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CORRESPONDENCE

Expression of MAP 2 by haemangioblastomas: an immunohistochemical study with implications for diagnosis

Sir,

Haemangioblastomas are uncommon central nervous system (CNS) tumours that usually occur in the cerebellum, brain stem or spinal cord of adults.[1] The tumours are composed of neoplastic stromal cells and abundant blood vessels, are low grade and occur sporadically or in association with von Hippel–Lindau syndrome. The histogenesis of the stromal cells is uncertain with glia, endothelial cells, arachnoid cells, fibrohistiocytic cells, neuroendocrine cells and neuroectodermal cells all proposed as origins.[2–6] Since it has been suggested that haemangioblastomas are glial or neuroepithelial in origin, we hypothesised that the stromal cells would express microtubule associated protein 2 (MAP 2), an antigen that is consistently expressed by neural and neoplastic glial cells. In addition, since studies have suggested that non-neuroendocrine carcinomas usually do not express MAP 2,[7,8] we hypothesised that its expression would distinguish haemangioblastoma from metastatic clear cell renal carcinoma. We further hypothesised that MAP 2 expression would distinguish haemangioblastoma from clear cell and microcystic meningiomas, two other tumours in the differential diagnosis.

With the approval of the Institutional Review Board of the University of Texas Southwestern Medical Center, formalin fixed, paraffin embedded sections of 48 haemangioblastomas, seven metastatic clear cell renal carcinomas, seven clear cell meningiomas and eight microcystic meningiomas were retrieved from the archives of the Department of Pathology, Division of Neuropathology (Table 1). Additional sections of the tumours were stained with an antibody to MAP 2 (monoclonal mouse IgG, 1:4000; Sigma-Aldrich, USA) using a Leica Bond-III automated stainer (Leica Biosystems, Germany). Expression of MAP 2 was defined as cytoplasmic staining of any intensity.

MAP 2 was expressed by stromal cells of 32 haemangioblastomas (67%); staining varied from focal to multifocal and weak to strong (Fig. 1). MAP 2 was not expressed by the neoplastic cells of any of the renal carcinomas or microcystic or clear cell meningiomas (Table 2).

Microtubule associated proteins are structural microtubule-binding proteins that bind to tubulin polymers to contribute to the regulation of microtubule functions.[9] The MAP 2 family is abundant in the mammalian CNS and composed of two groups of isoforms, high molecular weight, MAP 2A and 2B and low molecular weight, 2C and 2D. In the nervous system, high molecular weight forms are expressed in neurons while low molecular weight forms are also expressed in glia.[9] MAP 2 has also been identified by immunohistochemistry in cells of the adrenal medulla, pancreatic islets, exocrine pancreas, salivary glands and thyroid follicles, cells of monocyte/macrophage lineage, follicular dendritic cells and skeletal muscle.[7]

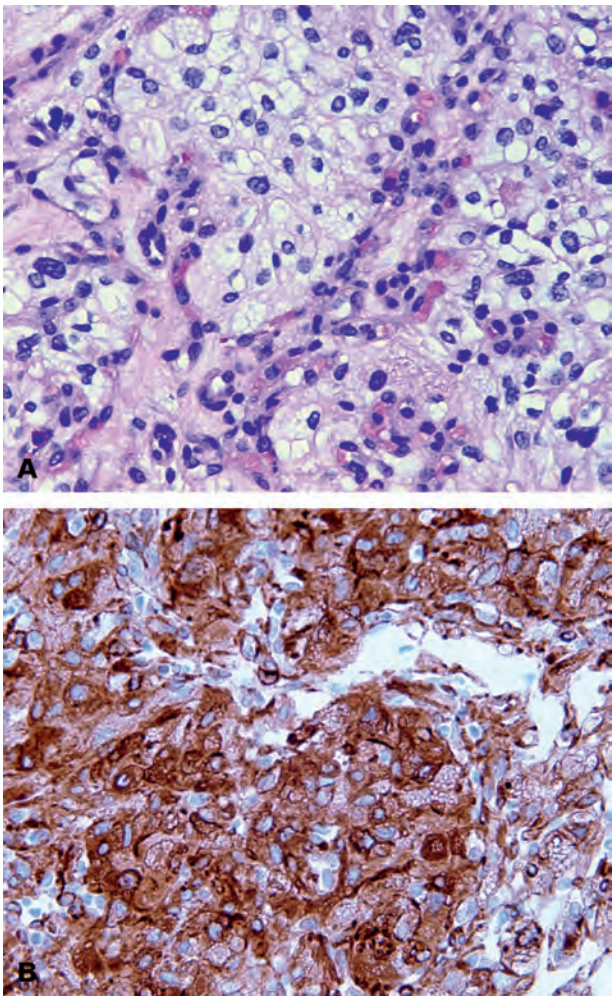

Fig. 1 (A) A cerebellar haemangioblastoma in a 47-year-old man (H&E). (B) Immunohistochemistry for MAP 2 with diaminobenzidine.

