Glomus Tumor of the Shoulder in a 25-Year-Old Woman: Case Report and Review of the Literature

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Abstract:
Correctly diagnosing and communicating results to patients is one of the most effective ways to ensure proper patient care and maximize effective treatment strategies. When nomenclature contradicts, it can create confusion and barriers between patients and physicians. One example is the diagnosis of a glomus tumor (GT), which has also been referred to as a paraganglioma (PG). However, a glomus tumor is not a paraganglioma and awareness of this distinction is essential. The case we present is a 25-year-old female who presented with a painful left shoulder mass. The mass was surgically excised, and the pathological examination diagnosed it as a glomus tumor. We review the literature regarding this tumor and clarify the distinction between glomus tumor and paraganglioma.

Keywords: Glomus Tumor, Paraganglioma, Differential Diagnosis, Immunohistochemistry

Introduction:
Glomus tumors are uncommon neoplasms arising from the arterial end of glomus bodies found in the reticular dermis of the skin. Glomus bodies are modified smooth muscle cells responsible for thermoregulation.1,2 They prevent heat loss by shunting blood away from the skin surface when exposed to cold temperatures, and they also allow maximal blood flow to the skin in warm weather to properly dissipate heat.1,2 Certain site-specific misnomers like glomus faciale, glomus jugulare, glomus tympanicum, glomus vagale, etc., are paragangliomas and not glomus tumors.3 Most GTs are benign, but they can also show malignant features. In 1877, Hoyer described the first case of glomus tumor, and in 1924, Masson described the first detailed clinical presentation of GT.1 Various types of deletions in the GLMN (glomulin) gene have been associated with familial glomangiomias. The mode of inheritance was reported as autosomal dominant with incomplete penetrance.4

We report a case of a 25-year-old female with the diagnosis of a small left shoulder glomus tumor. We review the literature on this uncommon tumor and how to differentiate it from another possible differential diagnosis. We also clarify the confusing nomenclature of GT and PG.

Case Presentation:
A 25-year-old female presented with a dark, painful, small nodule in her left shoulder. She noticed the nodule at least two years ago but did not seek medical attention until it became severely painful, especially in cold conditions. She described a history of sensitivity to cold weather but no significant medical history for herself or her family members. The patient was concerned about a possible skin malignancy and decided to see her physician. Physical examination showed a well-circumscribed dark nodular mass measuring 0.7 cm. The mass was surgically excised. Microscopic examination revealed a well-defined tumor mass (Figure 1A), with capillary-sized vessels lined with endothelial cells and collars of uniform glomus body cells forming nests, sheets, and trabeculae in a slightly hyalinized stroma (Figure 1B). Glomus body cells were round with indistinct borders and had a sharply punched-out nucleus in an amphophilic and eosinophilic cytoplasm. The cells showed homogenous chromatin and were bland with inconspicuous nucleoli. No atypia or mitosis were identified (Figure 1C). Some dilated vascular spaces showed endothelial cells growing into organized thrombi with recanalization (Figure 1D). The tumor cells were positive for smooth muscle actin, h-caldesmon, and vimentin and negative for cytokeratin, S100, chromogranin, and synaptophysin (Figure 2). The histomorphology and immunohistochemistry studies were consistent with the diagnosis of glomus tumor.
three-year follow-up showed no recurrence or change at the excision site.

Discussion:

The neuromyoarterial plexus is the site of origin for GTs, also called thermoregulator hamartomas. These are modified smooth muscles originating from the glomus body. Glomus tumors are primarily found in the deep dermis of the palm, wrist, forearm, foot, and feet and in the subungual or periungual area of the digits that are the farthest away. The typical benign solitary lesion is small, rarely exceeding 1.0 cm in greatest dimension. It usually forms a bulging, unencapsulated mass with an irregular, nodular, dark red surface. When multiple, the tumors are usually 0.1 to 0.3 cm in diameter, but lesions up to 3.0 cm have been reported. Patients typically present with a triad of symptoms, including excruciating paroxysmal pain (worse at night), temperature sensitivity, and severe point tenderness. The histology of a glomus tumor shows sheets of cells with oval nuclei arranged around blood vessels. GTs are characteristically and diffusely immunoreactive for α-SM muscle actin (αSMMA), Muscle Specific Actin (MSA), and h-Caldesmon. Although nonspecific, vimentin and collagen type IV are also expressed. Variable expression of CD34, and to a lesser extent desmin, has also been reported.

