# Cutaneous soft tissue tumours: an update on tumours with perivascular and myoid differentiation

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## Abstract

Cutaneous tumours showing pericytic features show a wide morphological spectrum with differentiation towards glomus cells, haemangiopericytomatous areas and outright myoid differentiation. This tumour group includes glomus tumour and its variants, myofibroma, myofibromatosis, myopericytoma and angioleiomyoma. The majority of these tumours are benign but criteria for malignancy are only poorly established. In the skin, malignant examples are particularly rare. Familiarity with these tumours and their wide histological range is important to avoid misdiagnosis as other mesenchymal neoplasms with more aggressive behaviour. This article emphasizes the clinical and histological features of the cutaneous tumours with pericytic differentiation. It also includes a discussion of cutaneous myoid tumours for which they may readily be mistaken.


**Keywords** glomus tumour; glomangioma; leiomyoma; leimyosarcoma; mesenchymal; sarcoma

## Introduction

The pericyte is a specialized contractile cell surrounding the endothelial cell layer of small vessels and capillaries. Tumours with pericytic differentiation show a wide morphological range and include glomus cell tumour and glomangioma, tumours with haemangiopericytomatous features, myofibroma and myopericytoma, and angioleiomyoma showing overt myoid differentiation at the opposite end of the spectrum.[1–5] These tumours share a perivascular proliferation of tumour cells, often in a concentric arrangement. Furthermore, they show significant morphological overlap and precise categorization is not always possible. These tumours are currently regarded as different morphological expressions of a single tumour group. Their behaviour is largely benign with only rare cases of malignancy reported in the skin. Due to the significant morphological overlap with cutaneous smooth muscle tumours, these are also discussed in detail.

## Glomus tumour

**Clinical presentation:** glomus tumour is a distinctive and not uncommonly encountered mesenchymal tumour. The majority of cases are sporadic and present as small solitary nodules, measuring less than 1 cm, often showing a red to bluish discoloration.[6] The distal limbs of middle-aged adults are typically affected and subungual presentation is commonly seen.[6] Subungual tumours occur three times more frequently in females than in males.[7] The tumours are painful and sensitive to cold and touch. A familial presentation has also been reported.[8,9] This rare form presents in childhood and may be congenital. It is multifocal and includes glomangiomas (glomuvenous malformation) and diffusely infiltrative tumours (glomangiomatosis). The disease has an autosomal-dominant inheritance trait and is associated with inactivating mutations in the glomulin (GLMN) gene on chromosome 1p21-22.[10–12] Multifocal presentation may also be seen in patients with neurofibromatosis 1(NF-1).[13–16] Sporadic glomus tumours commonly show NOTCH gene rearrangement.[1]

**Histology:** glomus tumours are nodular and relatively circumscribed but unencapsulated tumours based within dermis and superficial subcutis (Figure 1a). Presentation in deep soft tissues or at visceral sites is exceptional. The tumours are composed of sheets of uniform round cells with distinctive cell borders, palely eosinophilic cytoplasm and centrally located nuclei with inconspicuous nucleoli (Figure 1b). Cytological atypia is not a feature and mitoses are rare. Additional findings, present in varying amounts, are small, thin walled vessels containing 'glomus cells' in a subendothelial distribution and myoid differentiation with fascicles of smooth muscle cells (Figure 1c). A myxoid or hyaline stromal background is observed in a subset of tumours.[17,18]

Based on their cytological and architectural features distinctive variants of glomus tumour are recognized:

**Glomangioma (glomuvenous malformation):** these tumours are mainly composed of dilated vascular spaces containing a subendothelial proliferation of glomus cells (Figure 1d).

**Glomangiomyoma:** in addition to a proliferation of glomus cells, these rare tumours are characterized by prominent smooth muscle differentiation adjacent to vascular spaces.

**Glomangiomatosis:** these tumours show infiltrative borders and represent angiomatosis with an additional proliferation of glomus cells.[19]

**Oncocytic glomus tumour:** in this variant, the glomus cells display more pronounced epithelioid features are brightly eosinophilic cytoplasm (Figure 1e).[20]

**Symplastic glomus tumour:** areas of degenerative cytological atypia characterize this variant. Glomus cells are enlarged and contain nuclei with prominent nucleoli (Figure 1f). Mitotic activity is however not increased.[19,21,22]

**Immunohistochemistry:** tumour cells express SMA and h-caldesmon. CD34 expression is observed in a subset of cases. Desmin expression is rare and focal. S100 and CD31 are consistently negative.

**Behaviour and prognosis:** glomus tumours are entirely benign and only rarely recur after surgical excision. Recurrence rates are highest for tumours with infiltrative margins (glomangiomatosis).

