CASE REPORT

Clinically malignant atypical glomus tumour

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SUMMARY

Glomus tumours (GTs) resemble the normal glomus body and have a predilection for skin and subcutaneous tissue. Although the majority of glomus tumours are small, benign neoplasms that occur in the dermis or subcutis of the extremities and cases of atypical or malignant variants have been reported. We report a case of a man who presented with a 1-year history of subcutaneous nodule in the right scapular area which was mildly tender. The nodule measured 2 cm. Microscopic examination showed features of glomus tumour with increased mitotic activity. These features, by current definition, would suggest glomus tumour of uncertain malignant potential. Three months later, he presented with recurrence. During his metastasis work-up, we noticed bilateral pulmonary metastasis. Metastasising GTs are rare. The patient underwent wide local excision and received chemotherapy.

BACKGROUND

Glomus tumours (GTs) are uncommon mesenchymal perivascular tumours. They comprise of about 1.6% of all soft tissue tumours.[1] The lesion was probably first clinically described in 1912, and subsequently, a histological description was provided by Mason in 1924.[2] GTs are composed of cells histogenetically resembling cells present in glomus body. Most GTs are small, superficially located and benign.[1] Examples of histologically atypical, malignant and even rare metastasising GTs[3 4] have been reported in the literature. Atypical GT can mimic other entities. Here, we report a case of a man who presented with a 1-year history of subcutaneous nodule in right scapular area which was mildly tender. The nodule measured 2 cm. Microscopic examination showed features of GT with increased mitotic activity. On the basis of new criteria and the lack of atypical mitotic figures, we graded our case as GT of uncertain malignant potential. Three months later, he was presented with local regrowth. During his metastasis work-up, bilateral pulmonary metastasis was seen. The patient underwent wide local excision and received chemotherapy. Metastasising GTs are rare and, according to some reports, GTs of uncertain malignant potential did not metastasise.[3] However, it was not true about our patient.

CASE PRESENTATION

A 22-year-old man presented with a painful subcutaneous nodule in the right scapular area for the past 1 year. On examination, the mass was tender, firm and about 2 cm in diameter. Overlying skin was normal. Family history was not significant. There was no lymphadenopathy. Physical examination was unremarkable except for the region of the mass.

INVESTIGATIONS

Chest x-ray revealed no abnormality. The mass was excised and submitted for histopathological examination. Grossly, it was smooth, greyish white in colour. Histologically, the tumour was composed of sheets and nests of cells with uniform cytomorphology, including typical round cells with clear cytoplasm and well-defined borders interrupted by vessels of varying size and frequent mitotic figures (>5 mitotic figures/50 high power fields) were noted (figures 1 and 2). There were tumour plugs in the lumen of several vessels. Immunohistochemistry showed cytoplasmic and membranous expression of smooth-muscle actin, vimentin and focal reactivity for desmin (figure 3). The tumour was characterised by superficial location, relatively large size and high mitotic activity. The findings appeared to be consistent with the diagnosis of GT of uncertain malignant potential.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of atypical GT is broad, and to some extent, site dependent. In the skin, atypical GTs are most likely to be confused with the more common primary cutaneous round cell tumours, such as Merkel cell carcinoma, eccrine spiradenoma and melanoma, as well as rarer tumours such as cutaneous extraosseous Ewing sarcoma/primitive neuroectodermal tumour (PNET) and neuroblastoma.[5] Merkel cell carcinomas and eccrine spiradenomas differ from atypical GTs in that they express cytokeratins, including cytokeratin 20 in Merkel cell carcinomas. Muscle actin expression may be seen in eccrine spiradenoma, but only in basal cells.[6] Demonstration of S-100 protein expression and HMB-45 positivity

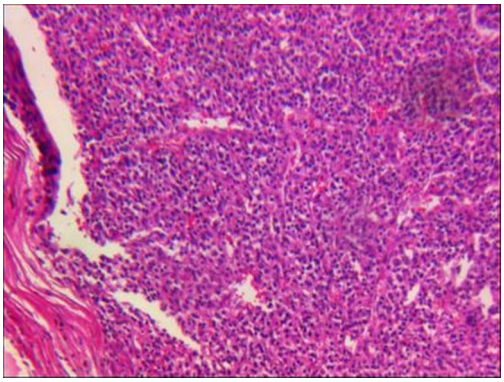

Figure 1 Section shows neoplastic round cells with well-defined borders interrupted by vessels (H&E ×10).

