Meningiomas do not express CD117 (KIT)

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Sir: The transmembrane receptor CD117 (KIT) has been shown to be constitutively expressed in gastrointestinal stromal tumours (GISTs), in most cases owing to activating mutations in the corresponding c-kit gene and resulting in increased tyrosine kinase activity of the KIT protein. The knowledge of this pivotal signalling pathway in GISTs has been the basis for successful adjuvant treatment using Imatinib mesylate (Gleevec®), in particular in metastatic and unresectable GISTs.1 Subsequently, a variety of other mesenchymal and non-mesenchymal cells and tumours have been shown to express CD117, such as seminoma, mastocytosis, malignant melanoma and several soft-tissue tumours.2 In tumours of the central and peripheral nervous system, CD117 expression has been reported for malignant peripheral nerve sheath tumours,3 neoplastic Schwann cells,4 gliomas5 and medulloblastomas.6 In addition, a case of meningeval solitary fibrous tumour has been reported to be CD117+.7 However, the expression of CD117 in meningiomas has not previously been studied. Meningiomas comprise about 25% of primary brain tumours. Most meningiomas are slowly growing benign tumours, but atypical World Health Organization (WHO) grade II and anaplastic WHO grade III meningiomas with aggressive clinical behaviour and substantially reduced survival rates occur in about 15–20% and 1–2%, respectively,8 Despite surgery, treatment options for these aggressive meningioma variants are currently limited to radiation.9 Moreover, meningiomas have been reported to occur rarely in other parts of the body, e.g. in the lung,10 and may pose a diagnostic challenge, in particular if a spindle-cell pattern (fibroblastic type) dominates. Therefore, knowledge of CD117 expression in meningiomas is of interest both for differential diagnosis from other mesenchymal tumours as well as for potential new treatment options of atypical or anaplastic meningiomas.

Therefore, we have investigated 37 intracranial meningiomas of different WHO grade (13 grade I tumours, including six meningothelial, five fibroblastic and two transitional meningiomas, 15 grade II and nine grade III meningiomas) by immunohistochemistry using an antibody directed against human KIT [MBL, Nagoya, Japan; dilution 1 : 200; microwave pretreatment (20 min/ethylenediaminetetraaceticacid)]. A GIST of the stomach served as positive control; a negative control (omission of the primary antibody) was also included.

CD117 was detected in 0/13 grade I meningiomas, 0/15 grade II tumours and in only one grade III meningioma (1/9). In this tumour, immunoreactivity showed a membranous and cytoplasmic staining pattern of moderate intensity (Figure 1A). It was unevenly distributed, with a cluster-like arrangement of immunopositive tumour cells, constituting approximately 20% of all tumour cells. In each tumour, several CD117+ mast cells were found that also served as an internal control (Figure 1B). Whereas brain mast cells are CD117–, mast cells within the normal meninges, as in other body parts, usually express
Owing to the immunohistochemical data, mutational analysis of exons of the c-kit gene was pointless and was not done. Our data demonstrate that, to all intents and purposes, CD117 is not expressed in meningiomas, irrespective of WHO grade, which may be of significant diagnostic utility in difficult cases. Although one single meningioma showed focal CD117 expression, it can also be assumed that KIT signalling is not of biological importance in this tumour entity. However, this does not totally rule out the possibility that imatinib therapy may be of benefit in selected cases of meningioma with malignant behaviour and at an advanced stage, as this therapy also substantially affects the protein product of another receptor tyrosine kinase, the platelet-derived growth factor receptor alpha (PDGFRα)12 and meningiomas have been reported to express PDGFRα, correlated tumour location and tumour grade.13

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Figure 1. A, Focal cytoplasmic and membranous CD117 expression in one single anaplastic meningioma. B, CD117− meningioma. The positive mast cell (arrow) serves as an internal control.

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Mucinous bronchioloalveolar carcinoma of lung with a rhabdoid component—report of a case and review of the literature

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Sir: Bronchioloalveolar carcinoma (BAC) of the lung with rhabdoid cells has been reported in only three