



Feline malignant lymphoma in an uncommon location as a differential diagnosis for neurological disease

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Abstract

Case summary A 12-year-old male castrated domestic shorthair cat exhibited right Horner's syndrome, right facial nerve paresis, difficulty swallowing, coughing, gait abnormalities and weight loss. Despite prior unspecific treatment by a primary care veterinarian with cortisone and antibiotics, the cat's condition worsened, culminating in tetraparesis and right hemispasms. Imaging studies, including CT and MRI, identified a mass extending from the carotid body into the neurocranium, causing displacement of adjacent brain structures and meningeal contrast uptake. Histopathology confirmed a malignant B-cell lymphoma. Differential diagnoses are explored, with a particular focus on carotid body tumours, which originate from the chief cells of the carotid body. These neoplasias are rare in non-human primates, dogs, cats and horses, possibly influenced by genetic predisposition and environmental factors such as hypoxia.

Relevance and novel information Carotid body tumours are rare in cats, as they are in other animal species. Although lymphomas are the most common feline neoplasms, to our knowledge, no previous case of a B-cell lymphoma in the carotid body has been described in the feline species to date. This case underscores the importance of considering rare and common neoplastic entities in feline patients with atypical clinical presentations and locations. Thereby highlighting the diagnostic challenges in veterinary oncology.

Keywords: Lymphoma; glomus caroticum; paraganglioma; chemodectoma

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Introduction

Lymphoma is a common neoplasm and the most common haemopoietic neoplasm in cats.¹ Lymphomas mainly arise from lymph nodes but can have their origins in a variety of other organs.² Their anatomical location is one basis for classification. The main locations of lymphoma include the multicentric, thymic/mediastinal, gastrointestinal, cutaneous, extranodal and central nervous system (CNS). This classification does not include lymphomas in uncommon locations, such as the carotid body.³ Of all lymphomas, approximately 13% are located in the CNS, mostly as part of a multisystemic neoplastic disease.⁴

In addition, lymphoid neoplasms are classified based on their ultrastructural morphology and their cellular origin, which is confirmed through immunohistochemical staining⁵ or through antigen aberrancies in flow

cytometry.^{6,7} These tools are essential for the explicit diagnosis of lymphomas, as a large number of subtypes play a role in this group, which are morphologically uniform but phenotypically different. Lymphomas can be differentiated between B-cell and T-cell, and there are other uncommon aberrant phenotypes.² In dogs, 60–70%

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of lymphomas are of B-cell origin; however, in cats, enteric T-cell lymphomas make up approximately 50% of all feline lymphomas since the vaccination for feline leukaemia virus (FeLV) is broadly available.⁸

The most established markers are CD3 for the detection of T cells and CD79a for the detection of B cells. CD20 and Pax-5⁹ can be used as further markers for the detection of B cells in cats. However, markers based on B220, a B-cell specific member of the T200 glycoprotein family, have also been established as B-cell specific markers.² These are used in CD45R antibodies.¹⁰ Other antibodies that can be used to further classify lymphomas, for example, are CD11b, CD11c, CD14, CD21 and CD34.²

The glomus caroticum, also known as the carotid body or paraganglion intercaroticum, is located at the bifurcation of the common carotid artery. It is approximately 1.5mm long, 1mm wide and 0.5mm thick. On cross section, it is spindle-shaped or triangular.¹¹ Neoplastic diseases of the carotid body are rare, but the aortic and carotid bodies are the most common sites of paragangliomas in dogs^{12,13} and cats.¹⁴ However, they have been described in the glomus pulmonale,¹⁵ in the adrenal gland¹⁶ and in the jugulotympanic paraganglia¹⁷ of dogs. In cats, chemodectomas are reported in the carotid body,¹⁸ in the aortic body,^{14,19–26} in the vena cava,²⁷ in the cauda equina²⁸ and, recently, in the glomus pulmonale²⁴ and in the orbita.²⁹ Metastases occur in approximately 3.3% of carotid body tumours³ and have been found in the lung,²⁸ myocardium, pericardium, cranial mediastinal lymph nodes,¹⁹ diaphragm and intercostal muscles of cats.³⁰

