Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Malignant carotid body tumor: a report of two cases

Abdullah A. Alfawaz, MD[a,b,*], Dalia Albloushi, MD[b], Danah Quttaineh, MD[b], Salman Alsafran, MD[a,b], Omar AlQabandi, MD[c], Marzouq Albader, MD[b]

Introduction and importance: Carotid body tumors (CBT) are neoplasms that originate from chemoreceptors of the carotid body. They are neuroendocrine tumors that are usually benign but may have malignant potential. Malignancy is diagnosed with evidence of lymph node metastasis, distant metastasis, or disease recurrence. Multiple imaging modalities are used to diagnose CBTs and the treatment of choice is surgical excision. Radiotherapy is used for unresectable tumors. In this case, series we describe two cases of malignant paragangliomas that were diagnosed and operated on at a tertiary hospital in Kuwait, by the vascular team. Malignant CBTs are rare, documentation of the cases encountered and the subsequent management and outcome is important to give us a better understanding of the disease.

Case presentation: *Case one*– A 23-year-old woman presented with a right-sided neck mass. History, physical examination, and appropriate imaging suggested malignant paraganglioma with evidence of lymph node, vertebral, and lung metastases. Surgical excision of the tumor and regional lymph nodes was done. Histopathological assessment of the retrieved specimens confirmed the diagnosis. *Case two* – A 29-year-old woman presented with a left submandibular swelling. She was appropriately investigated, and the diagnosis of a malignant carotid body tumor was made with evidence of lymph node metastasis. Surgical resection of the tumor with clear margins was done and histopathological analysis of the resected specimen confirmed the diagnosis.

Clinical discussion: CBT's are the most common tumors of the head and neck. Most are nonfunctioning, slow growing, and benign. They typically present in the fifth decade of life but can occur at a younger age in individuals who carry certain genetic mutations. Both cases of malignant CBT's that we encountered occurred in young women. Furthermore, the 4-year and 7-year history in case number one and two, respectively, supports the fact that CBTs are slow growing tumors. In our case series, the tumors were surgically resected. Both cases were discussed in multidisciplinary meetings and were referred for hereditary testing and radiation oncology for further management.

Conclusion: Malignant carotid body tumors are rare. Prompt diagnosis and treatment is important to improve patient outcomes.

Keywords: carotid body tumor, case series, chemodectoma, malignant, paraganglioma

Introduction and importance

Carotid body tumors (CBT) are neoplasms originating from chemoreceptors of the carotid body[1]. Paragangliomas, also known as Chemodectomas[1]. They are rare extra-adrenal neuroendocrine tumors that can present at any age; however, the incidence is highest in the fifth decade of life[2]. They usually present at a younger age in familial cases[3].

HIGHLIGHTS

- Carotid body tumors are neoplasms originating from the chemoreceptors of the carotid body.
- They are neuroendocrine tumors; that are mostly benign; however, they can be malignant.
- Local and distant metastasis can occur.
- Surgical resection of the carotid body tumors is the treatment of choice with or without adjuvant radiotherapy.

They are usually benign, but they have malignant potential[1]. Malignant disease makes up 4–10% of all CBTs[4,5]. They vary in presentation and there may be no correlation between clinical presentation and histopathological findings[1]. They usually present as a painless, gradually enlarging neck mass[1]. May also present with vagal, hypoglossal, glossopharyngeal, and recurrent laryngeal nerve neuropathy in larger tumors[6–8]. A functional CBT may result in catecholamine related symptoms such as palpitations, headaches, hypertension, tachycardia, and flushing[9,10]. Carotid vessel invasion can result in stenosis, occlusion, and rupture[11]. Malignant disease is usually diagnosed with lymph node metastasis, distant metastasis, or by disease recurrence[1]. There are no histopathological and immunohistochemical features of the primary CBT that may indicate malignancy[4,12–14]. It most commonly metastasizes loco-regionally to regional lymph nodes, distant metastasis usually occurs in the liver

[a]Department of Surgery, Kuwait University, [b]Mubarak Al Kabeer Hospital and [c]Ministry of Health, Kuwait

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Surgery, Faculty of Medicine, Kuwait University. P. O. Box 24923, Safat 13110 – Jabriya, Kuwait. Tel: +965-24636218, E-mail: Abdullah.alfawaz@hsc.edu.kw (A. A. Alfawaz).