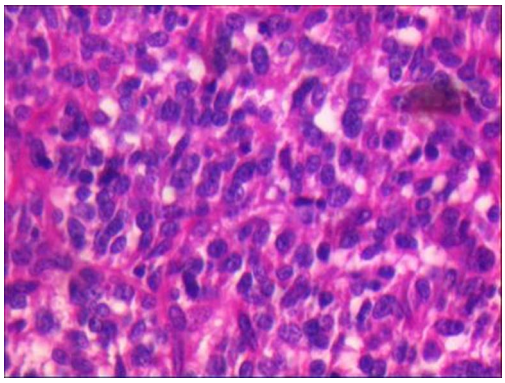

Figure 2 Section shows neoplastic cells with frequent mitotic figures (H&E ×40).

should allow the distinction of malignant melanomas from GTs, because GTs are seldom S-100 protein positive and are never HMB-45 positive.[6] Cutaneous ES/PNET would not be expected to express muscle actins and does not demonstrate pericellular type IV collagen expression.[7]

Unlike GTs, cutaneous neuroblastomas express markers of neural differentiation, such as neurofilament proteins, chromogranin and synaptophysin. Histological distinction between GT and nodular hidradenoma may present a difficult diagnostic problem. A helpful feature in distinguishing GT from hidradenoma or other adnexal tumours is the intimate localisation of glomus cells around blood vessels at the periphery of the tumour. Also, GT lacks ductular differentiation and any epithelial mucin production. Immunohistochemistry may be diagnostically useful, because hidradenomas typically stain for cytokeratin, and frequently express carcinoembryonic antigen and epithelial membrane antigen, features that the GT lacks.[8]

TREATMENT

The patient underwent wide local excision and surgical margins were free.

OUTCOME AND FOLLOW-UP

Three months later, he was presented with recurrence in the tumour bed. During his metastasis work-up, we noticed bilateral pulmonary metastasis (figure 4). The patient underwent wide local excision. Again microscopic examination was compatible with GT of uncertain malignant potential. Undoubtedly, the clinical course of the disease looked unfavourable, but histopathology alone did not allow for diagnosing glomangiosarcoma, so the final diagnosis was clinically malignant (metastasising) atypical GT. The patient received chemotherapy (paclitaxel (135) mg/m^2 on day 1 and gemcitabine (1000) mg/m^2 on days 1 and 8 on every 21 days regimen).

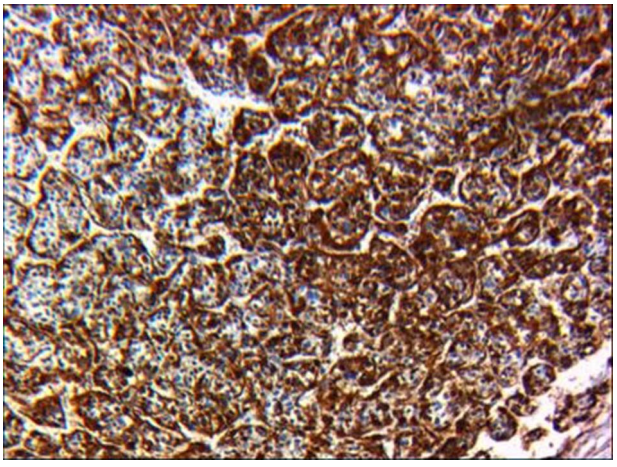

Figure 3 Section shows tumoral cells revealing smooth-muscle actin reactivity (Immunohistochemical staining ×10).

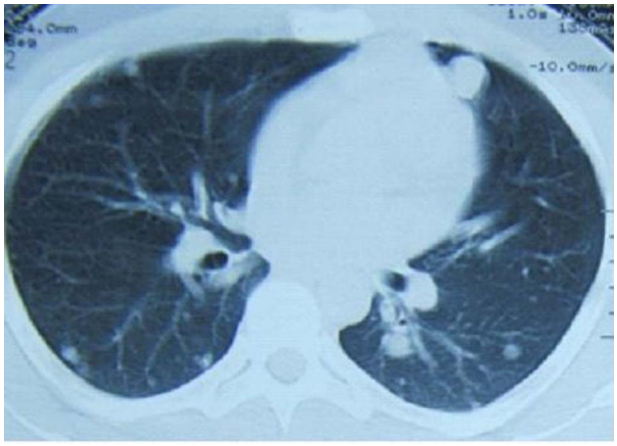

Figure 4 CT scan reveals bilateral pulmonary metastasis.