Immunostaining has been established for the detection of paragangliomas in humans. One study showed that S-100 protein is present in all carotid body tumours. In addition, most tumours also exhibit neuron-specific enolase (NSE), chromogranin A (CHA), serotonin (SER) and synaptophysin (SYN).^{31,32} In a feline aortic body tumour, the cells were immunohistochemically positive for CHA, for SYN and, faintly, for NSE, and negative for vimentin, cytokeratin, a smooth muscle actin, glial fibrillary acidic protein, thyroglobulin and calcitonin.²⁰

Case description

A 12-year-old male castrated domestic shorthair cat was admitted to the referral clinic with tetraparesis and right hemifacial spasms. The owner stated a 1-week history of right Horner's syndrome, right facial nerve paresis, constant swallowing, coughing and dysphonia. Gait was abnormal with stumbling on the right hindlimb and the cat was not able to open its jaw to the maximum, noticed by the inability to take in larger pieces of food and the absence of yawning. Pretreatment administered 1 week before presentation in the referral clinic by a primary care veterinarian consisted of cortisone and an unknown systemic antibiotic. Owing to a lack of improvement, the cat was admitted to the clinic 2 weeks after the first evident clinical signs.

On physical examination, the cat presented as apathetic and in lateral recumbency. The cat showed generalised muscle wastage and a reduced body condition score of 2/9. The cat presented with an inability to open its mouth completely. During palpation of the throat, the cat swallowed multiple times and showed discomfort.

On neurological examination, the cat showed an inability to stand and walk, while motor function was preserved. Postural and positional reactions as well as proprioception was reduced on all limbs. Spinal reflexes were moderately excessive on the left forelimb and hindlimb. During evaluation of the cranial nerves, the cat showed normal visual functions, anisocoria with a miosis on the right, right enophthalmos, resulting in prolapse of the nictitating membrane, consistent with the preliminary report of a right Horner's syndrome. Neuroanatomical location was suspected to be the cervical cord (C1-5) and/or the brainstem. Haematology and a biochemical analysis were unremarkable, as were paired radiographs of the thorax.

MRI was performed and showed a space-occupying mass reaching from the carotid angle to the tympano-occipital fissure (Figure 1). The fissure was mildly dilated and the bone of the skull base showed low-grade sclerosis. The mass entered the neurocranium via the fissure. Within the neurocranium, a poorly circumscribed large

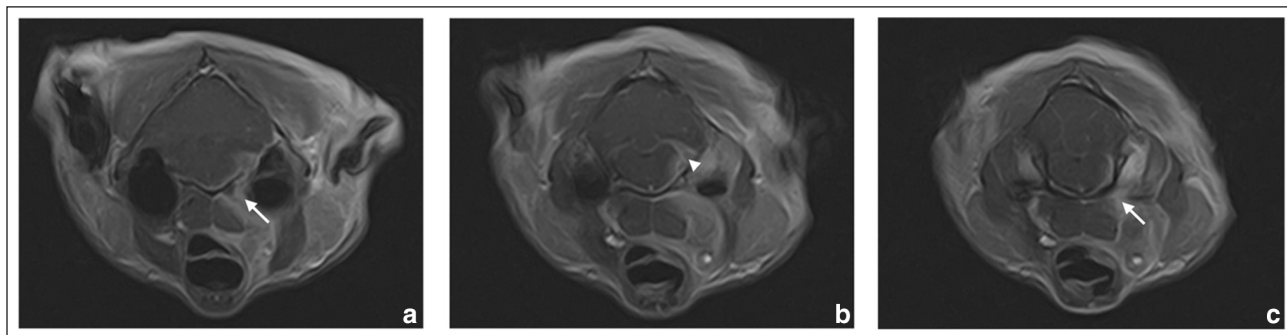


Figure 1 Set of MRI scans of the head. Starting from the region of the right medial retropharyngeal lymph node and carotid angle ([a,c] arrows), a space-occupying mass is visible, which extends towards the tympano-occipital fissure ([b] arrowhead)

mass with a diameter of approximately 4 mm was seen around the cerebellopontine angle, displacing the adjacent portions of the brainstem and cerebellum. There was a high degree of contrast enhancement in the intra- and extracranial regions of the mass and along the meningeal surface of the brainstem extending rostrally to the hypophyseal fossa. The meningeal contrast uptake was visible mainly on the right side, where it extended to the level of the flocculus. There was a high degree of contrast enhancement within the internal acoustic meatus along the facial nerve and vestibulocochlear nerve.