Annals of Medicine & Surgery (2023) 85:1857–1862

Received 10 September 2022; Accepted 12 February 2023

Published online 11 April 2023

http://dx.doi.org/10.1097/MS9.0000000000000402

and lungs[15,16]. Sympathetic paragangliomas are more likely to be malignant (15–23%) when compared to parasympathetic paragangliomas[17].

Preoperative work-up of a patient with a suspected CBT includes clinical history, physical examination, and MRI[18]. Radionuclide studies can be used to determine metastatic disease[2]. Angiographic embolization of blood vessels can be performed to decrease intraoperative blood loss[2]. The Shamblin classification is used to determine the resectability of the CBTs and surgical outcomes, and it is based on the relationship of the tumor to the adjacent carotid artery[9]. A biopsy of the tumor is contraindicated as it carries the risk of massive hemorrhage, thrombosis, pseudoaneurysm formation, and dissemination[19,20]. Surgical resection of the CBT is the treatment of choice with or without adjuvant radiotherapy[21]. Lymph node sampling should be performed during primary resection[22]. Radiotherapy is the treatment of choice for unresectable tumors[1].

Malignant CBT's are rare, documentation of the cases encountered and the subsequent management and outcome is important to give us a better understanding of the disease.

Method

Our report on the two cases of malignant CBT's is a retrospective study. Data was collected retrospectively from patient files. This case report has been reported in line with the Surgical CAse REport (SCARE) 2020 Criteria[23].

Case one

A 23-year-old woman, known case of epilepsy and diabetes mellitus. The patient did not have a past medical or surgical history, a nonsignificant family history, and not known to have any drug allergies. She initially presented to a tertiary care center with a 4-year history of a progressively enlarging right-sided neck swelling. The swelling was not associated with any other symptoms. Her vital signs were within normal limits. On examination of the neck, a right-sided neck swelling around 3 cm in diameter was noted at the anterior triangle of the neck. The mass was round, with a smooth surface, compressible, and had a positive Fontaine sign. A pulse was noted adjacent to the mass. Laboratory investigations revealed no abnormality.

A carotid doppler was done, which revealed a large heterogeneous mass, 3.39×3.76 cm in size, with some vascularity within its core. The internal carotid artery and the external carotid artery were completely encased by the tumor. The findings were highly suggestive of a carotid body tumor (chemodectoma) Shamblin type III.

A computed tomography angiography was performed, which showed a heterogeneous lesion at the right carotid sheath space, measuring $3.2 \times 3.7 \times 4.6$ cm, displacing and compressing the internal jugular vein laterally, and splaying the internal carotid artery, and the external carotid artery. The mass was encasing the internal carotid artery for more than 270 degrees. Those findings are suggestive of a carotid body tumor type III according to the Shamblin classification. Multiple bilateral cervical and submandibular lymph nodes were noted. (Fig. 1).

MRA was conducted displaying a well-defined lobulated mass with prominent vascular channels, measuring $5.5 \times 3.5 \times 3.8$ cm. The mass was splaying the right internal and external carotid arteries and the internal jugular vein, causing vascular compromise. The study also demonstrated bilateral prominent lymph nodes throughout the deep cervical chain. (Fig. 2).

