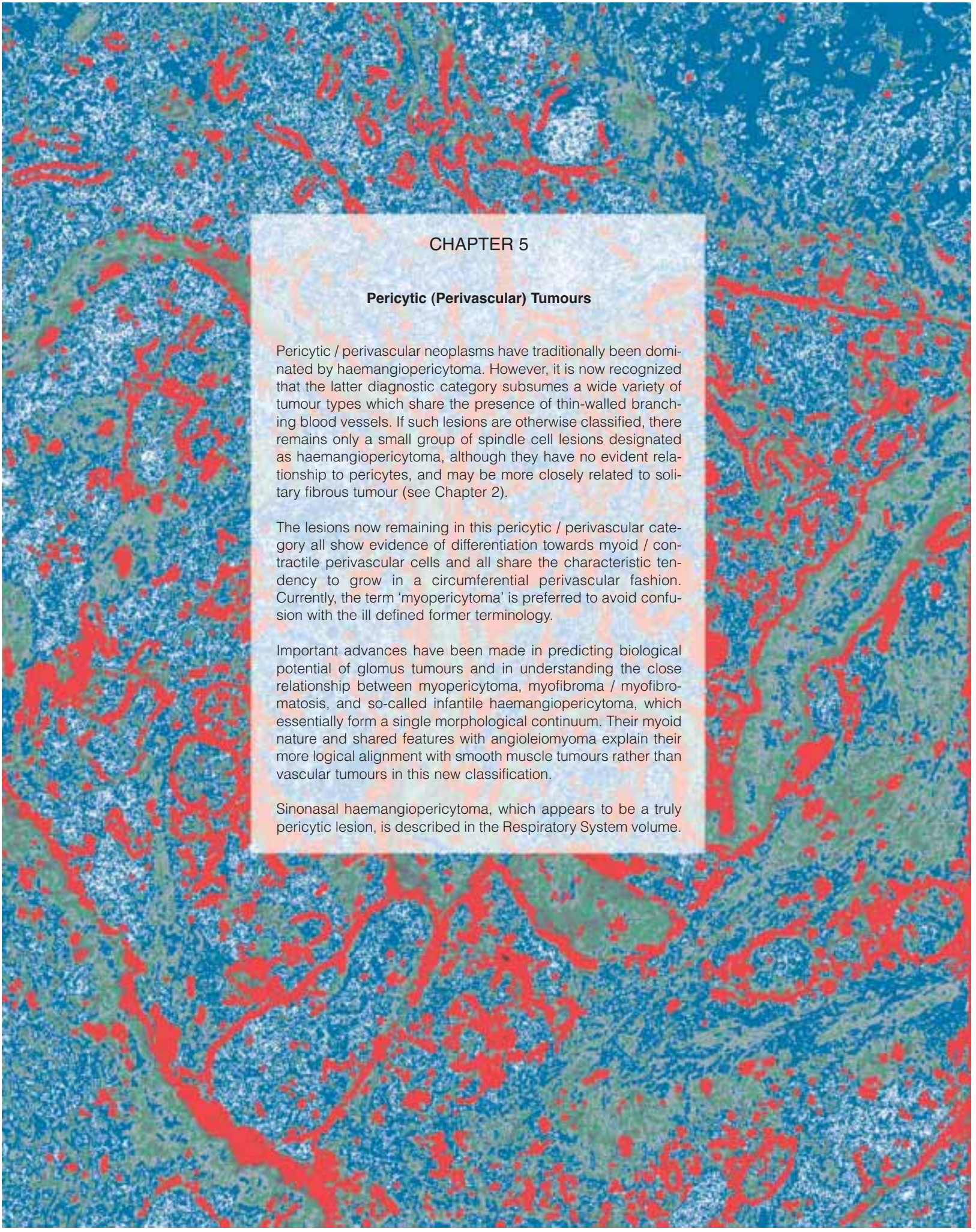


CHAPTER 5

Pericytic (Perivascular) Tumours

Pericytic / perivascular neoplasms have traditionally been dominated by haemangiopericytoma. However, it is now recognized that the latter diagnostic category subsumes a wide variety of tumour types which share the presence of thin-walled branching blood vessels. If such lesions are otherwise classified, there remains only a small group of spindle cell lesions designated as haemangiopericytoma, although they have no evident relationship to pericytes, and may be more closely related to solitary fibrous tumour (see Chapter 2).

