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Case Report

Glomus tumor of uncertain malignant potential

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ABSTRACT

Glomus tumors closely resemble the normal glomus body and have a predilection for skin and subcutaneous tissue. Clinically, Glomus tumors are present on the nail bed and are of less than 1 cm. We report a case of a male who presented with a 3 month history of swelling in the left thumb which was mildly tender. The swelling measured 6 x 6.5 cm. On microscopy the tumor showed mild atypia with increased mitotic activity. These features, by current definition, would suggest uncertain malignant potential.

INTRODUCTION

Glomus tumor is a distinct mesenchymal neoplasm composed of cells that resemble the normal glomus body. These neoplastic cells are closely arranged with variably sized vessels and smooth muscle cells. The various designations for benign glomus tumour include solid glomus tumor, glomangioma, or glomangiomyoma. Other rare types include symplastic glomus tumor, glomus tumor of uncertain malignant potential and malignant glomus tumour. [1- 4] The label of uncertain malignant potential has been applied to superficially located tumors with more than 5 mitotic figures/50 high-power fields (HPF), alternatively large size only or deep location only. Glomus tumor commonly presents as small, benign neoplasm occurring in the dermis or subcutis of the extremities.[5] However, occasionally glomus tumors show unusual features, such as large size, location in deep soft tissue or viscera, infiltrative growth pattern, and multicentricity. There are some reported cases of primary benign glomus tumors in the kidney despite this being an uncommon location for mesenchymal tumors.[6-9] This case differs from the published cases in being a glomus tumor of uncertain malignant potential.

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CASE REPORT

A 63 year old male presented with a 3 month history of swelling in the left thumb. The swelling was mildly tender and was rapidly increasing in size. An excisional biopsy was done and the specimen was sent for histopathological examination.

The gross specimen showed a skin bearing tissue measuring 6 x 6.5 x 2 cm. (fig. 1).

Figure 1. *Gross Specimen showing skin bearing tissue with ulceration.*

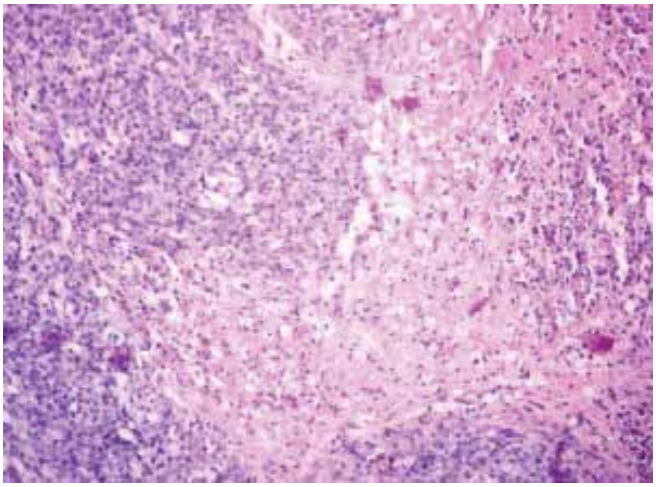

Figure 2: *Microscopic view showing necrosis. (HE stain, X10)*

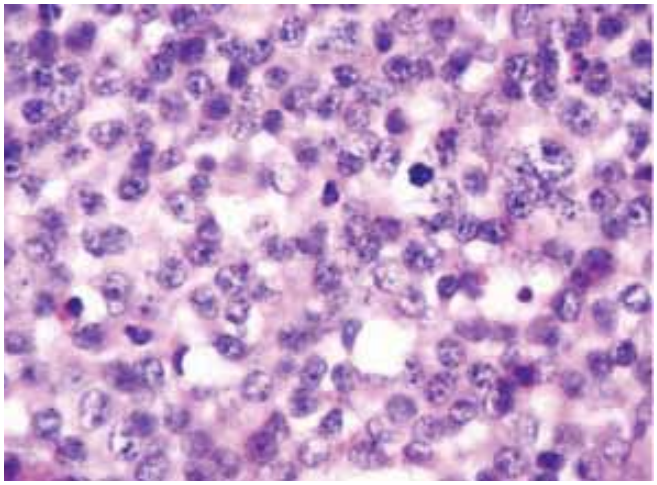

Figure 3. *Microscopic view showing Atypical mitosis (HE stain, X40)*

An ulcer was seen at one end of the specimen. Cut section showed solid tan white area with small slit like spaces. The tumor was well demarcated from the overlying skin. Areas of hemorrhage were seen towards the peripheral areas. Microscopic examination revealed a solid pattern of growth. The tumor was composed of uniform round cells with pale eosinophilic cytoplasm and sharply defined cell borders, with perivascular aggregation. Nuclear variation was moderate with mild cytological atypia and the chromatin was finely granular. The mitotic count was at 5 per 50 HPF with few atypical mitoses. Areas of necrosis with numerous acute and chronic inflammatory cells were seen. Many large and small blood vessels were seen. There was no evidence of lymphovascular invasion. (fig. 2. and fig. 3)