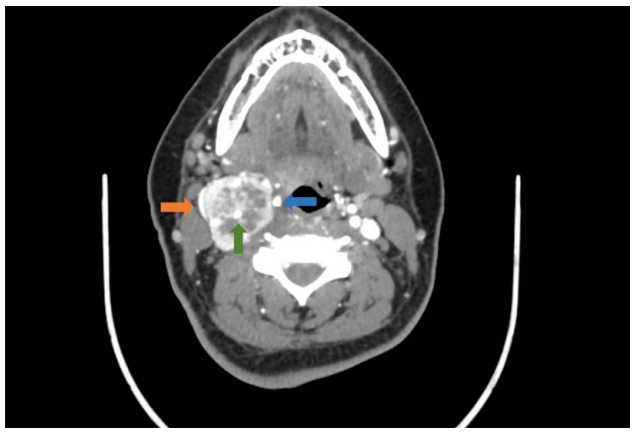

Figure 1. CT imaging showing a heterogeneous lesion at the right carotid sheath space. Orange arrow: carotid body tumor, green arrow: internal carotid artery, and blue arrow: external carotid artery.

A preoperative vocal cord assessment was done and revealed bilateral vocal cord movement.

The tumor was successfully excised by an experienced vascular surgical team, and repair of the right internal carotid artery was done with a reversed long saphenous vein bypass graft. An interposition graft with saphenous vein was performed, using a nonreversed saphenous vein graft after valve lysis. This was done to ensure no size discrepancy at the anastomosis. Additionally, lymph node sampling was also done. The excised specimens were sent for histopathological analysis. The patient had an uneventful postoperative course and was discharged on antiplatelet therapy. (Figs. 3, 4).

Histopathology later revealed carotid body malignant paraganglioma, 2/4 lymph nodes were positive. Mitosis is rare, 2/10 HPF. Immunohistochemical analysis revealed tumor cells that were positive for chromogranin, synaptophysin, and S100 stains in sustentacular cells. Ki67 (proliferation index was 18%). Her case was discussed at a multidisciplinary team meeting, and the patient was referred to radiation oncology for further management. She was referred to the hereditary cancer clinic to undergo genetic testing, which was negative for any known mutations.

Case two

A 29-year-old female patient, previously healthy, no past medical or surgical history, a nonsignificant family history, and not known to have any drug allergies, presented with a 7-year history of a left submandibular swelling, which was progressively increasing in size. There was no associated pain, shortness of breath, dysphagia, hoarseness, and overlying skin changes. The patient also denied any episodes of loss of consciousness or palpitations. On examination, the patient's vitals were within normal limits, there was a 4×6 cm fine immobile left submandibular mass. There was a positive Fontaine sign. The patient was initially worked up in a tertiary otolaryngology, head and neck hospital, where she was diagnosed with a carotid body tumor and was referred to our vascular service.

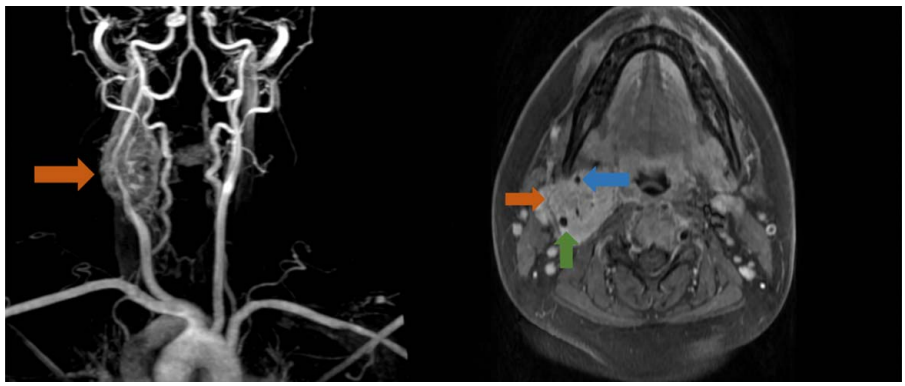

Figure 2. MRA imaging of the CBT. Orange arrow: carotid body tumor, green arrow: internal carotid artery, and blue arrow: external carotid artery.

Laboratory investigations demonstrated no abnormalities. A duplex ultrasound scan showed a large heterogeneous mass on the left side of the neck, measuring 7.10 × 3.63 cm with increased vascularity within its core. Both the internal and external carotid arteries were completely encased by the mass. No abnormalities were detected on the right side. MRI and MRA was performed. It revealed a left-sided carotid body paraganglioma with splaying of the carotid vessels. Preoperatively, the patient underwent vocal cord assessment, which revealed left vocal cord weakness.