MRI findings suggested a neoplasia in the carotid body extending to the neurocranium. Owing to the poor prognosis and at the owner's request, the cat was humanely euthanased.

A full post-mortem examination was performed and in the region of the carotid angle, a $2 \times 1.5 \times 0.5$ mm large firm mass with a homogeneously pale pink and round cross section was detected (Figure 2). The bulla and its surrounding tissue did not reveal any macroscopic changes. Other organs and lymphoid tissue were unaffected.

Histologically, an infiltration with a high number of monomorphic round cells in the carotid body with addi-

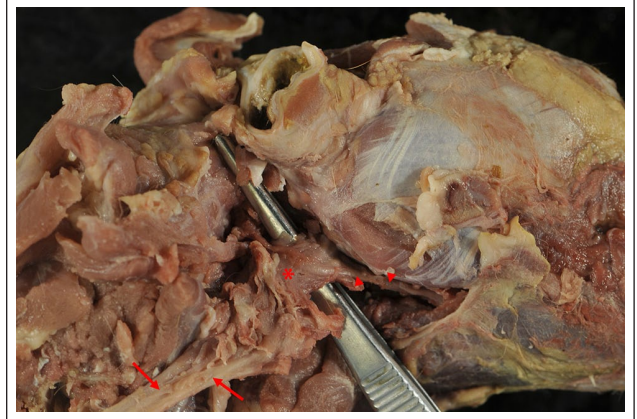


Figure 2 Right lateral view of the cranial neck and head. The mass (asterisk) is close to the common carotid artery (arrows) as well as the external carotid artery (arrowheads)

tional pronounced infiltration of nervous tissue was observed (Figure 3). Adjacent to the bulla, multiple regions with pronounced infiltration of monomorphic round cells of nervous tissue, presumably the