DISCUSSION

GTs are uncommon, comprising 1.6% of 500 consecutive soft tissue tumours reported from the Mayo Clinic.[9] The majority of GTs are small, benign neoplasms that occur in the dermis or subcutis of the extremities.[1] However, occasional GTs may show unusual clinical features, such as large size, deep soft tissue or visceral location, infiltrative growth pattern or multicentricity.[10] Over the years, the malignancy of GTs has been more of a concept than a reality. Although several histologically malignant GTs have been reported, biological confirmation of malignancy in these cases was lacking,[1] probably because many were superficial and therefore cured by therapy. A second compounding factor was the fact that the rare malignant GTs that produced metastases lacked a benign glomus component, and hence the accuracy of the diagnosis was questioned. The first report of a clinically malignant (ie, metastatic) GT is that of Brathwaite and Poppiti.[11] The new WHO classification categorises these tumours into GT, GT of uncertain malignant potential and malignant GT.[12] The diagnostic criteria of malignancy includes (1) size greater than 2 cm and a subfascial location, (2) atypical mitotic figures and (3) moderate-to-high nuclear grade and five or more mitotic figures per 50 high power fields.[3] Some GTs fail to meet the minimum criteria of malignancy but display features that are clearly beyond the realm of an ordinary GT. The first report of a clinically atypical infiltrating GT was in 1972,[13] in a case report of Lumley and Stansfeld. A classification of atypical GTs was proposed by Gould *et al* in 1990, with locally infiltrative tumours categorised into the following three groups: (1) locally infiltrative GT, which is cytologically bland with a frequent glomangioma appearance and possible recurrence; (2) glomangiosarcoma in benign GT; and (3) de novo glomangiosarcoma.[4] Enzinger[1] designate such lesions 'glomus tumour of uncertain malignant potential'. Most lesions falling into this category are superficial tumours with high mitotic activity and no significant nuclear atypia, or they are large or deep. In 2001, Folpe *et al*[3] reviewed 52 'atypical' or 'malignant'

GTs and evaluated tumour size, depth, growth pattern, cellularity, nuclear grade, number of mitotic figures per 50 high power fields, atypical mitotic figures, vascular space involvement and necrosis to define criteria for malignancy. Follow-up revealed seven recurrences, eight metastases, and seven related mortalities. Five-year cumulative metastatic risk increased significantly for tumours with a deep location, a size of more than 2 cm, and atypical mitotic figures. Mitotic activity of more than five mitoses/50 high power fields, high cellularity, the presence of necrosis and moderate-to-high nuclear grade approached but did not reach significance. The tumour in the present case was characterised by a relatively large size and high mitotic activity. On the basis of these criteria and the lack of atypical mitotic figures, at first, we graded the tumour as 'glomus tumour of uncertain malignant potential'. However, after recurrence (3 months later) and bilateral pulmonary metastasis, we considered it as clinically malignant (metastasising) atypical GT. Metastasising GTs are rare and according to some reports, GTs of uncertain malignant potential did not metastasise.[3] However, it was not true about our patient. In addition, Folpe reported that high nuclear grade, infiltrative growth and vascular space involvement were not associated with metastasis, however in our case, vascular invasion was present, even in the initial specimen, which shows vascular invasion is an ominous finding. It seems that the category of 'glomus tumour of uncertain malignant potential' should be defined more precisely.

Although the follow-up of GTs of uncertain malignant potential has been claimed to be good, however the number of cases is small and the follow-up is relatively short. Undoubtedly, the clinical course of the disease in the presented case looked unfavourable and aggressive clinical behaviour is expected to some extent. Our patient underwent wide surgical resection with free margins and received chemotherapy. He is currently undergoing appropriate clinical follow-up.

Learning points

- Although usually benign, some aggressive variants of glomus tumour have also been reported.
- In the light of its varied differential diagnoses, the possibility of atypical glomus tumour should be kept in mind, even in tumours which occur at sites where glomus cells are sparse or unrecognised.
- The label of glomus tumour of uncertain malignant potential warrants close follow-up.
- The infrequency of these tumours makes their diagnosis challenging, however careful examination, paired with immunohistochemical studies, can lead to correct diagnosis.
- Although the follow-up of glomus tumours of uncertain malignant potential has been claimed to be good, sometimes the clinical course of the disease looked unfavourable and aggressive.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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