DISCUSSION

The first report of a clinically atypical infiltrating glomus tumor was reported in 1972 in a case report of Lumley and Stansfeld.[6] One year later, Anagnostou et al.[7] illustrated a case they claimed to be a pathologically malignant glomus tumor, and mentioned that another such case had been presented at the 40th assembly of the Greek Pathological Society. Enzinger and Weiss,[5] in the first edition of Soft Tissue Tumors, noted having seen four cases of otherwise typical glomus tumors that contained within them areas of malignant spindle cell growth "having features somewhat intermediate between fibrosarcoma and leiomyosarcoma." A detailed clinical and pathologic description of these four tumors was, however, not given, and no follow-up information was provided. In 1988, Aiba et al.[8] described a pathologically malignant glomus tumor, characterized by a pleomorphic spindle cell tumor with frequent mitotic figures that arose within a typical glomus tumor of the back. The patient was reported to be disease free 3 years after resection.

Gould et al.[3] first attempted the classification of aggressive and/or potential malignant glomus tumors in 1990. They studied 6 atypical glomus tumors, and proposed the terms locally infiltrative glomus tumor for cytologically bland tumors with infiltrative growth, and glomangiosarcoma arising in a benign glomus and glomangiosarcoma de novo for malignant-appearing tumors with and without identifiable benign glomus respectively. The four specimens considered to be malignant were histologically similar and

Table 1: Summary of clinical features[2]

Malignant glomus tumor	Symplastic glomus tumor
1) Large size and deep Location or 2) Atypical mitotic figures or 3) Marked atypia with mitotic activity	1) Lacks criteria for malignantglomus tumor and 2) Marked nuclear atypia only
Glomus tumor of uncertain malignant potential	**Glomangiomatosis**
1) Superficial location withhigh mitotic activity or 2) Large size only or 3) Deep location only	1) Lacks criteria for malignantglomus tumor or glomus tumor of uncertain malignant potential and 2) Diffuse growth, resembling angiomatosis, with excess glomus cells

consisted of pleomorphic, hypercellular and mitotically active round cell tumors that were cytoarchitecturally and immunohistochemically similar to typical glomus tumors. Follow-up information, available for three of the patients with malignant appearing tumors revealed two local recurrences but no metastases. Between 1990 and 1996, a very small number of additional case reports of histologically malignant glomus tumors were published.[4, 9, 10]

The first outcome study was done by Andrew Flope et al in 2001[2] of a large number of glomus tumors having one or more atypical features. Such lesions are admittedly rare and comprised less than 5% of all glomus tumors which was referred to them. Combining the features of necrosis, mitotic activity of more than 5 mitoses/50 HPF, and the combination of high nuclear grade and high mitotic activity they proposed an empirically useful classification of glomus tumors with atypical features: (Table 1)

In all locations, the identification of areas of typical glomus tumor is the most important clue to the diagnosis of atypical glomus tumors. In general, typical glomus tumor is found at the periphery of both round cell and spindle cell forms of atypical or malignant glomus tumor. Atypical glomus tumors of the round cell type may be seen without a component of typical glomus tumor. In these tumors, histologic features that allow the correct diagnosis include the prominent, branching capillary vasculature, the perivascular arrangement of the tumor cells, the generally uniform cell shape and size, and the presence of distinct cell borders and uniform cellular investment by basement membrane (demonstrated best on periodic acid–Schiff or reticulin histochemical stain). In difficult cases, immunohistochemical demonstration of smooth muscle actin expression and individual cell investment by type IV collagen may be valuable in the diagnosis of both typical and atypical glomus tumors.[11]

The differential diagnosis of malignant glomus tumor is broad, and to some extent site dependent. In the skin, atypical glomus tumors are most likely to be confused with the more common primary cutaneous round cell tumors, such as Merkel cell carcinoma, eccrine spiradenoma and melanoma, as well as rarer tumors such as cutaneous extraosseous Ewing Sarcoma/primitive neuroectodermal tumor (PNET) and neuroblastoma.[11] Merkel cell carcinomas and eccrine spiradenomas differ from atypical glomus tumors in that they express cytokeratins,[12] including cytokeratin 20 in Merkel cell carcinomas.[13] Muscle actin expression may be seen in eccrine spiradenoma, but only in the basal cells.[12] Demonstration of S-100 protein expression and HMB-45 positivity should allow the distinction of malignant melanomas from glomus tumors, because glomus tumors are seldom S-100 protein positive and are never HMB-45 positive.[12] Cutaneous ES/PNET would not be expected to express muscle actins and does not demonstrate pericellular type IV collagen expression.[14] Unlike glomus tumors, cutaneous neuroblastomas express markers of neural differentiation, such as neurofilament proteins, chromogranin, and synaptophysin.

CONCLUSION

Glomus tumors are usually considered benign with infiltrative or malignant cases being exceedingly rare. Prognosis of glomus tumor of uncertain malignant potential is good but the number of cases is small and the follow up relatively short. The label of glomus tumor of uncertain malignant potential warrants close follow-up.

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