

# Neck glomangiomyoma: A case report and literature review

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Received April 26, 2021; Accepted January 21, 2022

DOI: 10.3892/mco.2022.2587

**Abstract.** Glomus tumors are rare and the hand is classically the most commonly affected site. The present study performed a literature review on the topic and reported on an unusual case of neck glomangiomyoma in a female adult patient. A 31-year-old woman presented with a 4-year history of a growing submandibular tumor with localized non-irradiated pain. A previous fine needle aspiration biopsy had suggested a glomus tumor, and immunohistochemical analysis showed positive staining for smooth muscle actin, H-caldesmon, muscle-specific actin and collagen type IV. The MRI revealed a well-defined nodular lesion measuring 38x28x33 mm. The patient underwent surgery with no complications. After the histopathological examination and immunohistochemical staining, a diagnosis of glomangiomyoma was established. Glomangiomyomas are extremely rare but should be considered in the differential diagnosis of an adult presenting with a neck mass and localized tenderness, especially if no other risk factors for head and neck tumors are present.

## Introduction

The glomus tumor (GT) is a distinctive neoplasm that resembles the normal glomus body, and accounts for approximately 1.6% of all soft tissue tumors (1). GTs are rare, and usually present in adults between the third and fourth decade of life. The classical triad of symptoms is localized tenderness, severe pain and cold hypersensitivity, and usually present as a small solitary tumor (2).

When first described as a distinct clinical entity by Wood in 1812 (3), it was considered a form of angiosarcoma until its histopathology was accurately described by Masson in 1924 (4,5). These lesions show varying proportions of glomus

cells, blood vessels and smooth muscle cells and are classified accordingly into solid glomus tumor (25% of cases), glomangioma (60% of cases) and glomangiomyoma (15% of cases) (6).

In this study, we report a rare form of glomus tumor: a glomangiomyoma of the neck. To our knowledge this is the second glomangiomyoma of the neck reported in the literature and the first described in an adult.

## Case report

A 31-year-old woman presented to the Ear Nose Throat department of Son Espases University Hospital in Palma de Mallorca, Spain with a 4-year history of a growing right submandibular tumor with localized non-irradiated pain. The physical examination revealed a localized tenderness and a well-defined ovoid mass of approximately 4x3 cm, with no neurological deficit. The oral cavity, oropharynx and larynx examination were unremarkable. She reported no previous personal or family history of glomus tumor, no evidence of cold sensitivity and no previous history of trauma.

Before she was sent to our hospital, a core needle biopsy had been performed in another center in 2018, suggesting the diagnosis of glomangioma. The histopathology showed a homogenous cellularity with cells arranged diffusely and perivascularly. Immunohistologically, the tumor cells featured a cytoplasmic staining for SMA (smooth muscle actin), H-caldesmon, vimentin and collagen IV, whereas the reactions with antibodies against CD3, CD20, CD138, desmin, S-100, CD138, CD1 and CD34 were negative. No mitotic activity was observed, and Ki-67 cell proliferation index was 2%.

The first MRI was performed in June 2019, showing a solid nodular lesion measuring 25x21x20 mm, with a decreased signal intensity on T1 and increased signal intensity on T2-weighted images. After the diagnosis, the patient decided not to proceed with the surgery. She returned in October 2020 due to increased pain and a second MRI was performed, showing a significant growth of the tumor, measuring 38x28x23 mm; the enhancement pattern remained unchanged (Fig. 1).

She underwent excision of the tumor under general anesthesia and facial nerve monitoring with no complications. Intraoperatively the tumor was solid and well delimited, with no sign of tumor spread into the adjacent tissue (Fig. 2A). A meticulous dissection was performed preserving the marginal nerve. Postoperatively the patient was free of complications.

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**Key words:** head and neck, glomangiomyoma, neoplasm, glomus tumor, oncology

The histopathology exhibited a well circumscribed solid lesion, composed of uniform elongated cells with a round and ovoid central nuclei with no signs of atypia, and lightly eosinophilic cytoplasm with well-defined cell margins. These cells were distributed near vascular spaces.

Immunohistochemical analysis was performed showing a positive stain for smooth muscle actin, H-caldesmon, muscle specific actin and collagen type IV. The tumor cells were negative to desmin, calponin, melan-A, Sox-10, S100 and CD34. Ki-67 proliferation index was 1% (Fig. 2B-F).

## Discussion

GTs are usually benign perivascular neoplasms, most likely derived from modified smooth muscle cells of the neuromyo-arterial glomus body. The normal glomus body is a specialized form of arteriovenous anastomosis that regulates heat, and is located in the stratum reticularis of the dermis and most frequently encountered in the subungual region, the lateral areas of the digits and the palm (7).

