Epithelioid perineurioma: an unusual variant

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ABSTRACT
An unusual epithelioid variant of perineurioma of the groin occurring in a 53-year-old man is described. The lesion appeared to be associated with a femoral nerve branch. The tumour was characterised by the presence of a syncytial proliferation of epithelioid cells, mimicking a meningioma of syncytial type. In addition there was a minor component of a conventional perineurioma. The tumour cells were EMA+; claudin-1+ and collagen type IV+. Bcl 2 was focally expressed. This case highlights the possibility of a common histogenetic pathway for meningiomas and perineuriomas. Although ultrastructural evidence of possible meningiomatous differentiation within an otherwise histologically typical perineurioma has been described, this is the first reported case of an unconventional epithelioid variant of perineurioma, histologically resembling meningioma.

Perineurioma, first described in 1978, is a relatively rare neoplasm in the spectrum of benign peripheral nerve sheath tumours that may present a morphological mimic of a number of benign and malignant soft tissue lesions. Perineuriomas are usually localised in skin and subcutaneous tissue but they may also be found in the deep soft tissue. These tumours can be broadly divided into two main types: the rare intraneural perineurioma, and a more common extraneural perineurioma of soft tissue. The extraneural type may be further divided into a conventional form, and a number of variants, including sclerosing and reticular types. Additional variants have been described, and knowledge of these is important as they may form part of the differential diagnosis of other mesenchymal tumours with different lines of differentiation, including clinically more aggressive neoplasms. We present a case of a perineurioma arising in the groin, which had a highly unusual epithelioid morphology that closely mimicked that of a meningioma. The epithelioid perineurioma may be a form of perineurioma with a range of differentiation akin to that seen in meningioma, reflecting the close relationship between perineurium and meningothelium. We believe that this is the first report of this pattern of differentiation in this tumour and we discuss the relationship between perineurioma and meningioma.

CASE REPORT
A 53-year-old man presented with a slowly growing painless lump in the groin. The lesion appeared to be associated with a femoral nerve branch. The patient had received radiotherapy for testicular teratoma 30 years previously. A 1 cm lesion was identified in the left kidney on CT scanning. There were no additional features to suggest an association with neurofibromatosis. As it was not possible to reach a secure diagnosis following initial biopsy of the groin mass, a therapeutic and diagnostic excision was performed. Macroscopically the mass measured 75×70×55 mm; it was well circumscribed and unencapsulated with a smooth outer surface and fleshy consistency. Histologically, the lesion was predominantly composed of a syncytial like proliferation of epithelioid cells with moderate amounts of eosinophilic cytoplasm and moderately pleomorphic nuclei with a very low mitotic index (2/50 high-power field). In some areas there were prominent intranuclear pseudoinclusions (fig 1). Psammoma bodies were not identified. The overwhelmingly predominant epithelioid component of the tumour was reminiscent of a meningioma of syncytial type.

A minor component of the tumour featured slender non-atypical spindle cells with tapering nuclei in an amorphous eosinophilic stroma. This minority component had morphological characteristics consistent with a conventional perineurioma (fig 2). The tumour contained a number of thin walled vessels, many of which had a perivascular space containing a few inflammatory cells. Immunohistochemical studies showed strong and diffuse positive staining for epithelial membrane antigen (EMA) (fig 3), claudin-1 and pericellular collagen type IV. Staining for Bcl 2 was positive in a patchy distribution. The tumour cells were negative for CD54, CD99, CD117, cytokeratins, S100 protein, HMB45, smooth muscle actin, desmin and H-caldesmon.

 ultrastructural examination of tumour tissue retrieved from paraffin embedded material was performed. This revealed an epithelioid cell proliferation showing interdigitating processes with junction formation and incomplete external lamina around many of the cells. The tumour cells displayed elongated nuclei with peripheral condensation of chromatin. The cytoplasmic processes appeared thin with focal vesicle formation. These did not have classical features of pinocytic vesicles; however, material had been reprocessed from paraffin and thus preservation was suboptimal.

Following simple excision of the tumour, the patient remains well without recurrence one year later.

DISCUSSION
We have reported an unusual epithelioid tumour with a meningiomatous appearance and intense EMA positivity arising in the groin. The morphology, and immunohistochemical and ultrastructural findings led us to believe that this is a variant of perineurioma. Indeed careful examination of the tumour revealed a minor component with more conventional perineuriomatous appearance. To our
knowledge there are no previous reports of a perineurioma with this peculiar epithelioid and meningiomatous morphology. The presence of epithelioid cells, however, has previously been reported in the cutaneous sclerosing form of perineurioma, where the author describes the presence of clusters of epithelioid cells giving a superficial similarity to epithelioid histiocytoma. However, in the current case the epithelioid morphology is the overwhelming feature.