The lesions now remaining in this pericytic / perivascular category all show evidence of differentiation towards myoid / contractile perivascular cells and all share the characteristic tendency to grow in a circumferential perivascular fashion. Currently, the term 'myopericytoma' is preferred to avoid confusion with the ill defined former terminology.

Important advances have been made in predicting biological potential of glomus tumours and in understanding the close relationship between myopericytoma, myofibroma / myofibromatosis, and so-called infantile haemangiopericytoma, which essentially form a single morphological continuum. Their myoid nature and shared features with angioleiomyoma explain their more logical alignment with smooth muscle tumours rather than vascular tumours in this new classification.

Sinonasal haemangiopericytoma, which appears to be a truly pericytic lesion, is described in the Respiratory System volume.

Glomus tumours

A.L. Folpe

Definition

Glomus tumours are mesenchymal neoplasms composed of cells that closely resemble the modified smooth muscle cells of the normal glomus body.

ICD-O codes

Glomus tumour	8711/0
Glomus tumours of uncertain malignant potential	8711/1
Malignant glomus tumour	8711/3

Epidemiology

Glomus tumours are rare, accounting for less than 2% of soft tissue tumours {1946}. Multiple lesions may be seen in close to 10% of patients. Malignant glomus tumours are exceedingly rare, comprising less than 1% of glomus tumours {697}.

Glomus tumours typically occur in young adults but may occur at any age. No sex predilection is seen, except in subungual lesions, which are far more common in women {2079,2177}.

Sites of involvement

The vast majority of glomus tumours occur in the distal extremities, particularly the subungual region, the hand, the wrist and the foot {2246}. Rare tumours have however been reported in almost every location, including the stomach {885}, penis {1132}, mediastinum {952}, nerve {293}, bone {1815} and lung {751}. Glomus tumours almost always occur in the skin or superficial soft tissues, although rare cases occur in deep soft tissue or viscera. Malignant glomus tumours are usually deeply seated, but may be cutaneous {697}.

Clinical features

Cutaneous glomus tumours are typically small (<1 cm), red-blue nodules that are often associated with a long history of pain, particularly with exposure to cold or minor tactile stimulation.

Deeply seated or visceral glomus tumours may have either no associated symptoms or symptoms referable to the involved organ.

Histopathology

Typical glomus tumours

Typical glomus tumours are subcategorized as "solid glomus tumour", "glomangioma", and "glomangiomyoma" depending on the relative prominence of glomus cells, vascular structures and smooth muscle. Glomus cells are small, uniform, rounded cells with a centrally placed, round nucleus and amphophilic to lightly eosinophilic cytoplasm. Each cell is surrounded by basal lamina, seen best on PAS or toluidine blue histochemical stains. Occasionally cases show oncocytic {1967} or epithelioid change {1737}.

Solid glomus tumours are the most common variant, comprising approximately 75% of cases {2242}. They are composed of nests of glomus cells surrounding capillary sized vessels. The stroma may show hyalinization or myxoid change. Small cuffs of glomus cells are often seen around small vessels located outside of the main mass. Glomangiomas, comprising approximately 20% of glomus tumours, are characterized by dilated veins surrounded by small clusters of glomus cells. Glomangiomas are the most common type of glomus tumour in patients with multiple or familial lesions. Glomangiomyomas, the least common subtype of typical glomus tumour, are characterized by an overall architecture similar to solid glomus tumour or glomangioma and by a transition from typical glomus cells to elongated cells resembling mature smooth muscle. In some glomus tumours a branching, haemangiopericytoma-like vasculature is present and such cases have been designated "glomangiopericytoma" {825}.

Glomangiomatosis

Glomangiomatosis is an extremely rare variant of glomus tumour with an overall architectural resemblance to diffuse angiomatosis (see page 161) {697, 823, 1294}. Glomangiomatosis is distinguished from angiomatosis by the presence of multiple nodules of solid glomus tumour investing the vascular walls. It is benign despite its infiltrative growth.

Symplastic glomus tumours

Symplastic glomus tumours show striking nuclear atypia in the absence of any other worrisome feature (e.g., large size, deep location, mitotic activity, necrosis) {697}. The marked nuclear atypia that characterizes these tumours is believed to be a degenerative phenomenon. All cases reported to date have behaved in a benign fashion.