The most affected site is the hands (particularly the subungual region and palm), followed by the foot and forearm (6). These lesions can also be found in regions where no normal glomus have been identified, including deeper tissues such as joint capsule and striated muscle (8).

A 20-year-long series published by Schiefer *et al* (9) shows that the extra digital location could be more common than we thought, comprising approximately 61% of glomus tumors seen at the Mayo Clinic during this time frame. This finding is also supported by the experience of Heys *et al* (10) in a 43-patient-series (1992), where 67% of tumors were extradigital, like the findings reported by Chou *et al* (2).

In our literature review, we found that only a few extradigital locations of glomangiomyoma (less frequent histological variant of glomus tumor) have been reported: Laryngeal (11), trachea (12,13), pancreas (14), kidney (15,16), forearm (17,18), vagina (19), knee (20), periurethral (21), lung (22), gastrointestinal (23), chest wall (24), nasal cavity (25) and only one other case of neck glomangiomyoma in a child in Nepal (26).

Classically described, the glomus tumor presents as a solitary, small (<1 cm), blue-red nodule with paroxysmal pain, worsened by cold temperature and pressure (2,27). In a patient series reported by Schiefer *et al* (9) and Heys *et al* (10) the most common symptom was localized pain, while pain elicited by cold temperature was rare. A prior history of trauma in the affected area has also been described (9).

Our patient presented a growing large neck mass, differing from the classical presentation described in the literature. We think that the patient may not have noticed the mass during the first years of presentation due to its submandibular localization, and the only symptom she presented was localized non-irradiated pain, which worsened with growth.

While most glomus tumors are benign; malignant, and aggressive tumors have been published in the literature. In 2001, Folpe *et al* (28) published a classification of atypical GTs identifying a size larger than 2 cm, deep location, nuclear atypia, mitotic activity, and diffuse growth as potentially malignant features.

In our case, even though the tumor fulfills the malignancy criteria proposed by Folpe *et al* due to its deep location and size, intraoperatively it was a well circumscribed lesion with no macroscopic signs of adjacent tissue infiltration. The histopathology of the core needle biopsy and the surgical specimen showed no signs of atypia or mitotic activity and a low Ki-67 cell proliferation index. In deep soft tissues, the differential diagnosis of an atypical GT should consider hemangiopericytoma, leiomyosarcoma with epithelioid change, rhabdomyosarcoma, and pPNET (peripheral primitive neuroectodermal tumor) (28). Given the patient's characteristics we also considered HPV associated oropharyngeal cancer, salivary gland neoplasm and lymphoma. Distinctive characteristics of these lesions are described in Table I.

The molecular mechanisms that may lead to a glomus tumor have also been researched. In their series of 93 patients with GTs, Agaram *et al* observed that 54% of GTs harbor NOTCH-gene fusions. NOTCH2-MIR143 was the most common fusion, detected in 76% of the cases (29). BRAF V600E mutation has also been studied potentially related to malignancy and tumor progression (30).

During diagnostic evaluation an image test should be performed, with MRI being shown to be the most sensitive imaging modality for diagnosing glomus tumors (9,31). Most lesions are surrounded by a capsule and are iso- or slightly hyper intense on T1 and strongly hyperintense on T2-weighted images relative to the muscle, as seen on this patient (Fig. 1A). Vascular predominant GT could show a stronger contrast enhancement (31-34).

These lesions immunohistochemically and ultrastructurally exhibit smooth muscle characteristics. Cells usually stain for smooth muscle actin, H-caldesmon, muscle-specific actin, and myosin. Staining for collagen type IV shows prominent pericellular positivity. Desmin has occasionally been found to be positive and S100 positivity is rare. Studies show conflicting results for CD34 positivity, classically considered as an endothelial marker, but its role in glomus tumors remains unclear (27,28,35-40).

The immunohistochemical analysis of our patient showed positivity for smooth muscle actin, H-caldesmon, muscle-specific actin and collagen IV, similar to what has been classically described in the literature.

Glomangiomyomas share the architectural pattern of a classic glomus tumor showing transitions between glomus cells and cells with partial smooth muscle features (4). It has been proposed that glomangiomas and glomangiomyomas designate the same lesion; the latter with transitional areas from glomus cells to well defined smooth muscle cells, and to identify these areas, extensive sampling and analysis should be made (38,41). We believe this is why our case was initially diagnosed as a glomangioma through a core needle biopsy with the final diagnosis of glomangiomyoma only being established after the final specimen had been obtained.

