Case Report

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A Large Malignant Glomus Tumor involving Bones and Soft tissues of the Wrist: A Rare Case Report

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Abstract

Malignant glomus tumor, involving the bones is rare. A 24-year-old lady was referred with a gradually increasing recurrent tumor over her right wrist since 7 years, for which she previously underwent incomplete resections. Presently, a 9cm x 4cm-sized swelling was noted on her right wrist. Plain radiograph revealed an osteolytic lesion in her distal radius, extending into the adjacent carpal bones and soft tissues. Microscopy revealed a tumor comprising round to oval cells arranged around blood vessels; focally displaying moderate nuclear atypia, with mitoses ranging from 2-3/10 high-power-fields, including atypical forms; focal necrosis along with bone infiltration. Immunohistochemically, the tumor cells expressed smooth muscle actin. Ki-67/MIB1 highlighted 30% tumor nuclei. Computed tomogram revealed multiple bilateral pulmonary metastases. This forms the third case of a large malignant glomus tumor, involving bones and soft tissues. It underscores the value of a timely diagnosis, followed by wide-excision in such cases, as these tumors can metastasize. Differential diagnoses are discussed herewith.

Keywords: Glomus Tumor; Malignant Glomus Tumor; Unusual Soft Tissue Tumors; Uncommon Bone Tumors; SMA.

Introduction

Glomus tumor forms less than 2% soft tissue tumors and comprises cells resembling modified smooth muscle cells of the glomus body. Most cases occur in the distal extremities of young adults, especially in the subungual region, hand, wrist and foot [1]. Rare cases have been reported within the bones [2,3]. Histopathologically, a glomus tumor may be benign, atypical or malignant subtype [1]. Malignant glomus tumor in musculoskeletal sites has been rarely documented [1, 4-7].

Case Report

A 24-year-old lady was referred to us with a gradually increasing tumor over her right wrist since 7 years. Previously, she underwent tumor excisions with unclear resection margins, for smaller lesions, on two occasions, 7 and 4 years back, respectively. Lately, she developed pain along with sudden increase in the tumor for which she underwent a biopsy six months back that was submitted to us for a review.

Presently, a 9cm x 4cm sized firm to hard tender swelling was noted on the radial aspect of her right wrist, involving the dorsal and palmar surfaces, along with healed scars on the volar aspect of her right hand, as a result of prior excisions [Figure 1a].

Recent plain radiograph revealed an osteolytic lesion in the distal radius, extending into carpal bones and adjacent soft tissues [Figure 1b].

Magnetic resonance imaging disclosed, a large lobulated, poorly marginated, enhancing lesion measuring 6.6cm x 6.5cm x 9.7cm on the lateral aspect of right wrist, involving the lower end of radius, infiltrating into adjacent muscles and subcutaneous planes; anterolaterally extending up to the base of first and second metacarpals, along with mild erosion of

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the scaphoid and trapezium. The lesion was seen indenting the medial and ulnar neurovascular bundles [Figures 1c-d].

Histopathological Findings

Microscopy showed a tumor comprising polygonal cells with well-defined cell borders, arranged around blood vessels(pericytic). Focal areas displayed moderate nuclear atypia, prominent nucleoli; mitotic figures, ranging from 2-3 per 10 high power fields (hpfs), including atypical forms; focal tumor necrosis and bone infiltration [Figures 2b-d).

By immunohistochemistry, the tumor cells were diffusely positive for smooth muscle actin (SMA) in most areas, except focally in the malignant areas, while negative for desmin, CD34, AE1/AE3, EMA, CD10, S100-P and HMB45. Ki-67/MIB1 highlighted 30% tumor nuclei in the most proliferating tumor areas [Figure 3a-c]. Diagnosis of malignant glomus tumor was offered.

Six months post-biopsy, a transaxial helical computed tomography computed tomogram of thorax showed bilateral 3 to 6 mm-sized metastatic lesions in bilateral lungs [Figure 4].