Malignant glomus tumours (glomangiosarcomas) and glomus tumours of uncertain malignant potential

Histologically malignant glomus tumours are exceedingly rare and clinically malignant ones (e.g., metastatic) rarer yet. Prior to 2000, fewer than 20 histologically malignant and 2 clinically malignant tumours had been reported {21,54,247,823,885,952,953,1575, 2219,2220, 2255}. Criteria for the diagnosis of malignancy in glomus tumours were only recently elaborated {697}. The diagnosis of "malignant glomus tumour" should be reserved for tumours showing: 1) Size >2 cm and subfascial or visceral location; 2) Atypical mitotic figures; or 3) Marked nuclear atypia and any level of mitotic activity. These features frequently co-vary in a given case. A component of pre-existing benign-appearing glomus tumour is often but not always present. There are two types of malignant glomus tumour.

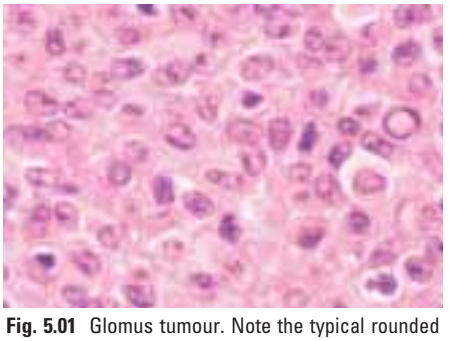


Fig. 5.01 Glomus tumour. Note the typical rounded cytomorphology and well defined cell membranes.

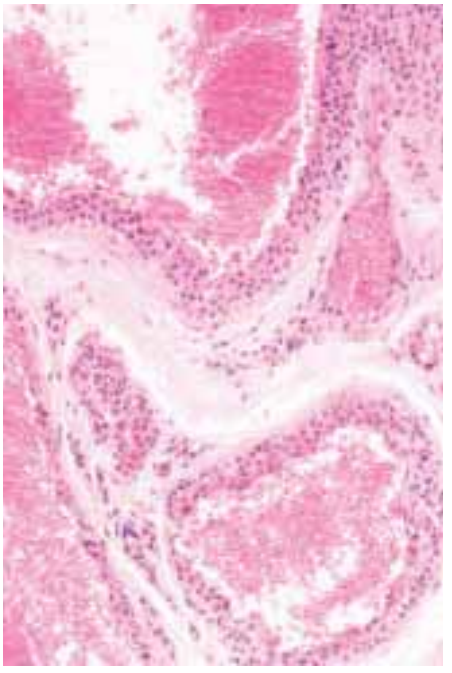


Fig. 5.02 Glomangioma. The lesion is composed of dilated vascular spaces, the walls of which contain several layers of glomus cells.

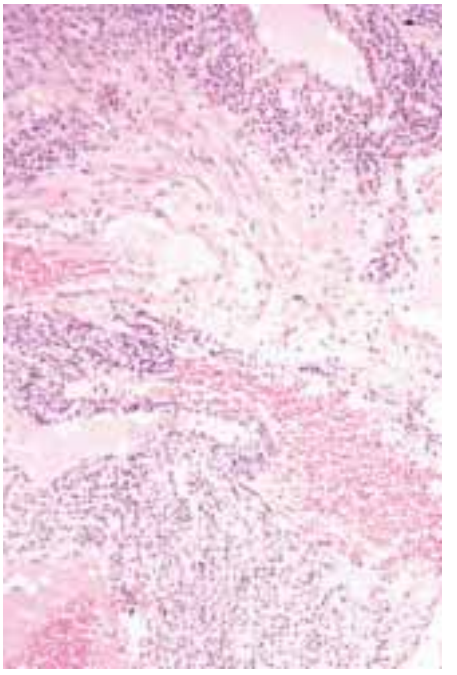


Fig. 5.03 Glomangioma, composed of dilated vascular spaces, the walls of which contain several layers of glomus cells.