A glomus tumor is a rare neoplasm, more so if localized in the head and neck region. It should be considered in an adult presenting with a neck mass and localized tenderness especially if no other risk factors for head and neck tumors are present. Imaging technique and fine needle aspiration biopsy are mandatory to characterize the mass properly as complete surgical excision continues to be the treatment of choice.



Figure 1. Last head and neck MRI before surgery showing T2 weighted images. (A) Axial view showing a hyperintense (relative to muscle) well circumscribed mass measuring 38x28x23 mm. (B) Coronal view.

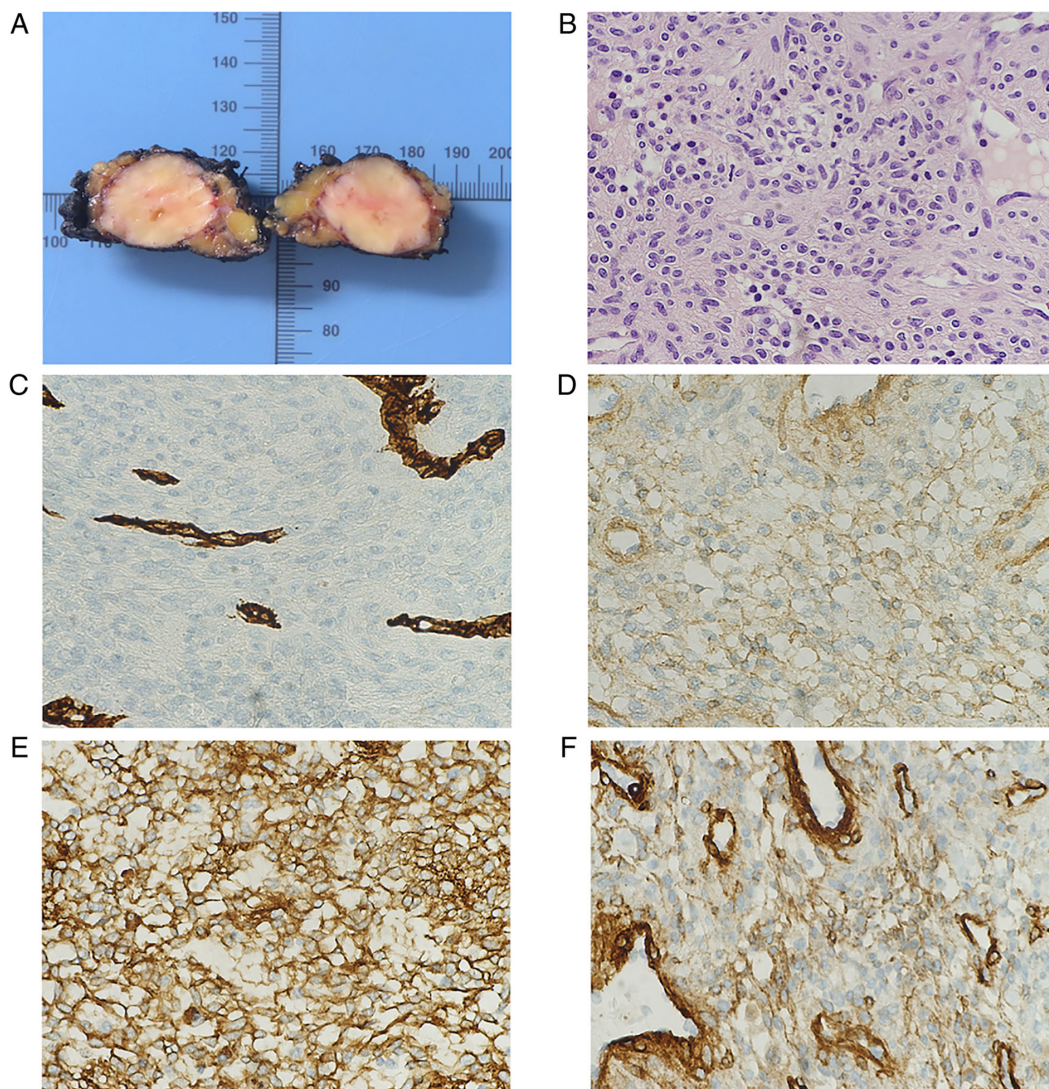


Figure 2. Immunohistochemical staining and surgical specimen. (A) Surgical specimen reveals a uniform well circumscribed tumor. (B) Hematoxylin-eosin (magnification, x60), showing uniform rounded glomus cells with a central nucleus. (C) Negative staining for CD 34 (magnification, x60). (D) Tumor cells stained positively for smooth muscle actin (magnification, x60). (E) Collagen IV pericellular positivity (magnification, x60). (F) Intense staining for muscle specific actin (magnification, x60).