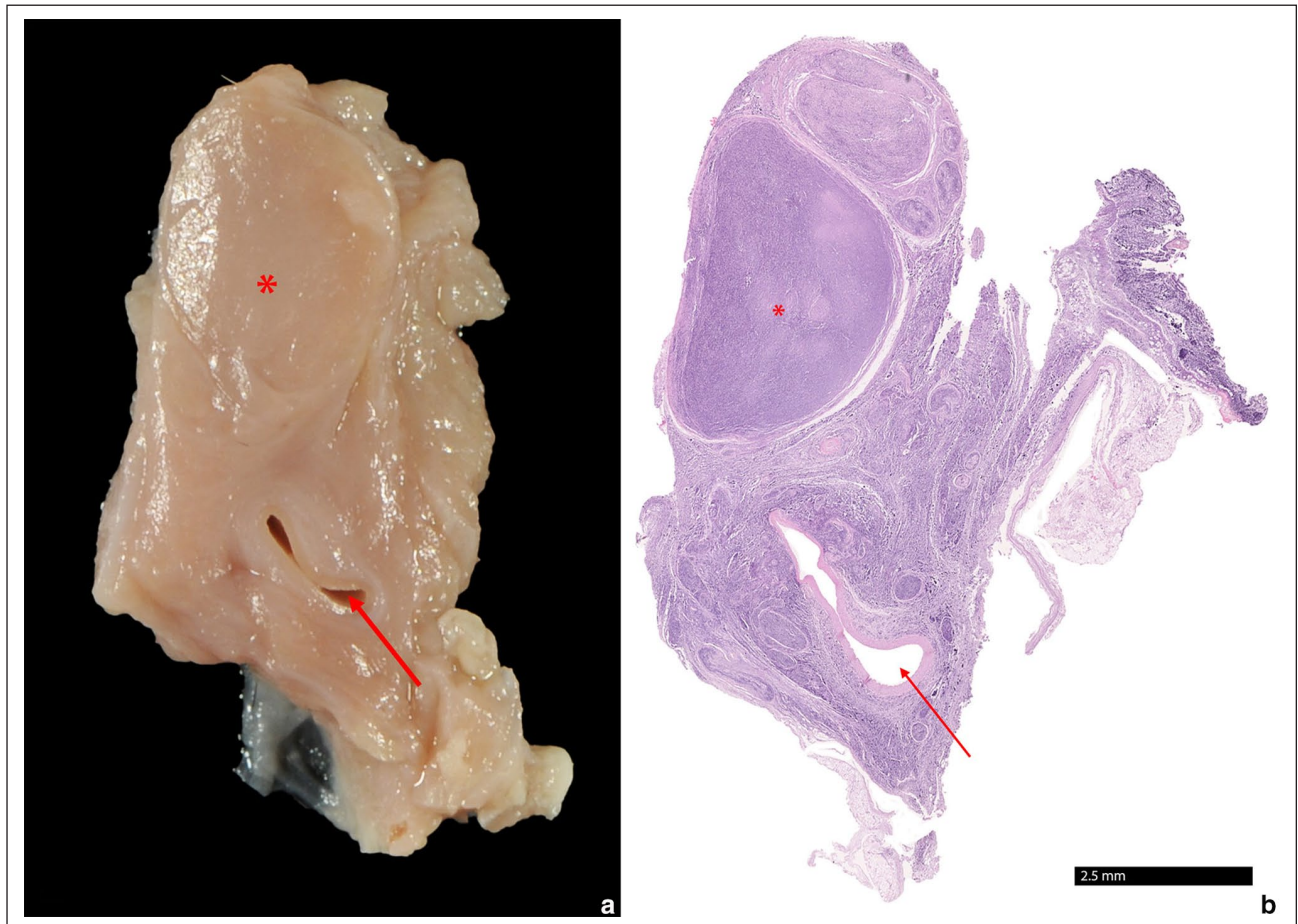


Figure 3 (a) A $2 \times 1.5 \times 0.5$ mm large firm mass (asterisk) with a homogeneously pale pink and round cross section is located close to the common carotid artery (arrow). (b) Histologically, the mass is encapsulated and of high cellularity