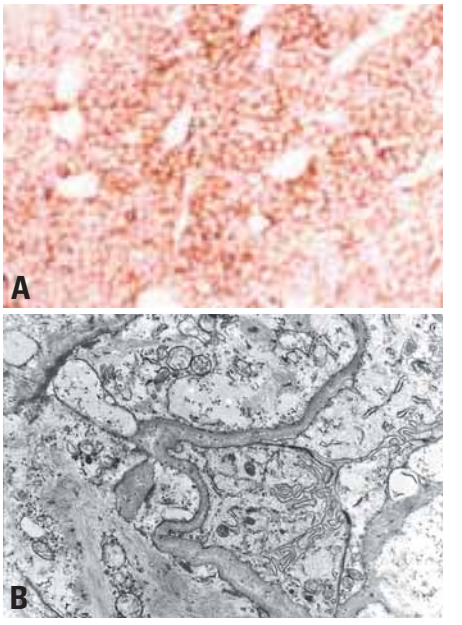


Fig. 5.04 Glomus tumour. **A** Tumour cells show consistently strong immunoreactivity for smooth muscle actin. **B** Ultrastructure showing prominent external lamina, pinocytotic vesicles and intracytoplasmic actin microfilaments.

In the first type, the malignant component resembles a leiomyosarcoma or fibrosarcoma. In the second type, the malignant component retains an overall architectural similarity to benign glomus tumour and consists of sheets of highly malignant appearing round cells. Immunohistochemical demonstration of smooth muscle actin and pericellular type IV collagen is required for the diagnosis of this second type of malignant glomus tumour, in the absence of a clear-cut benign precursor. Malignant glomus tumours are highly aggressive with metastases in approximately 40% of cases, resulting in the death of the patient {697}. Glomus tumours not fulfilling criteria for malignancy, but having at least one atypical feature other than nuclear pleomorphism should be diagnosed as "*glomus tumours of uncertain malignant potential*".

Immunohistochemistry

Glomus tumours of all types typically express smooth muscle actin and have abundant pericellular type IV collagen production. H-caldesmon is also positive. Other markers, including desmin, CD34, cytokeratin and S100 protein are usually negative {697}.

Ultrastructure

Ultrastructurally glomus cells have short interdigitating cytoplasmic processes, bundles of thin actin-like filaments with dense bodies and occasional attachments plaques to the cytoplasmic membrane and prominent external lamina {1449}.

Genetics

Multiple familial glomus tumours appear to have an autosomal dominant pattern of inheritance {164,884,1363}. An association between subungual glomus tumours and neurofibromatosis type I has been reported {1109,1602,1867}. The gene for multiple inherited glomus tumours has been linked to chromosome 1p21-22 {229,297}. The genetic events underlying sporadic glomus tumours are not known.

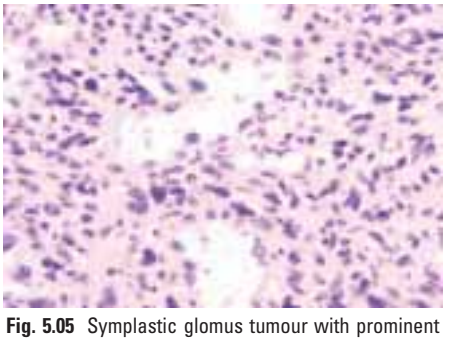
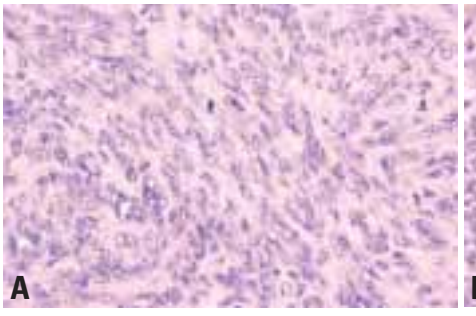


Fig. 5.05 Symplastic glomus tumour with prominent nuclear atypia but without mitotic activity.



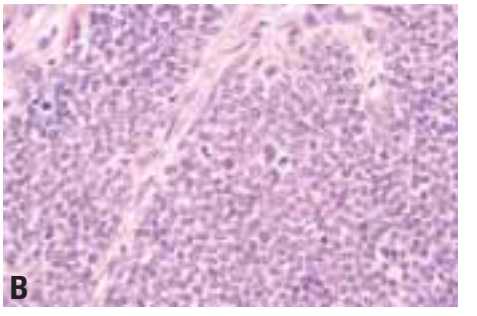


Fig. 5.06 **A** Malignant glomus tumour, spindle cell type. **B** Malignant glomus tumour, round cell type. Note the brisk mitotic activity.