In view of a large unresectable tumor with conspicuous bilateral pulmonary metastatic lesions, the patient was recommended best supportive care. She undertook few cycles of chemotherapy, elsewhere and is presently alive-with-disease.

Table 1: Literature review of malignant glomus tumors involving deep musculoskeletal sites, including soft tissues and bones

Sr No.	Authors (Year)	Age/Sex	Site	T Size	Treatment and Outcome
*1	Hiruta, et al[5] (1997)	44/M	Thigh (Femur and adjacent muscles)	NK	Wide excision. Free of disease (57 months)
2	Matsumoto, et al[6](2001)	16/F	Arm (muscles)	5 cm	Wide excision. Free of disease (21 months)
3	Folpe, et al[2] (2001)	63/M	Shoulder	5 cm	Re-excision. Mets (Lung, Bowel). DOD (1yr.)
		52/M	Arm	1 cm	Re-excision. Follow-up till 6 yrs.
		**38/M	Buttock	2.5 cm	Resection +adjuvant CT. Mets (Lung, Brain, Bone). DOD (9 mo.)
		*47/M	Vertebra(L5)	NK	
		37/M	Paraspinal	12 cm	Resection. Follow-up NK.
		38/M	Finger	0.5 cm	Resection. Follow-up till 1 yr.
		**39/M	Thigh	2.5 cm	Resection. Follow-up till 16 yrs.
		32/M	Foot	5.5 cm	Resection. Mets (Lung). DOD (1yr.)
		48/M	Buttock	5.8 cm	Re-excision. Follow-up NK.
		23/F	Ankle	10 cm	Resection. Recur (5yrs.), Mets (Mesentery)(1yr)AWD(19yrs.)
		61/M	Thigh	2.5 cm	Resection. Follow-up till 4 yrs. Resection. Mets (Lung). DOD (3yrs.)
3	Khoury, et al[7] (2005)	48/F	Hand (muscles)	2.8 cm	Wide excision. Mets (Lung. Multiple B/L). AWD (8 months)
4	Terada, et al[8] (2011)	21/M	Hand (Deep-seated)	2.5	Resection. Recur(12 months)
*5	Present case (2014)	**24/F	Wrist (radius, carpal bones, soft tissues)	9 cm	Resection (twice). Large recur. Mets (Lung. Multiple B/L). AWD (7 yrs).

*: Tumors with bone involvement.
**: Cases with metastasis at presentation
NK: Not known, M: Male, F: Female, S/C: Subcutaneous, CT: Chemotherapy, Recur.: Recurrence, B/L: Bilateral, Mets. : Metastasis, DOD: Died-if-Disease, AWD: Alive with disease yr: year.

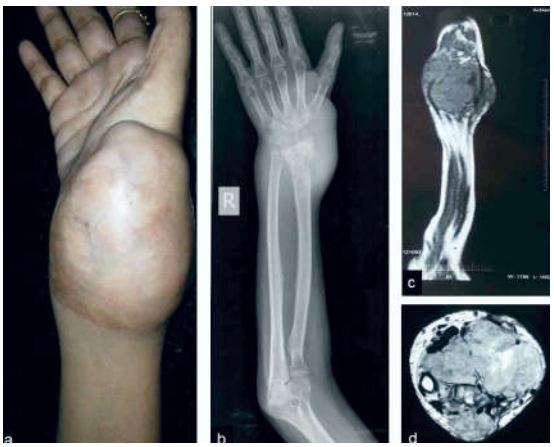

Fig. 1.(a) Clinical photograph revealing a large nodular tumor over the right wrist. **(b).** Plain radiograph revealing an osteolytic lesion in the distal radius with a wide zone of transition; a large soft tissue component, along with involvement of carpal bones. **(c)** T1-Sagittal **(d)** T2-Axial magnetic resonance imaging showing a large, lobulated poorly marginated, enhancing lesion involving distal radius extending to involving dorsal and palmar surfaces and extending up to head of 1st and 2nd metacarpal bones

