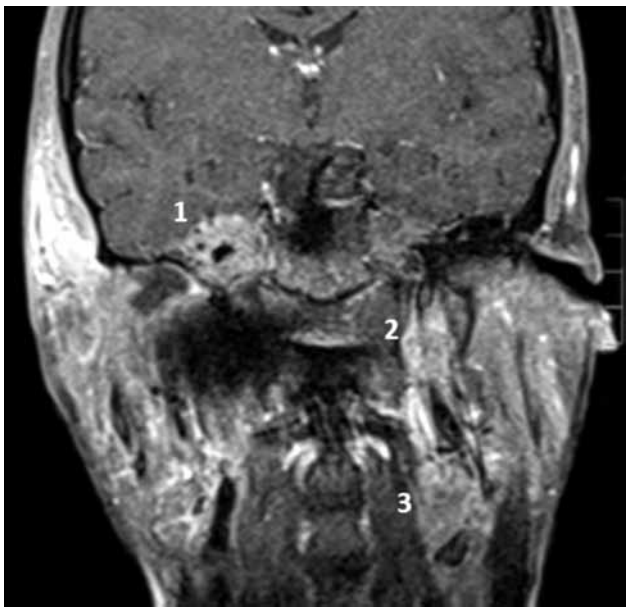

Figure 2. *T_1-weighed coronal magnetic resonance image with contrast enhancement. Glomus jugulare on the right is marked with (1), glomus vagale on the left is marked with (2) and glomus caroticum with (3).*

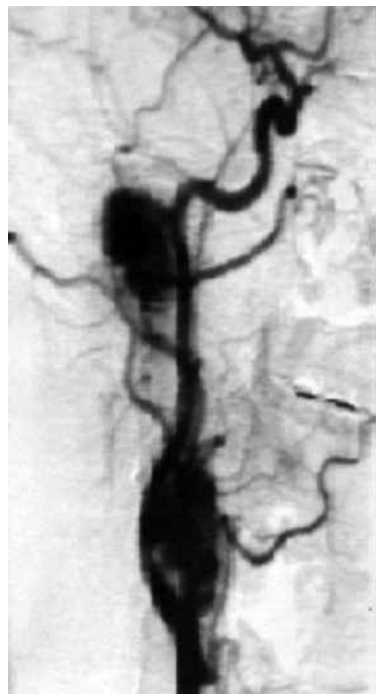

Figure 3. *Angiography revealed glomus vagale and glomus caroticum on the left side.*

The patient had subtotal removal of right glomus jugulare and removal of the lymph node via infratemporal fossa approach. Some part of the tumor in the posterior fossa was left behind due to extensive bleeding despite preoperative embolization. The patient had additional House-Brackmann (HB) grade-III facial paralysis due to facial re-routing; this recovered to HB grade-II in six months. Six months later, she had complete removal of glomus caroticum on the left. Pathology confirmed nodal metastasis (Figure 4a, b). Glomus vagale on the left was subjected to follow-up or radiotherapy if necessary due to previous vocal cord paralysis on the right side after glomus jugulare surgery. Currently, the patient has total hearing loss on the right with closed external auditory canal (cul-de-sac), vocal cord paralysis on the right (paramedian fixation), right facial paralysis (HB grade-II) and right glossopharyngeal paralysis. The patient will be followed with MRI every six months. Glomus remnant on the right and glomus vagale on the left are stable. She will be evaluated for radiotherapy if tumor re-growth is documented.

DISCUSSION

Paragangliomas are generally slow-growing painless benign tumors. Aggressive pattern of spread is seldom and is a subject of clinical discussion. The malignant type of the tumor can be defined when paraganglionic cells are found outside the original tumor bed with isolated growth in another tissue where neuro-endocrine cells are normally absent although cytological features of the primary and the metastatic tissues are identical.[5] No reliable studies including growth characteristics, cellularity, vascular invasion, mitotic figures, and necrosis are available to distinguish the benign from the malignant tumor. Some studies focus on immunohistochemical and molecular markers to analyze functioning malignant behavior of the tumor. High levels of catecholamines or their metabolites may be predictive of malignancy.[5,6] However, it is not sufficiently accurate to be considered diagnostic. Hereditary paraganglioma is inherited in an autosomal dominant manner. Paragangliomas in people with succinate dehydrogenase B (SDHB) gene mutation are more likely to become malignant than sporadic or succinate dehydrogenase C (SDHC) and succinate dehydrogenase D (SDHD) gene mutations.[3,7,8] However, penetrance for SDHB mutation is lower. Therefore some sporadic cases are likely to have SDHB gene. Klein et al.[8] have