Morphologically the differential diagnosis included an extracranial meningioma, a benign epithelioid peripheral nerve sheath tumour of soft tissue and smooth muscle tumour. The lack of any significant S100 positivity effectively excludes most peripheral nerve tumours with any Schwann cell component. Similarly the lack of staining for SMA or other smooth muscle markers rules out a tumour of myofibroblastic or smooth muscle origin. Perineural cells, which normally surround the nerve fascicles within a nerve, can be distinguished from Schwann cells by their immunoreactivity for EMA and lack of reactivity for S100 protein. Type IV collagen and laminin, two components of the basement membrane, also stain the abundant basal lamina elaborated by the perineural cells, as does the more recently described claudin-1, which is a tight junction associated protein. In our case the immunohistochemical findings are thus entirely consistent with a perineuriomatous histogenesis.

Given the morphology and immunohistochemical findings, the closest diagnostic differential is extracranial meningioma. Although true extracranial meningiomas probably arise from ectopic arachnoid lining cells, their presentation and localisation suggest at least two possible pathogenetic mechanisms. One is similar to that proposed for meningoceole, which complicates abnormalities of neural tube closure associated with relocation of meningeal tissue in the surrounding skin and subcutis of the scalp, forehead and paravertebral areas. The other is that proposed for extracranial meningiomas, which are situated in the vicinity of the sensory organs (eye, ear, nose) or along the paths of the cranial and spinal nerves. Accordingly meningiomas of soft tissue are unusual and probably arise from ectopic meningotheial cells; thus they typically arise in the soft tissues overlying the skull and spinal column. In this particular case, we consider that the location of the lesion in the groin effectively rules out soft tissue meningioma as a tenable diagnosis. Many perineuriomas from sclerosing spindle cell variants to this unusual epithelioid form are structurally similar to meningiomas. Therefore, morphologically it is not always possible to distinguish them. Problematic cases can be resolved by immunohistochemistry for EMA, S100, claudin-1, collagen type IV and cytokeratins. The positivity for EMA is seen in both perineurioma and meningioma, and hence is not a distinguishing marker. Claudin-1 and collagen type IV are of particular interest as they only stain the perineural cells. In contrast, meningiomas stain for S100, may show nuclear positivity for progesterone and focal reactivity for cytokeratin, in the absence of claudin-1 and collagen IV immunoreactivity.

The ultrastructural examination provides a gold standard for distinguishing these tumours. The meningiomas often display complex, jigsaw puzzle-like arrays of interdigitating cytoplasmic processes, containing abundant intermediate filaments, joined by desmosomes. On the other hand, perineuriomas have

Figure 1 Typical appearance of the tumour with a syncytial like appearance of epithelioid cells with copious eosinophilic cytoplasm. Occasional intranuclear inclusions are present. Note the thin walled vessel with a perivascular space. Original magnification x200.

Figure 2 A minority of the tumour showed areas more typical of perineurioma (bottom right) admixed with the dominant epithelioid component (top left). Original magnification x200.

Figure 3 Intense and diffuse positivity for EMA. Negatively stained vessels are shown as negative internal control. Original magnification x200.
characteristic cytoplasmic processes with prominent pinocytotic vesicles. These cytoplasmic processes are covered by an external lamina and are joined by tight junctions. Thus despite the unusual morphology of the lesion, the immunohistochemical findings and other features suggest that this case represents an unusual form of soft tissue perineurioma. Perineuriomas are rare tumours derived from normal perineurium. They are usually, but not always, located superficially. The relationship of meningiomas to perineuriomas is interesting as the perineurium is in continuity with the pia mater of the central nervous system. Furthermore, both tumours may show cytogenetic abnormalities of chromosome 22 and deletion of the NF2 gene. Meningiomas are morphologically diverse. They feature a spectrum of appearances that show a morphological overlap with perineurioma. Further evidence of a link between the two tumours is provided by Castellvi et al, who reported a perineurioma from the mesentery that, on ultrastructural analysis, showed both meningiomaticous and perineuriomaticous differentiation, although the light micrograph provided with their report shows the storiform morphology typical of a perineurioma.

In summary, we wish to draw attention to a case of a rare type of perineurioma with peculiar epithelioid features that shows morphological overlap with those of the syncytial type of meningioma. In our opinion, this lesion has sufficient light microscopic, immunohistochemical and ultrastructural features to propose it as a distinct variant of perineurioma. We believe that this is the first report of such a variant. This case raises the possibility that meningiomas and perineuriomas may partly share a common histogenetic pathway.

Competing interests: None.

Patient consent: Obtained.

REFERENCES