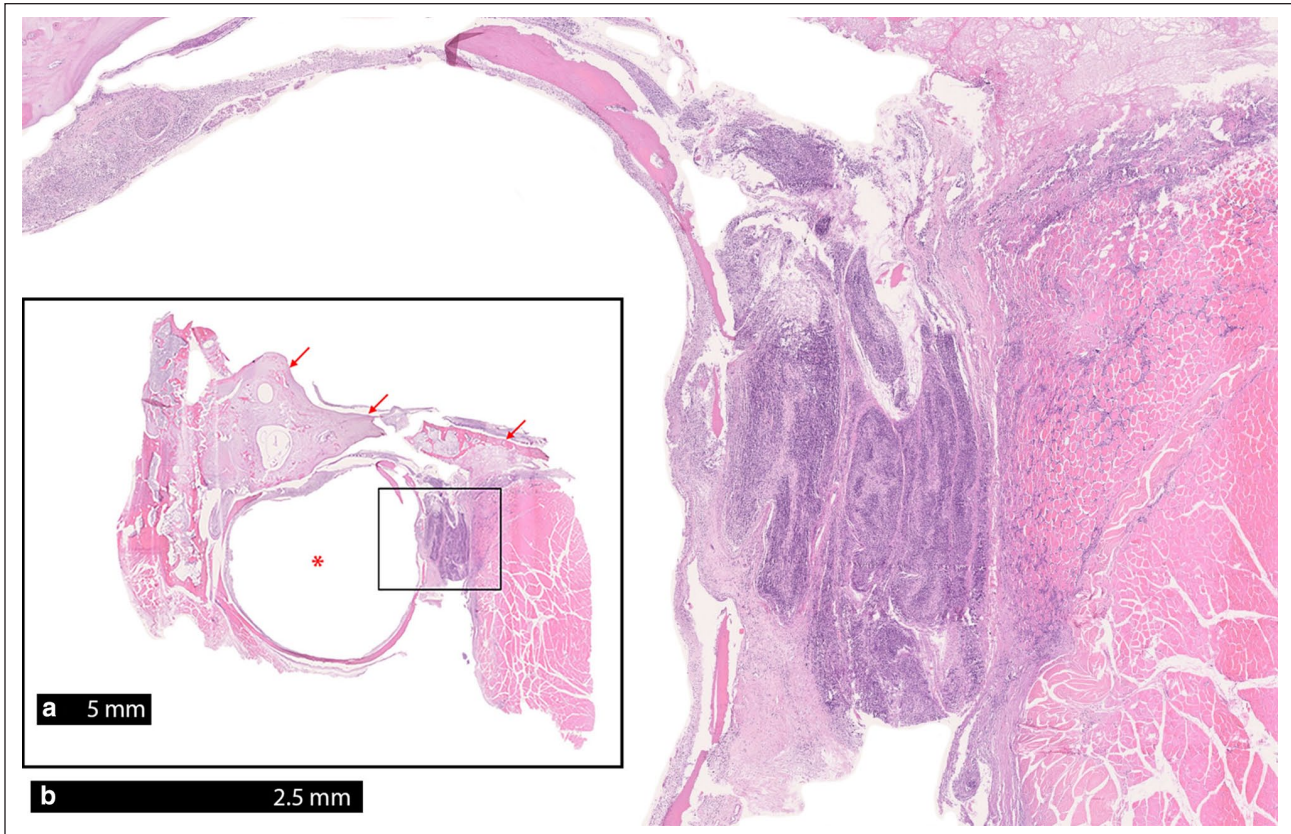


Figure 4 (a) There is evident cellular infiltration medially to the bulla (asterisk), but not in the ventral cranium (arrows). (b) Pronounced infiltration of the nervous tissue and parts of the skeletal muscles with monomorphic round cells (inset of panel [a])

glossopharyngeal nerve, and portions of skeletal muscle were evident (Figure 4). Immunohistochemistry was performed using the primary antibodies listed in Table 1. Paraffin sections were deparaffinised in xylene and rehydrated through graded alcohols. Endogenous peroxidases were inhibited by incubation (30 mins) in methanol-hydrogen peroxide. Slides were labelled with corresponding antibodies. Chromogenic methods were either ABC (Avidin-biotin complex; Linaris Biologische Produkte) for CD45R, NSE, SYN, cytokeratin, vimentin or PAP (peroxidase-antiperoxidase; Dako/Agilent Technologies) for CD3, CHA, S-100 and thyroglobulin. For each antibody, a positive control was included. For negative controls, primary antibodies were replaced by non-reacting antibodies. The neoplastic cells were immunopositive for CD45R and a low number of cells were immunopositive for CD3 (Figure 5). CD45R has been shown to be a specific B-cell marker in cats, as it detects the epitope of the B220 antigen of the CD45 glycoproteins,^{10,33–36} resulting in the diagnosis of a malignant B-cell lymphoma.

Discussion

The clinical signs, the unique location and the regional spread of the tumour in the MRI led clinicians to the first

differential diagnosis of a paraganglioma of the glomus caroticum. In human medicine, invasion of nearby nerves or tissue adjacent to the base of the skull, as seen in this case, has been reported.³⁷ Even though the neoplasm in this case turned out to be a malignant B-cell lymphoma, several differentials to neoplasms in the region near the angle of the mandible should be considered. As a result of the anatomic proximity, tumours of the mandibular lymph nodes, the medial retropharyngeal lymph nodes, the mandibular gland and the parotid gland would be valid differential diagnoses for tumours in this region, which are more frequent than tumours of the carotid body. However, these locations could be excluded as the origin of the tumour, owing to the performed diagnostic imaging.

During the post-mortem examination, the mass could be confirmed to be located in the glomus caroticum and the surrounding tissues, such as glossopharyngeal nerve and skeletal muscle. Through histopathology and immunohistochemical staining, the neoplasm was diagnosed as diffuse large B-cell lymphoma (DLBCL). According to the Revised European-American Lymphoma (REAL) classification of lymphoid neoplasms adopted by the World Health Organization, the DLBCL is part of the

Table 1 List of the antibodies used and results of immunohistochemical staining

Antibody	Origin, clone/polyclonal	Supplier	Dilution	Reactivity
CD3	Rabbit, polyclonal	Agilent Dako	1:100	(+) some interspersed cells
CD45R	Rat, clone B220 (Ly 5)	Cedarlane	1:1000	+
SMA	Mouse, clone 1A4	Agilent Dako	1:500	–
S-100 protein	Rabbit, polyclonal	Agilent Dako	1:400	–
NSE	Mouse, clone BBS/NC/M-H14	Agilent Dako	1:100	–
Cytokeratin	Mouse, clone AE1/AE3	Agilent Dako	–	–
SYN	Mouse, clone SY 38	Agilent Dako	1:100	–
CHA	Rabbit, polyclonal	Origene	1:10	–
Vimentin	Mouse, clone V9	Agilent Dako	1:50	–
Thyroglobulin	Rabbit, polyclonal	Agilent Dako	–	–
Glial fibrillary acidic protein (GFAP)	Rabbit, polyclonal	Agilent Dako	1:500	(+) some interspersed cells