Among neoplasms, MAP 2 is expressed by cells of most neural, glial, neuroectodermal, neuroendocrine and neural crest tumours.[7,8] In this regard, MAP 2 has emerged as a sensitive marker of primary and also metastatic neuroblastoma, particularly in bone marrow.[7] Expression has also been observed in tumours of the haemangiopericytoma/solitary fibrous tumour family, glomus tumours, Kaposi's sarcoma, isolated cases of gastrointestinal stromal tumour, endometrial stromal sarcoma,

Table 1 Clinicopathological features of 70 CNS clear cell tumours

	M/F	Age, years	Cerebellum	Brain stem	Spinal cord	Supratentorial
Haemangioblastoma	26/22	15–78	28	2	11	6
Renal cell carcinoma	4/3	46–69	1	0	4	2
Clear cell meningioma	3/4	35–66	2	0	3	2
Microcystic meningioma	3/5	44–72	0	0	0	8

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Table 2 Expression of MAP 2 by CNS clear cell tumours

	Positive	Negative	% Positive
Haemangioblastoma	32	16	67
Renal cell carcinoma	0	7	0
Clear cell meningioma	0	7	0
Microcystic meningioma	0	8	0

liposarcoma and leiomyosarcoma and in tumours containing histiocytes/macrophages.[7]

Among non-neuroendocrine carcinomas, focal expression of MAP 2 was observed in six of 50 (12%) non-small cell lung carcinomas, although areas of neuroendocrine differentiation (confirmed by synaptophysin expression) were noted in four of the six tumours.[8] Other investigators noted punctate, apical expression in five of five papillary thyroid carcinomas and weak expression in one of five adenocarcinomas of the lung.[7] MAP 2 was not expressed by neoplastic cells in five of five papillary carcinomas of the kidney.[7]

We demonstrated MAP 2 expression by stromal cells in 32 of 48 (67%) haemangioblastomas by immunohistochemistry; MAP 2 was not expressed by neoplastic cells of seven clear cell meningiomas, eight microcystic meningiomas or seven metastatic clear cell renal carcinomas. In their study of the utility of MAP 2 expression in the diagnosis of low grade neuroepithelial tumours, Blumcke *et al.* detected MAP 2 in seven of 10 (70%) haemangioblastomas.[10] The studies suggest that MAP 2 is a moderately sensitive marker of haemangioblastoma and, in the CNS, highly specific inside of the usual differential diagnosis. Compared with inhibin, recent series[11–13] suggest that MAP 2 is less sensitive but, with regard to differentiation of CNS clear cell neoplasms, perhaps more specific.[13,14] We conclude that addition of MAP 2 to a panel of immunohistochemical stains may aid in the diagnosis of clear cell tumours of the brain and spinal cord.

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Patrick J. Malafronte
Ella M. LePage
Kimmo J. Hatanpaa
Dennis K. Burns
Charles L. White III
Jack Raisanen

Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Contact Dr J. Raisanen.
E-mail: jack.raisanen@utsouthwestern.edu

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Primary pulmonary hyalinising spindle cell tumour with giant rosettes

Sir,

Hyalinising spindle cell tumour with giant rosettes (HSCT) is an uncommon variant of low grade fibromyxoid sarcoma (LGFMS) which usually occurs in the deep soft tissues of the lower extremities in young to middle aged adults.[1] Primary soft tissue HSCT can metastasise to the lung[2] but primary pulmonary HSCT are very rare with only two cases described previously in the literature.[3,4] Herein we report a third case.

A 66-year-old woman, with a history of breast carcinoma and bronchiectasis, had a right lung nodule diagnosed as an incidental finding on chest X-ray. A positron emission tomography (PET) scan showed the nodule to be FDG avid with no FDG avid lesions elsewhere in the body. A right lower lobe thoracotomy and wedge excision was performed. The gross specimen showed a very well circumscribed, lobulated, firm, cream coloured tumour, 26 mm in maximum dimension, which had a gritty texture on sectioning.

The histological features were consistent with a HSCT. The tumour had well circumscribed margins and was composed of variably sized, well defined, prominent rosettes scattered throughout a relatively loose spindle cell background. The rosettes consisted of central hyalinsed collagenous material surrounded by palisading, mildly anisomorphic epithelioid cells (Fig. 1A). Areas of the tumour resembled a sclerosing epithelioid fibrosarcoma with epithelioid cells dispersed within a densely sclerotic hyalinsed stroma with pericellular clearing