The patient underwent excision of the carotid body tumor by the vascular surgical team. An oblique incision was made along the anterior border of the sternocleidomastoid, exposing the common carotid and obtained proximal control. Intraoperative findings revealed a tumor arising from the Vagus nerve, encasing the common, internal, and external carotid arteries, and invading the internal jugular vein. The hypoglossal nerve was identified and preserved, the internal jugular vein was then divided and ligated both proximally and distally. Distal control of the distal internal carotid just below the skull base was then performed after several maneuvers to facilitate the exposure (subluxation of the mandible, nasotracheal intubation, division of the digastric muscle, and mobilization of the hypoglossal nerve). The tumor was resected en bloc with the inseparable carotid bifurcation successfully. The decision to revascularize was then made based on ICA backpressure quality and measurements. Internal carotid back bleeding was pulsatile. The common carotid was ligated as well as all the external branches of the carotid artery. Lastly, hemostasis was adequate, a drain was placed, and the wound was closed in layers. The Postoperative course was uneventful, and the patient was discharged home.

Histopathology later revealed carotid body malignant paraganglioma, 2/13 lymph nodes were positive. Mitosis is rare, 1-2/10 HPF. Immunohistochemical analysis revealed tumor cells that were positive for chromogranin, synaptophysin, and S100 stains in sustentacular cells. Ki67 (proliferation index was 3%). The patient was referred to radiation oncology for further management. She was referred to the hereditary cancer clinic to undergo genetic testing, which was negative for any known mutations.

The CBT's encountered were nonfunctional. Preoperative stenting or embolization was not required in both cases. Patients were seen at the outpatients department after discharge, they were both doing well, there were no postoperative residual deficits. They furthermore continued their follow-up at the Kuwait Cancer Control Center for further treatment.

Discussion

Paragangliomas are rare extra-adrenal neuroendocrine tumors. There are two types of paragangliomas, sympathetic and

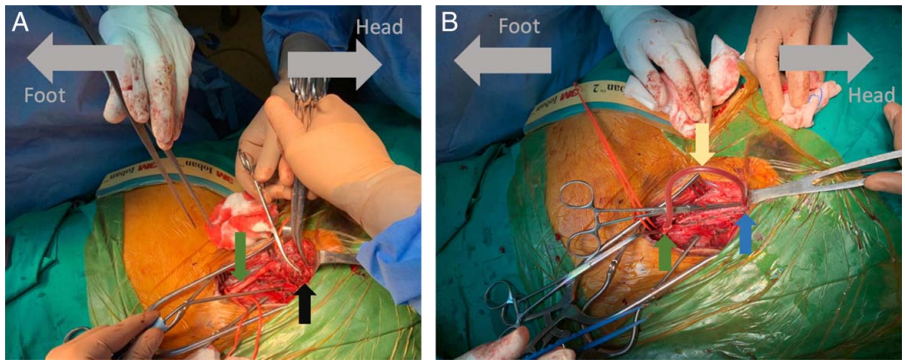

Figure 3. Intraoperative findings. A: Green arrow: common carotid artery, black arrow: carotid body tumor. B: Green arrow: common carotid artery, yellow arrow: shunt, and blue arrow: internal carotid artery.

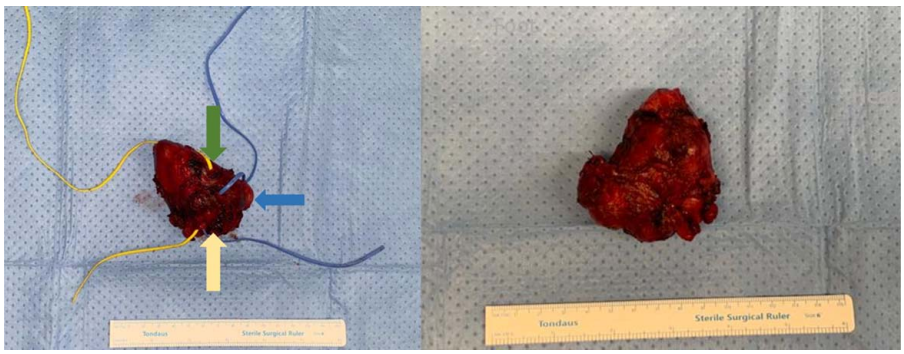

Figure 4. CBT after excision. Green arrow: internal carotid artery, blue arrow: external carotid artery, and yellow arrow: common carotid artery.

