CD34 and dural fibroblasts: the relationship to solitary fibrous tumor and meningioma

Abstract Intracranial solitary fibrous tumors (SFTs) are typically dural-based, CD34-positive neoplasms of uncertain histogenesis. We examined ten cases of meninges obtained at autopsy from patients with no history of neurological illness, head trauma, or neurosurgical intervention, and ten cases of typical meningiomas with attached dural margins not involved by tumor. All cases were immuno-stained with CD34. CD34 reactivity was noted in the long, thin delicate processes of dural fibroblasts preferentially located in the meningeal portion of the dura rather than the periosteal portion. No CD34 reactivity was identified in the arachnoid or pia mater, except in some endothelial cells. One supratentorial dural-based fibrous nodule and one SFT within the confines of the fourth ventricle showed strong and diffuse reactivity to CD34, bcl-2, and vimentin, and were negative for epithelial membrane antigen (EMA), S-100 protein, glial fibrillary acidic protein, smooth muscle actin, and desmin. We also describe a meningothelial meningioma within which a well circumscribed SFT-like nodule was embedded. The SFT-like nodule was strongly CD34 positive and EMA negative, and the meningioma was strongly EMA positive and CD34 negative. Fibroblasts of the dural border cell layer are attached to the underlying arachnoid, and their inclusion with arachnoidal stromal elements and pial-based tela choroidea during formation of choroid plexus interstitium may account for intraventricular SFTs. Our results suggest that SFTs and dural-based fibrous nodules derive from CD34-positive dural-based fibroblasts, and that CD34 reactivity in meningiomas may result from inclusion of dural fibroblasts within the neoplasm.

Keywords CD34 · Solitary fibrous tumor · Dural fibroblasts

Introduction

CD34 is a sialylated transmembrane glycoprotein that has been identified in myeloid progenitor cells in bone marrow, endothelial cells, and fibroblast-related mesenchymal cells [31, 44, 46]. Immunogold electron microscopy methods have localized CD34 to the cytoplasmic processes of fibroblasts [13, 14], and Northern analysis has detected CD34 mRNA in fibroblast cell lines [4, 21]. CD34 reactivity has been described in tumors of the central and peripheral nervous system, including meningiomas [10], neurofibromas [10, 47], and meningeal hemangiopericytomas [7, 10, 36], and in Antoni B but not Antoni A regions of schwannomas [47]. CD34 reactivity has been described in neoplastic and malformative lesions associated with chronic focal epilepsy, including gangliogliomas, astrocytomas, oligodendrogliomas, and glio-neuronal hamartomas [31].

Solitary fibrous tumors (SFTs) were initially described in 1931 by Klemperer and Rabin as pleural-based tumors arising in adults [19]. Since then, they have been described in numerous non-pleural locations [2, 9, 28, 29]. Intracranial and spinal SFTs typically are meningeal-based lesions that may mimic meningiomas clinically and radiographically [1, 6, 7, 8, 24, 32, 35, 37, 41, 42]. They have been reported as intraventricular lesions [43], and they rarely metastasize [30]. They are spindle cell neoplasms that histologically and immunohistochemically resemble pleural-based SFTs, and are characterized immunohistochemically by CD34, vimentin, and bcl-2 [1, 11, 17, 18] reactivity. The differential diagnosis of meningeal-based SFT includes fibroblastic meningioma, meningeal hemangiopericytoma, schwannoma, neurofibroma, and fibrosarcoma [7, 32, 36].

CD34 has shown its utility in the identification of intracranial SFTs. We describe the pattern of CD34 reactivity in normal meninges, and hypothesize that intracranial SFTs, dural-based fibrous nodules, and CD34-positive cells in meningiomas derive from fibroblasts of the dural border cell layer.
Materials and methods

Ten specimens of dura and leptomeninges obtained at autopsy from patients with no history of neurological illness, head trauma, or neurosurgical intervention, and ten meningiomas with intact strips of attached dural margins resected at Duke University Medical Center were reviewed. India ink was used to identify the periosteal aspect of the dura mater. The meningiomas were diagnosed and classified according to WHO criteria [35]. All were WHO grade I meningiomas and subtyped as follows: five meningothelial, two fibroblastic, two psammomatous, and one transitional type. Also reviewed were the three following surgical specimens: one SFT within the confines of the fourth ventricle from a 52-year-old male with a 2-month history of ataxia, one right frontal dural-based fibrous nodule occurring in a 55-year-old female with a complaint of vertigo, and one left parietal meningothelial meningioma with an embedded SFT-like nodule from a 43-year-old male with a chief complaint of headache. Paraffin blocks and original hematoxylin and eosin-stained slides were available for all cases.