CHA = chromogranin A; GFAP = glial fibrillary acidic protein; NSE = neurone-specific enolase; SMA = smooth muscle actin; SYN = synaptophysin

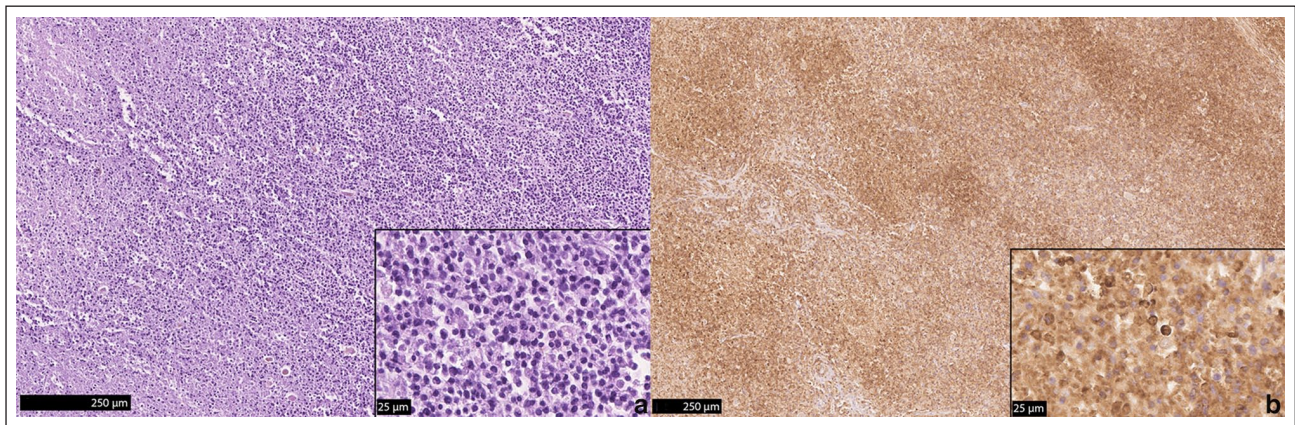


Figure 5 (a) The carotid body is infiltrated with a high number of monomorphic round cells. (b) The majority of cells is immunopositive for CD45R

mature (peripheral) B-cell neoplasm. DLBCL is the most common lymphoma in most domestic species.³⁸ In cats, B-cell lymphoma is common and many of them were located in the mediastinum,³⁹ but were also found in the upper respiratory tract, segments of the bowel or were multicentric.^{1,39–41} Therefore, this case represents an outlier of a B-cell lymphoma in an unusual location.

In the present case, a tumour arising from the carotid body is most probable. On the other hand, a primary CNS lymphoma extending towards the carotid body is a possibility, but the prevalence of primary CNS lymphomas is very low, at only 3% of primary CNS tumours,⁴² with even less showing extension into the extracranial tissues. Extension into extracranial tissues has been reported in the nose in feline patients,⁴³ but none can be found along the tympano-occipital fissure; however, there are reports of tumours originating from the carotid body invading nearby tissues in humans.³⁷ In addition,

the intracranial changes described in diagnostic imaging could not be histologically confirmed, reinforcing the assumption of the glomus caroticum being the origin of the tumour.

Other neoplasms of the nervous system have been ruled out and the unique dispersion of the lymphoma from the carotid body along the glossopharyngeal nerve with probable invasion of the neuropil can be held accountable for the observed signs.

Conclusions

The present case report describes the clinical findings, diagnostic imaging and pathohistological changes in a cat with a tumour of the glomus caroticum. Even though the neoplasm turned out to be a malignant lymphoma, the unique location, the infiltration along nervous tissue and the absence of neoplastic cells in other examined organs, led at first to the assumption of a paraganglioma

in the glomus caroticum. Therefore, this case shows the importance of keeping a common neoplasm at the top of the differential diagnoses.

Author note Parts of the findings and figures have been displayed as a poster at the regional conference '67. Jahrestagung der DVG-Fachgruppe Pathologie 2024'.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers, tissues and samples) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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