parasympathetic paragangliomas. Sympathetic paragangliomas arise from the sympathetic nervous system. These are chromaffin tumors, which are usually functional, and 15–23% are metastatic[3,10,12]. In contrast, tumors arising from the paraganglia of the head and neck are parasympathetic paragangliomas[13,24], these are nonfunctional and are rarely malignant[17]. Carotid paragangliomas, also known as CBT, are the most common tumors of the head and neck, comprising ~60% of them[1]. Most of these tumors are nonfunctioning, slow growing, and benign. Despite that, literature suggests that 5–10% of those tumors are malignant in nature[25]. These tumors can occur at any age with an equal division between the two genders. However, the literature suggests that it most commonly presents in the fifth decade[2,21]. Presentation at a younger age can occur in individuals that carry genetic mutations in the succinate dehydrogenase subunit B gene (SDHB) or succinate dehydrogenase subunit D gene (SDHD)[3]. SDHB mutations are associated with malignant paragangliomas of the head and neck[26]. It typically presents with a painless and slow growing mass on the neck[18]. As reported by Zhang *et al.*[27], the average duration of growth is 6.4 years. In order to make a proper diagnosis, history, clinical examination, appropriate imaging, and histopathology findings are imperative[17]. It is important to note that a biopsy of the mass is contra-indicated as it is associated with risks such as hemorrhage and fibrosis[1]. In both cases of malignant CBT's we encountered occurred in young women, genetic testing was offered to identify genetic mutations that may have played a role in the development of the tumor. Furthermore, the 4-year and 7-year history in case number one and two, respectively, supports the fact that CBTs are slow growing tumors.

Malignancy of the CBT is confirmed by pathological findings in lymph nodes or other distant organs such as the liver or lungs, as opposed to histological findings of the primary tumor[13,25] or disease recurrence[1]. There are no reliable histopathological findings to make the diagnosis of malignancy[25]. However, some studies reported that those histopathological findings that can raise the suspicion of malignancy include: central necrosis of clusters, invasion of vascular space, and mitosis[28]. Poor prognosis is associated with malignant CBT, in particular those presenting with distant metastasis, with a 11.8% survival chance at 5 years[16,29]. There was evidence of lymph node metastasis in both cases, which was initially suspected in the imaging and confirmed postoperatively with histological analysis of the retrieved specimens. In case number one there was evidence of distant metastasis, which was evident on nuclear imaging.

Investigations that are used to confirm the diagnosis of CBT include arteriography, duplex ultrasound scan, computed tomography angiography (CTA), MRI, and MRA. Arteriography is the gold-standard, however, nowadays it is reserved for larger CBT's[30]. A color flow duplex ultrasound scan is very specific and sensitive, demonstrating a well-defined hypoechoic mass that splays at the carotid bifurcation. CTA is used to determine the size of the tumor and the relationship it has to bony landmarks. This is useful for operative planning. MRI and MRA are used to establish possible vascular involvement, as well as the attachment of the tumor to surrounding structures. Lastly, full body scans and radionuclide studies are performed to determine the presence of distant metastasis[30]. Duplex ultrasound scan, CTA, MRI, MRA, and PET scans were used to confirm the diagnosis and assist in operative planning in both cases.