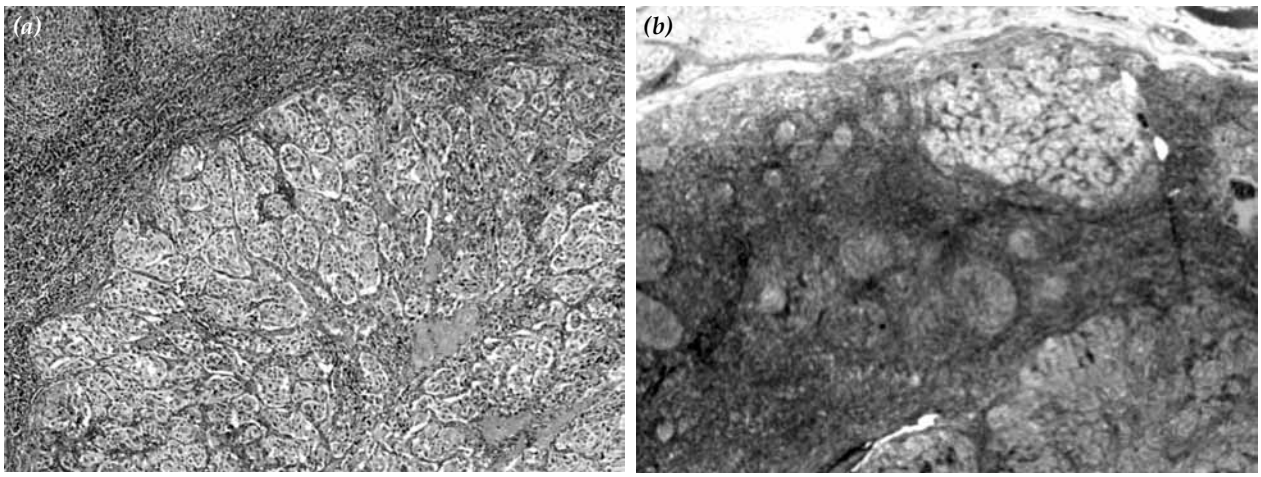

Figure 4. *Lymph node with paraganglioma metastasis [**(a)** H-E x 100, and **(b)** H-E x 50].*

pointed out SDHB gene mutation in patients with sporadic sympathetic or secretory tumors. SDHB gene mutation analysis should be performed for all patients with paraganglioma.

Imaging modalities widely used for detection of these tumors include computed tomography, MRI, ultrasound and angiography with varying sensitivity and specificity. Magnetic resonance imaging seems to be superior to tomography. Increased signal intensity on T_2-weighted images is characteristic, but not diagnostic.

Imaging can be replaced by immunohistochemical analysis if whole body screening is needed to investigate metastatic or multiple lesions. Functional imaging can be performed by using radiolabelled ligands. 18F-fluorodopamine positron emission tomography/computed tomography ([18F]-FDA PET-CT), 131I and 123I-metaiodobenzylguanidine (123I-MIBG), somatostatin receptor imaging with 111In-octreotide scintigraphy are useful tools to detect occult paraganglioma.[9]

The main therapeutic method for extra-adrenal sympathetic paragangliomas of the head and neck is surgery since they tend to metastasize even if the rate is low. Catecholamine excess has to be controlled prior to surgery by alpha and beta adrenergic blockade. Radiopharmaceutical treatment using I-MIBG (radiolabeled metaiodobenzylguanidine) as an adjunctive therapy to surgery either alone or in combination with chemotherapy has been successfully used in some patients.[10] Positive response or stabilization of the tumor growth after MIBG therapy has been reported especially in those patients with high I-MIBG or somatostatin analogue uptake.[11] Radiation therapy can also be used, but potential long-term risks include malignant transformation of the primary tumor. Surgery is the main therapeutic option. Non-surgical methods, especially in elderly individuals or those with clinically important comorbidities are preferable. Genetic counseling has great importance to understand malignant progression particularly in familial cases.[4]

Through analysis of the literature it appears that the metastatic paraganglioma of the neck is a rare clinical condition. Clinical awareness and application of different radiological tools confirm the diagnosis. These problems can have favorable prognosis if managed effectively. However, radiological and clinical follow-up for a long time is important due to their slow-growing pattern.

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