Myopericytoma

M.E. McMenamin

Definition
Myopericytoma is a benign, generally subcutaneous tumour that is composed of oval-to-spindle shaped myoid appearing cells with a striking tendency for concentric perivascular growth. It is believed that the lesional cells show apparent differentiation towards perivascular myoid cells or myopericytes. Myopericytoma forms a morphological continuum with myofibroma, angioleiomyoma and so-called infantile haemangiopericytoma.

ICD-O code 8713/1

Synonyms
In the past, myopericytoma may have been diagnosed as a solitary myofibroma or "haemangiopericytoma."

Epidemiology
Myopericytoma arises most commonly in mid adulthood; however, lesions can arise at any age. Familial cases have not been reported.

Sites of involvement
Myopericytoma generally arises in subcutaneous tissue. There is a predilection for lesions to involve the distal extremities; however, tumours can also arise at other sites, including the proximal extremities and neck. It is likely that a wider site distribution will be described with increased recognition of this tumour.

Clinical features
Myopericytoma generally presents as a painless, slow-growing subcutaneous nodule that can be present for years. Some lesions are painful. Myopericytoma most commonly arises as a solitary lesion but multiple lesions are not infrequent. Multiple lesions generally arise metachronously and usually involve a particular anatomic region such as a foot.

Macroscopy
Myopericytoma tends to be a well circumscribed nodule measuring less than 2 cm in diameter.

Histopathology
Myopericytomas are unencapsulated and most lesions are fairly well circumscribed. Lesions are composed of relatively monomorphic oval-to-spindle shaped myoid appearing cells that show striking multilayered concentric growth around lesional blood vessels. The cells have eosinophilic or amphophilic cytoplasm. Lesions can be solidly cellular; however some cases have prominent myxoid stroma. In occasional cases, the spindle cells fall apart in the intervascular regions. In many cases, blood vessels outside the