In 1971 a classification system was introduced by the Shamblin research group, which is based on the size of the tumor and carotid artery involvement. It is mainly used to assess and establish the risk of cranial nerve injury and intraoperative blood loss, as well as help determine the possibility of carotid artery resection and reconstruction[7]. Shamblin Type I tumors are small lesions located at the carotid bifurcation; their excision is usually done without difficulty. Shamblin Type II tumors tend to be larger in size and splay the carotid bifurcation, however, these tumors do not encase the carotid arteries. The last classification is the Shamblin Type III, which includes large tumors that encase the vessels, and their excision tends to be associated with difficulty and a greater degree of intraoperative neurovascular compromise. Both cases had large tumors, encasing the vessels and were Shamblin type III.

Surgical resection of the CBT is recommended. However, due to the rarity of the CBT, treatment protocols are not well-defined[29]. Preoperative angiography embolization is occasionally used, to prevent massive blood loss. In those that are considered inoperable or have had incomplete resection, radiotherapy is the management of choice[1,12] Common complications associated with surgical intervention include: Horner's syndrome, hoarse voice, glossal deviation, and upper limb weakness[27,31]. In our case series, the tumors were surgically resected. Both cases were discussed in multidisciplinary meetings and were referred to hereditary testing and radiation oncology for further management.

Limitations

Disease recurrence and prognosis could not be determined as of yet, as limited time has lapsed since the diagnosis was made and patients were appropriately treated.

Conclusion

CBTs are rare neuroendocrine tumors that arise from the chemoreceptors of the carotid body. They are usually benign but have malignant potential. They are often diagnosed at a later stage of the disease with symptoms arising secondary to the mass effect or distant metastasis. Early diagnosis and an appropriate work-up allows for prompt treatment and better outcomes.

Ethical approval

Ethical approval was not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

None.

Author contribution

Dr Alfawaz has full access to the data used in the following study and takes full responsibility for the integrity and accuracy of the data. A.A. and S.A.: concept and design; D.A. and D. Q.: drafting of the manuscript; D.A.: imaging analysis. Critical revision of the manuscript for intellectual content is done by all authors. A.A.: supervision.

Conflicts of interest disclosure

All authors declare no conflict of interest.

Research registration unique identifying number (UIN)

1. Name of Registry: Research Registry.
2. Unique Identifying Number of Registration ID: research registry 8262.
3. Hyperlink to your specific registration: https://www.researchregistry.com/browse-the-registry#home/registrationdetails/6314dfdec4a4990021897a3d/

Guarantor

Abdullah A. Alfawaz, Department of Surgery, Faculty of Medicine, Kuwait University. P. O. Box 24923, Safat 13110 – Jabriya, Kuwait. E-mail: Abdullah.alfawaz@hsc.edu.kw