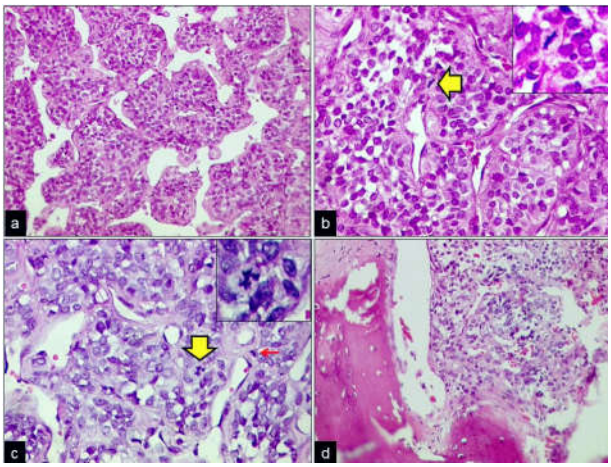

Fig. 2: Microscopy of malignant glomus tumor. **(a)** Round to oval cells with well-defined cell borders arranged around blood vessels. Hematoxylin and Eosin (H and E), x 200. **(b)** Higher magnification showing mild nuclear variation within tumor cells and scattered mitotic figures. H and E, x 400. **Inset:** Typical mitotic figure. (H and E) x. 1000 **(c)** Tumor cells with moderate nuclear atypia and scattered mitotic figures (arrow), including "atypical" forms (arrow head). H and E, x 400. **Inset:** Atypical mitotic figure. H and E, x1000 . **(d)** Tumor infiltrating the bone. H and E, x 100

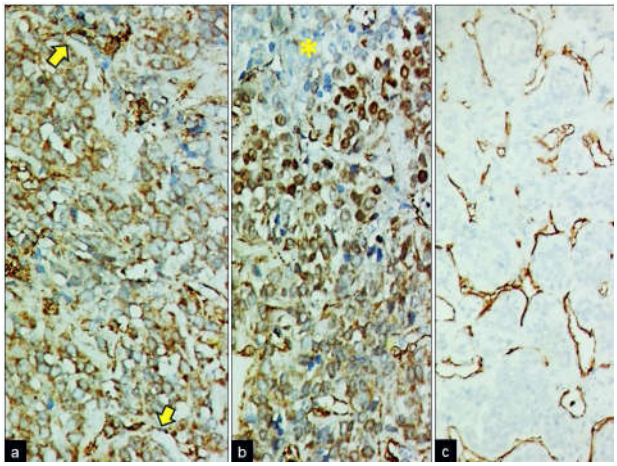

Fig. 3: (a) Diffuse smooth muscle actin (SMA) positivity. 3'-3'Diaminobenzidine, x 200. **(b)** SMA positivity in tumor cells with focal areas (marked with asterix) showing reduced staining pattern. Smooth muscles of interspersed blood vessels (arrow heads) acting as internal positive controls DAB x 400. **(c)** CD34 showing negative expression, highlighting interspersed "hemangiopericytoma-like" vasculature. DAB x 200

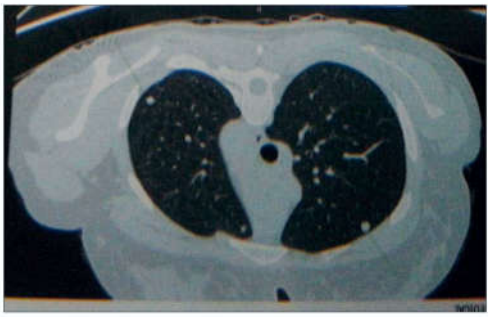

Fig. 4: Computed tomography scan showing multiple metastatic lesions in bilateral lungs