Table I. Differential diagnosis and its distinctive cytological and immunohistochemical features (42-60).

Differential diagnosis	History/physical exam	Cytological features on fine needle aspiration biopsy/biopsy	Immunohisto-chemistry
Atypical glomus tumor	Large size mass >2 cm, deeply located. Presents with paroxysmal pain elicited by cold	Glomus cells, blood vessels and smooth muscle cells	H-caldesmon, MSA, SMA, collagen type IV, +/- CD34
Salivary gland malignancy	Painless unilateral growing mass. That appears immobile without defined borders. Marginal nerve palsy. Cervical lymphadenopathy	Atypical mitotic figures and mitotic activity	ACC: CK7, CAM 5.2, calponin, p63, SOX10, S100, SMA MEC: CK5, CK6, CK7, CK8, CK14, CK18, CK19, EMA, CEA, and p63
Hodgkin lymphoma	Painless lymphadenopathy. Constitutional symptoms	Large neoplastic cells may be mononucleated (hodgkin cell) or bi or multilobated (Reed-Sternberg cell) with prominent nucleoli and abundant cytoplasm	CD30, CD15, PAX5, CD20
Non-Hodgkin lymphoma	Painless lymphadenopathy. Constitutional symptoms	DLBCL: lymphoid cells with nuclear size more than twice the size of normal lymphocytes FL: small mature-appearing lymphocytes with angulated, elongated, or cleaved nuclei and inconspicuous nucleoli, corresponding to the centrocytes. Large, non-cleaved cells corresponding to the centroblasts are present	CD19, CD22, CD79a CD19, CD20, CD10, BCL-6
HPV oropharyngeal squamous cell carcinoma	Painless neck mass and sore throat in usually non-smoker patients	Squamoid cytoplasm and cohesive streaming groups	Keratin, p63, p40 HR-HPV by PCR or ISH
Metastatic melanoma	History of exposure to intense UVR at a young age. Large number of naevi. Painless fixed adenopathy	Nuclear molding and nuclear crush artifact, necrosis, mitosis and apoptosis	S100, HMB-45, Melan-A, tyrosinase
Hemangiopericytoma	Usually large painless mass. Present in several anatomical sites	Homogenous vascular pattern, uniform cell population with ovoid/round cells enmeshed but reticulin and collagen fibers	Vimentin, STAT6, BCL2 +/- CD34 CD57, CD99
Leiomyosarcoma	Nonspecific symptoms caused by displacement of structures, slowly enlarging, discrete, firm, non-ulcerated painless mass	Intersecting, sharply margined fascicles of spindle cells with abundant eosinophilic cytoplasm and elongated and hyperchromatic nuclei	SMA, desmin, CK, EMA
Rhabdomyosarcoma	Children and adolescents presenting with a visible or palpable mass, symptoms develop from compression or invasion of adjacent structures	Primitive mesenchymal cells recapitulating various stages of myogenesis with variable presence of rhabdomyoblasts	Desmin, Myogenin, CD56, muscle-specific actin, Myoglobin, Vimentin and MyoD1
Peripheral primitive neuroectodermal tumor	Young patients with rapidly enlarging, often painful mass	Sheets of small, round to oval cells, often arranged in lobules, separated by fibrous septa Homer-Wright rosettes	MIC2, Vimentin, NSE (neuron specific enolase), synaptophysin

MSA, muscle-specific actin; SMA, smooth muscle actin; ACC, adenoid cystic carcinoma; MEC, mucoepidermoid carcinoma; CEA, carcinoembryonic antigen; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HR-HPV, high risk human papilloma virus; PCR, polymerase chain reaction; ISH, *in situ* hybridization; UVR, ultraviolet radiation.

## Acknowledgements

This article has been revised by Mr. Jonathan McFarland (Associate Professor at Autonomous University of Madrid, and Senior Lecturer at Sechenov University, Moscow).

## Funding

No funding was received.

## Availability of data and materials

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the current study.

## Authors' contributions

PSE and GTP are the main surgeons and provided substantial contributions in the design of this article. CMO and CC drafted the final manuscript, acquired all data, revised it critically and wrote the final version to be published. EMH performed the immunohistochemical staining and histopathology. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

The patient provided oral informed consent for the use of their surgical samples in scientific research and the use of images for publication (November 5, 2020).

## Competing interests

The authors declare that they have no competing interests.

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