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Nishijima H, Asakage T, Sugasawa M. Malignant carotid body tumor with systemic metastases. Ann Otol, Rhinol Laryngol 2011;120:381–5.
[2] Jeevan DS, Saleh M, LaBagnara M, *et al*. Malignant carotid body tumor presenting with myelopathy: case report. J Neurosurg Spine 2016;24:660–3.
[3] Havekes B, Corssmit EP, Jansen JC, *et al*. Malignant paragangliomas associated with mutations in the succinate dehydrogenase D gene. J Clin Endocrinol Metabol 2007;92:1245–8.
[4] da Silva AD, O'Donnell S, Gillespie D, *et al*. Malignant carotid body tumor: a case report. J Vascular Surg 2000;32:821–3.
[5] Sajid MS, Hamilton G, Baker DM. A multicenter review of carotid body tumour management. Europ J Vascular Endovascular Surg 2007;34:127–30.
[6] Shamblin WR, ReMine WH, Sheps SG, *et al*. Carotid body tumor (chemodectoma): clinicopathologic analysis of ninety cases. Am J Surg, 1221971:732–73.
[7] Knight TT Jr, Gonzalez JA, Rary JM, *et al*. Current concepts for the surgical management of carotid body tumor. Am J Surgery 2006;191:104–10.
[8] Frijns JH, van Dulken H, van der Mey AG, *et al*. Does intervention improve the natural course of glomus tumors? A series of 108 patients seen in a 32-year period. Ann Otol, Rhinol Laryngol 1992;101:635–42.
[9] Davis FM, Obi A, Osborne N. Carotid Body Tumors. In: Hans S, editor. Extracranial Carotid and Vertebral Artery Disease. Springer; 2018:253–260.
[10] Albsoul NM, Alsmady MM, Al-Aardah MI, *et al*. Carotid body paraganglioma management and outcome. Eur J Sci Res 2009;37:567–74.
[11] Plukker JTM, Brongers EP, Vermey A, *et al*. Outcome of surgical treatment for carotid body paraganglioma. Br J Surg 2001;88:1382–6.
[12] Dinges S, Budach V, Stuschke M, *et al*. Malignant paragangliomas–the results of radiotherapy in 6 patients. Strahlenther Onkol 1993;169:114–20.
[13] Romanski R. Chemodectoma (non-chromaffinic paraganglioma) of the carotid body with distant metastases: with illustrative case. Am J Pathol 1954;30:1.
[14] Lv H, Chen X, Zhou S, *et al*. Imaging findings of malignant bilateral carotid body tumors: a case report and review of the literature. Oncol Letters 2016;11:2457–62.
[15] Moskovic DJ, Smolarz JR, Stanley D, *et al*. Malignant head and neck paragangliomas: is there an optimal treatment strategy? Head Neck Oncol 2010;2:1–8.
[16] Lee JH, Barich F, Karnell LH, *et al*. American College of Surgeons Commission on Cancer and the American Cancer Society. National Cancer Data Base report on malignant paragangliomas of the head and neck. Cancer 2002;94:730–7.
[17] Plouin PF, Gimenez-Roqueplo AP. Pheochromocytomas and secreting paragangliomas. Orphanet J Rare Dis 2006;1:1–7.
[18] Pellitteri PK, Rinaldo A, Myssiorek D, *et al*. Paragangliomas of the head and neck. Oral Oncol 2004;40:563–75.
[19] Chengazi HU, Bhatt AA. Pathology of the carotid space. Insights Imaging 2019;10:1–6.
[20] Muduroglu A, Yuksel A. Carotid body tumors: a report of three cases and current.
[21] Williamson J, Leopold G, Prabhu V, *et al*. Successful treatment of a rare metastatic malignant carotid body tumour in a young adult, with conservative surgery and local radiotherapy. J Laryngol Otol 2012;126:428–31.
[22] Carroll W, Stenson K, Stringer S. Malignant carotid body tumor. Head Neck 2004;26:301–6.
[23] Agha RA, Franchi T, Sohrabi C, *et al*. for the SCARE Group. The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84:226–30.
[24] Branham GH, Gnepp DR, O'McMenomey S, *et al*. Malignant paraganglioma—a case report and literature review. Otolaryngol Head Neck Surg 1989;101:99–103.

[25] Zbären P, Lehmann W. Frequency and sites of distant metastases in head and neck squamous cell carcinoma. An analysis of 101 cases at autopsy. Arch Otolaryngol Head Neck Surg 1987;113: 762–4.
[26] Boedeker CC, Neumann HPH, Maier W, *et al*. Malignant head and neck paragangliomas in SDHB mutation carriers. Otolaryngol Head Neck Surg 2007;137:126–9.
[27] Zhang WC, Cheng JP, Li Q, *et al*. Clinical and pathological analysis of malignant carotid body tumour: a report of nine cases. Acta Otolaryngol 2009;129:1320–5.
[28] Lack EE, Cubilla AL, Woodruff JM. Paragangliomas of the head and neck region. A pathologic study of tumors from 71 patients. Hum Pathol 1979;10:191–218.
[29] Pacheco-Ojeda L. Malignant carotid body tumors: report of three cases. Ann Otol Rhinol Laryngol 2001;110:36–40.
[30] Gu G, Wang Y, Liu B, *et al*. Distinct features of malignant carotid body tumors and surgical techniques for challengeable lesions: a case series of 11 patients. Eur Archives Oto-Rhino-Laryngol 2019;277:853–61.
[31] Kim GY, Lawrence PF, Moridzadeh RS, *et al*. New predictors of complications in carotid body tumor resection. J Vasc Surg 2017;65:1673–9.