Discussion

Glomus tumor constitutes as one of the pericytic (perivascular) tumors [1]. Malignant glomus tumors or glomangiosarcomas are mostly documented in skin, subcutaneous tissues and visceral sites and rarely in musculoskeletal sites [1,4-9]. In the largest documented series, 11 out of 32 such cases were identified in the deep tissues, including musculoskeletal sites, with age ranging from 23-63 years; male preponderance and tumor size ranging from 0.5-12 cm. Only a single case was identified in the bone (L3 vertebra) [1]. To the best of our knowledge, the present case forms the third case of a malignant glomus tumor, involving bones and soft tissues (Table 1) [1, 4] .

Characteristic histopathological features and SMA immunoreactivity were helpful in forming an objective diagnosis in the present case. Differential diagnoses included a hemangiopericytoma/solitary fibrous tumor, synovial sarcoma, metastatic renal cell carcinoma (RCC) and a perivascular epithelioid cell tumor (PEComa). While lack of CD34 immunostaining ruled out the former, absence of AE1/AE3 and EMA(epithelial markers) along with BCL2 negativity ruled out a synovial sarcoma. Lack of epithelial markers and CD10, with unremarkable abdominal imaging ruled out a metastatic RCC. HMB45 and Melan A negativity ruled out a PEComa.

Folpe *et al* [1] described two histopathologic forms of malignant glomus tumors. In the first form, the malignant component resembles a leiomyosarcoma or fibrosarcoma. The second form consists of sheets of highly malignant-appearing round cells. They designated malignant glomus tumors as those occurring in deep location with size exceeding 2cm, or tumors characterized by atypical mitotic figures, or with moderate to high nuclear grade and ≥ 5 mitoses/ 50 hpfs. Symplastic glomus tumors display a high nuclear grade in the absence of any other malignant feature. Tumors lacking criteria for malignant glomus tumor or symplastic glomus tumor, but with high mitoses and superficial location only; or large size only; or deep location only are labelled as "glomus tumors of uncertain malignant potential". The importance of identifying a malignant glomus tumor relates to its relatively aggressive clinical course with metastasis and death in 38% cases. In another study, the authors observed metastasis in 12 out of 45 (26.6%) previously documented malignant glomus tumors of skin and soft tissues [6]. Apart from the aforementioned histopathological features, presence of a large, destructive, recurrent tumor mass, leading to lung metastasis were indicators of malignancy in

the present case. There has been documentation of malignancy in a glomus tumor in the clinical context of a superficial typical glomus tumor [8]. Invariably, atypical or malignant glomus tumors have a rim of benign-appearing glomus tumor, like the present tumor [1]. Probably our patient initially harboured a benign and / or an atypical glomus tumor that eventually became malignant. Recently, a case was documented that histopathologically fulfilled criteria of a glomus tumor of uncertain malignant potential, but eventually resulted in pulmonary metastasis and was designated as a malignant glomus tumor, treated with local wide-excision, and adjuvant chemotherapy [9]. Therefore, cases with atypical features or with "uncertain malignant potential" should preferably undergo a timely wide-excision and follow-up. In view of a large recurrent, unresectable tumor with multiple pulmonary metastases, the present case was recommended "best supportive care". Presently, after undergoing few cycles of chemotherapy, she is AWD. Literature review of similar cases forecasts a grim prognosis [1].

Lately, *NOTCH2* rearrangement has been identified in malignant glomus tumors [10]. This would further provide additional insights towards targeted therapy, especially in unresectable and metastatic lesions.

To conclude, a malignant glomus tumor involving bones and soft tissues is extremely rare. This should be identified from amongst its mimics, in view of different treatment implications. Large, deep-seated glomus tumors have more chances of malignancy. Cases with "atypical or malignant" clinicopathological features should undergo a timely wide-excision, metastatic "work-up" and follow-up.

Conflict of Interest Statement

I declare that I have no conflict of interest.

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