For immunohistochemistry, sections from formalin-fixed paraffin-embedded tissue blocks were cut at 4–5 µm, placed on positively charged glass slides, deparaffinized in organic solvents, treated with methanolic H2 O2 to quench endogenous peroxidase activity, and rehydrated. Sections from the intraventricular SFT and the dural-based fibrous nodule were reacted with CD34 (1:30, monoclonal, Becton Dickinson, San Jose, Calif.), epithelial membrane antigen (EMA; 1:100, monoclonal, Dako, Carpinteria, Calif.), vimentin (1:150, monoclonal, Dako), glial fibrillary acidic protein (GFAP; 1:1,000, polyclonal, Dako), smooth muscle actin (1:400, monoclonal, Dako), desmin (1:50, monoclonal, Dako), S-100 protein (1:1,200, polyclonal, Dako), and bcl-2 (1:40, monoclonal, Zymed, San Francisco, Calif.). The meningioma with embedded SFT-like nodule was reacted with EMA, CD34, and bcl-2. All sections of the meninges were reacted with CD34 and EMA. Heat-induced epitope retrieval and pepsin enzyme-induced epitope retrieval were utilized for bcl-2 and vimentin, respectively. Negative controls consisted of either isotype-matched monoclonal antibodies to an irrelevant antigen or concentration-matched non-immune rabbit serum that were run in parallel with the positive reagents in each assay (Southern Biotechnologies, Birmingham, Ala.). Appropriate positive tissue controls were also tested in parallel with each assay. The unlabeled bound primary antibodies were linked with biotinylated secondary antisera (1:300; Vector Laboratories, Burlingame, Calif.), and detected with horseradish peroxidase-labeled streptavidin (1:800; Jackson Immuno Research, West Grove, Pa.). Immunoreactivity was visualized using diaminobenzidine as the chromogen, with Harris’ modified hematoxylin as the counterstain.

Results

The ten cases of meninges obtained from patients at autopsy and the ten cases of typical meningiomas with dural margins not involved by tumor showed CD34 reactivity in dural fibroblasts. The cytoplasmic CD34 reactivity was within long tapering dendritic processes arranged parallel to the long axis of the dura mater, and staining was preferentially more intense in the meningeal portion of the dura compared to the periosteal dura (Fig. 1). Others were oriented in a pattern surrounding blood vessels, similar to descriptions of dendritic interstitial cells [31]. Endothelial cells of intradural and intratumoral blood vessels were also CD34 positive. No CD34 reactivity was present in the leptomeninges except for occasional endothelial cells. Histological sections of the dural-based fibrous nodule showed a pattern of interweaving slender spindle cells embedded in dense fibroconnective tissue reminiscent of dura mater (Fig. 2a), and CD34 reactivity was prominent in tapered dendritic processes similar to those seen in normal dura mater (Fig. 2b). Magnetic resonance images of the intraventricular SFT showed a homogeneously enhancing mass within the fourth ventricle that pre-operatively was considered to be an intraventricular meningioma (Fig. 3a). The SFT exhibited elongated fibroblast-like spindle cells among dense collagen bundles (Fig. 3b), and reactivity to CD34 was strong and diffuse (Fig. 3c). Both the dural-based fibrous nodule and the intraventricular SFT were negative for EMA, S-100 protein, GFAP, smooth muscle actin, and desmin, and, in addition to CD34, showed strong and diffuse immunoreactivity to bcl-2 and vimentin. The SFT-like nodule embedded within a meningothelial meningioma (Fig. 4a) was composed of elongated cells with tapered ends reminiscent of dural fibroblasts, whereas the meningioma portion was composed of round to oval and plump meningothelial cells. The SFT-like nodule showed strong and diffuse reactivity to CD34 (Fig. 4b) and was EMA negative. The meningioma was strongly EMA positive, and CD34 neg-

![Image](303x115 to 548x452)