**Malignant glomus tumour:** Malignant glomus tumour is an exceptionally rare but aggressive disease, typically of deep soft tissues. The proposed diagnostic criteria for malignancy include:

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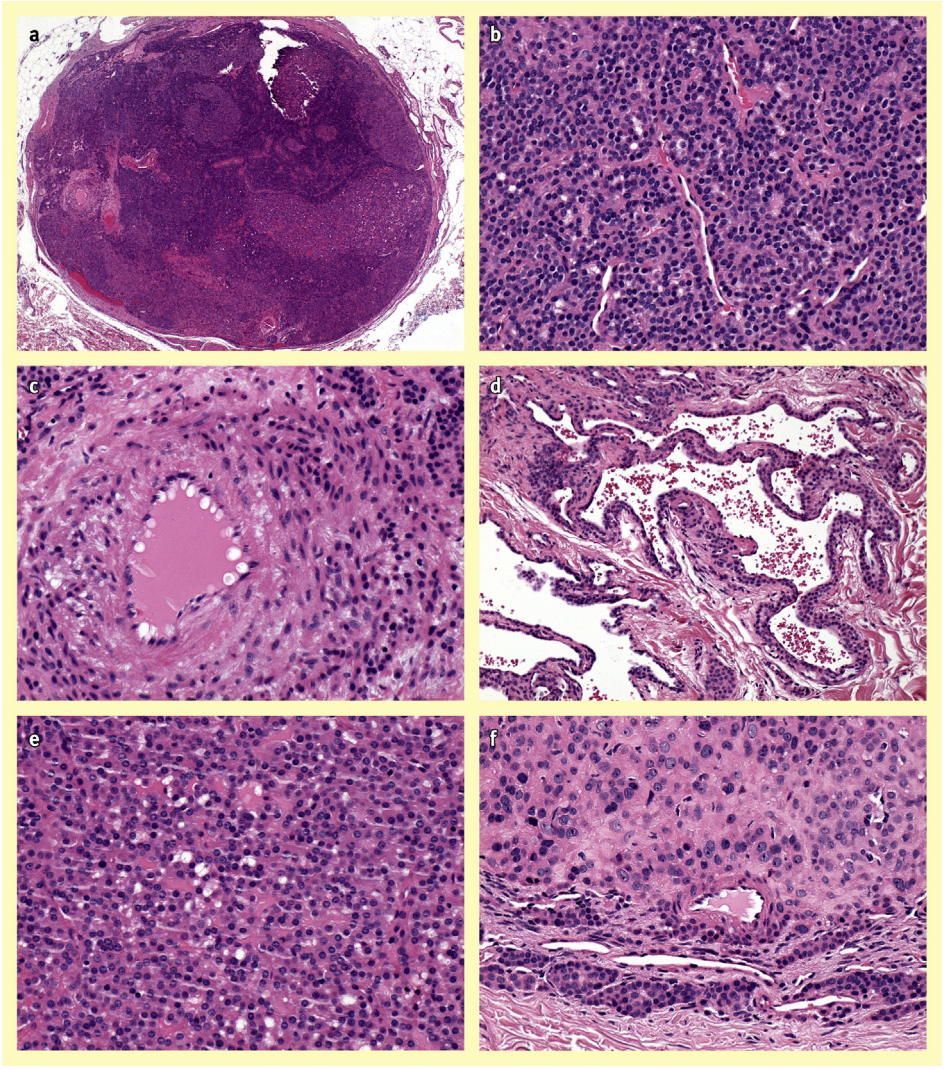


**Figure 1** Glomus tumour: This well-circumscribed nodular tumour is situated in the superficial subcutis (**a**). It is cellular and composed of uniform small round cells. Numerous small vascular channels are also present within this tumour (**b**). The tumours are arranged around pre-existing blood vessels and a focal spindle cell component is evidence of myoid differentiation (**c**). Glomangioma is characterized by a proliferation of dilated vascular channels with surrounding glomus cells (**d**). Occasionally, tumour cells show abundant eosinophilic cytoplasm (oncocytic change) (**e**). Marked cytological atypia but lack of mitotic activity characterizes the symplastic glomus tumour (**f**).

deep location and size >2 cm, or atypical mitoses, or moderate to high-grade nuclear atypia and >5 mitoses/50 HPF.[19] These tumours show a metastatic rate of 38%, and metastatic disease is associated with high mortality.[19] Tumours that do not meet outright criteria for malignancy but show high mitotic activity and superficial location only, or large size only, or deep location only, are currently regarded as '*glomus tumour of uncertain malignant potential*'.[19] They appear not to be associated with metastatic disease or mortality. Similar to its benign counterpart, malignant glomus tumours frequently show rearrangement of the *NOTCH* gene.[1]

**Differential diagnosis:** the solid variants of glomus tumour may easily be mistaken for melanocytic tumours but negativity for S100 or other markers of melanocytic differentiation allows reliable separation. Nodular hidradenoma shows significant morphological overlap. On careful examination, these tumours show true duct differentiation, which can be highlighted by EMA and CEA immunohistochemistry. In addition, glomus tumour lacks cytokeratin expression, which also excludes metastatic carcinoma. The identification of glomus cells allows distinction of glomangioma from cavernous haemangioma or vascular malformation.

## Myopericytoma

**Clinical presentation:** myopericytoma and myofibroma show at least some morphological overlap and they are currently regarded as a spectrum of the same disease rather than two distinct entities.[4,5] Myopericytoma affects a wide age range. It is most commonly observed in middle-aged adults with a slight male predilection.[3–5] The tumours present as small, painless and slowly enlarging nodules, typically less than 2 cm in diameter. The lower extremities are most frequently affected followed by the upper extremity, the head and neck area and the trunk.[3–5] The majority of lesions are solitary but multicentric presentation involving the same or different anatomic locations may