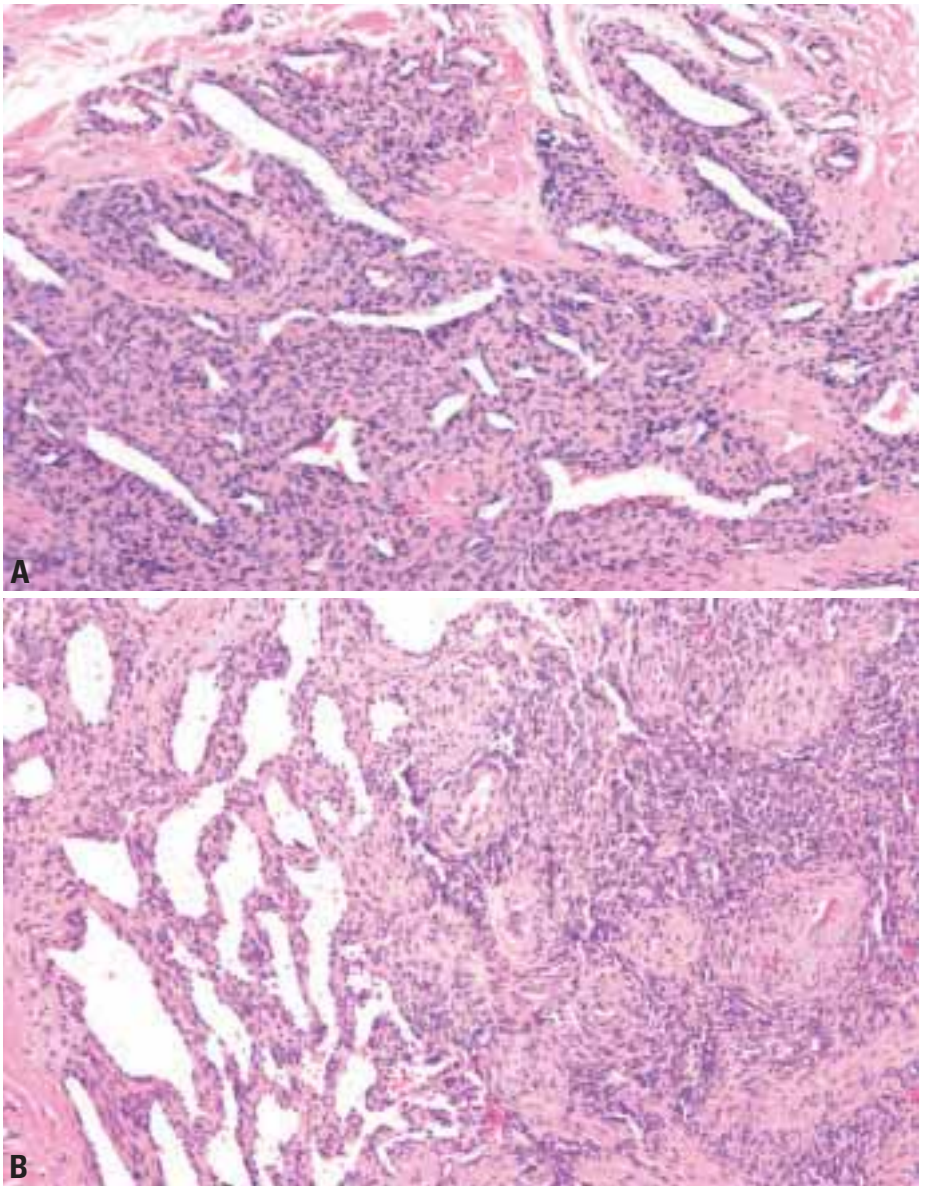


Fig. 5.07 Myopericytoma. **A** Typical proliferation of tumour cells around blood vessels at the periphery of this poorly circumscribed example. **B** Prominent gaping thin-walled blood vessels (left) and formation of whorls of spindle cells.

lesion also show concentric perivascular proliferation of spindle cells. Lesional blood vessels tend to be numerous and can be variable in size. In some cases, numerous thin walled branching or gaping blood vessels are present. Fasicular or whorled arrangements of spindle cells with abundant eosinophilic cytoplasm, embedded in myxoid stroma, are present in some cases. These areas are similar to the myoid whorls of myofibromatosis/myofibroma and invagination or bulging of these areas into the lumina of lesional blood vessels is frequently seen. Subendothelial proliferation of lesional cells in vessel walls is frequently seen and, indeed, myopericytoma can be located entirely within the lumen of a vein. Some myopericytomas have a component of cells with glomus-type features including cuboidal shape, distinct cell borders, clear to eosinophilic cytoplasm and central round nuclei and the term *glomangiopericytoma* can be used in such cases. In reality a spectrum of lesions exists that includes myofibromatosis, myofibroma, infantile haemangiopericytoma, glomangiopericytoma and myopericytoma {295,825}. Rarely, lesions show marked hyalinization, cystic change or focal metaplastic bone. Mitoses are not conspicuous (generally much less than 1/10 HPF). Coagulative necrosis has been described in a glomangiopericytoma; however, this appears to be a very unusual finding {825}.

Immunophenotype

The spindle cells in myopericytomas are positive for smooth muscle actin (SMA). SMA staining is generally diffusely positive, but can be only focally positive, generally in a perivascular distribution.