Familial generalized multiple glomangiomyomas have been associated with various deletions in the GLMN (glomulin) gene and are inherited in an autosomal dominant manner, with incomplete penetrance. The current literature on sporadic GTs records no molecular findings. A familial variant of glomangioma has recently been linked to chromosome 1p21 and involves truncating mutations in the glomulin gene, which encodes a 68-kDa protein with unknown function. So far, a mutation in glomulin has manifested in all affected families tested, thus demonstrating locus homogeneity. Mosquera et al. report that MIR143-NOTCH gene fusions are present in more than half of benign and malignant glomus tumors. Glomangiosarcomas, also known as malignant glomus tumors, are uncommon and typically indicate a locally infiltrative malignancy. Nonetheless, metastases do happen and are typically lethal. A few cases of cancerous GTs have been reported; however, they are usually only locally invasive, and metastases are exceedingly rare. There is one report of widespread metastases of a malignant GT involving the skin, lungs, jejunum, liver, spleen, and lymph nodes.

On histopathology, GTs can be termed as follows: Solid glomus tumor (75% of cases) consists predominantly of glomus cells, with poor vasculature and rare smooth muscle cells. Glomangioma (20% of cases): tumors with a prominent vascular component. Glomangiomyoma (5% of cases): tumors with prominent vascular and smooth muscle components. Our case showed a mix of these three types. Differential diagnosis includes other lymphovascular and adnexal tumors such as hidradenoma, intradermal nevi, or malignant melanomas. It is related to other pericytic tumors like myopericytoma and myofibromatosis (myofibroma) because it comes from perivascular cells (pericytic cells) and is a member of the pericytic family. Other differential diagnoses include smooth muscle, vascular, or nerve sheet origin tumors, that is, angioleiomyoma, hemangioma, or peripheral nerve sheet tumors. Immunohistochemistry (IHC) studies are instrumental in distinguishing glomus tumors from paragangliomas. As in our case, the strong positivity of the glomus bodies with actin and h-caldesmon and the negative reaction with neuroendocrine and cytokeratin markers aided in the diagnosis of GT. The selection of treatment modalities for GTs, such as sclerotherapy, laser therapy, or surgical excision, is predicated on the lesional location and clinical presentation. Surgical excision is the preferred treatment for benign glomus tumors. Glomus tumors are generally benign but painful lesions that may be exacerbated by pressure or temperature change and impair one’s quality of life.

Paragangliomas (PGs) are rare neuroendocrine neoplasms that may develop at various body sites (including the head, neck, thorax, and abdomen). When the same type of tumor is found in the adrenal gland, it is referred to as a pheochromocytoma. PGs are rare tumors, with an estimated incidence of 1 in 300,000. PGs are hypervascular, slow-growing, usually benign, uncommon catecholamine (norepinephrine)-secreting neuroendocrine neoplasms that arise from glomus cells that are commonly found in the head, neck, thorax, and abdomen. There are 500 to 1000 cases diagnosed per year in the United States.

The benign paraganglioma/pheochromocytoma incidence is estimated at 0.7 to 1.0 per 100,000 person-years. The classic clinical presentation of PG has the triad of headache, palpitations, and profuse sweating due to excessive catecholamine release, but other manifestations occur depending on the PG site. There are two types of glomus cells. Type 1 are peripheral chemoreceptors that detect pH, oxygen, and CO2 changes and appropriately adjust the body’s breathing. Type 2 glomus cells are sustentacular cells that provide structural support in various body areas, including the carotid and aortic bodies. The first step in diagnosing PGs and pheochromocytomas is measuring plasma fractionated metanephrines, with a sensitivity of 97% and a specificity of 93%, and surgical resection is the first line of treatment. IHC studies are used after excision to diagnose PGs. The adrenal gland secretes chromogranin A, and the neuroendocrine tumor marker represents chromogranin A. Other positive markers include PGP 9.5, N-CAM, and SYN. Complete surgical excision is the main form of treatment for PGs.
Paragangliomas were originally (and erroneously) known as glomus tumors. Our literature review in this report clarified that glomus tumors are not paragangliomas and should not be synonymous. We hope this report will raise pathologists’ and clinicians’ awareness of the distinction between glomus tumors and paragangliomas for better patient understanding, education, future research studies, and optimal management.

**Figures:**

![Figure-1: Microscopic examination of left shoulder glomus tumor](image)

1A: Whole slide view showing well-circumscribed dermal mass (H&Ex10)
1B: Intermediate view showing glomus body cells with no atypia and no mitosis (H&Ex40)
1C: Intermediate power view showing glomus body cells pushing endothelial cells and organized thrombus (arrowhead) through a vascular space (H&Ex40)
1D: Glomus body cells are positive for actin, and organized thrombus cells are negative for actin

**References:**


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