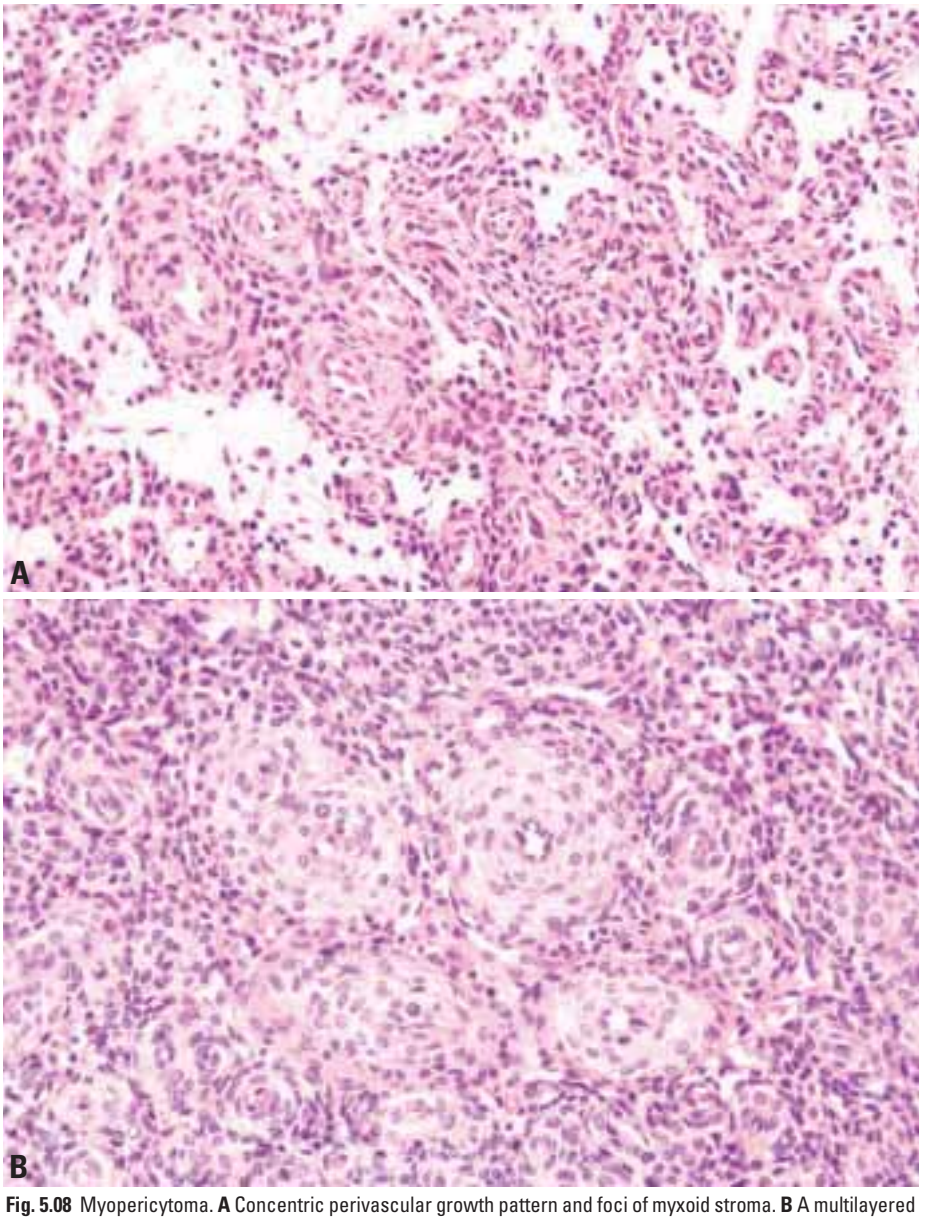


Fig. 5.08 Myopericytoma. **A** Concentric perivascular growth pattern and foci of myxoid stroma. **B** A multilayered concentric proliferation of spindle cells with myoid features around blood vessels.

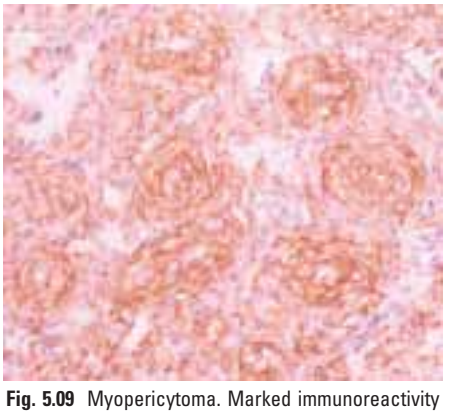


Fig. 5.09 Myopericytoma. Marked immunoreactivity for smooth muscle actin accentuates the perivascular growth pattern.

Occasional cases are focally desmin positive {825}. Focal CD34 staining by lesional cells occurs in some cases. Lesional cells are negative for S100 protein and most cases are negative for cytokeratin.

Prognostic factors

Most myopericytomas do not recur following excision. Recurrence may be related to poor circumscription of a lesion. Sometimes it is difficult to know whether a myopericytoma has recurred or whether a new lesion has developed in the same anatomic area. Very rare malignant myopericytomas exist {1383}.

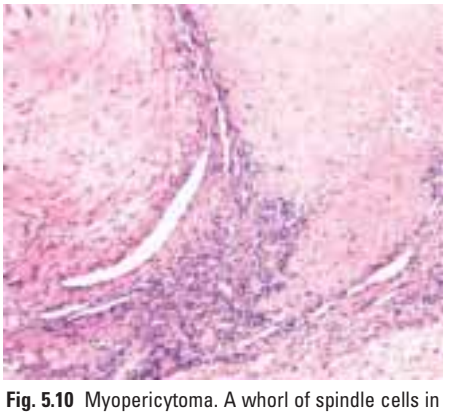


Fig. 5.10 Myopericytoma. A whorl of spindle cells in myxoid stroma bulges into the lumen of a blood vessel reminiscent of myofibromatosis / myofibroma.