The histopathological features of cerebellar hemangioblastoma: two case reports

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Capillary hemangioblastomas are benign, highly vascular tumors of controversial origin limited almost exclusively to the central nervous system. These tumors make up about 1 to 2 percent of all intracranial neoplasms and occur primarily in the posterior fossa. Most commonly they develop in the cerebellum of male adults in the third through fifth decades of life. Although the majority of the cases arise sporadically, some hemangioblastomas are associated with the autosomal dominantly inherited disease, von Hippel-Lindau syndrome. In this article, 2 cases of hemangioblastoma, diagnosed in our department of pathology are presented and the histopathological and the clinical features are discussed. [Turk J Cancer 2000;30(4):167-174]

Key words: Capillary hemangioblastoma, von Hippel-Lindau syndrome, posterior fossa

Capillary hemangioblastomas are benign and highly vascular central nervous system tumors of controversial origin. They comprise about 1 to 2 percent of all intracranial neoplasms and about 10 percent of the tumors are localized in the posterior fossa (1,2). They occur predominantly in the third through fifth decades of life and are more common in males than in females. Ninety-five percent of hemangioblastomas begin in the posterior fossa of which 70 to 80 percent are located in the cerebellar hemispheres, 10 to 15 percent in the cerebellar vermis and 10 percent in the brain stem. Hemangioblastomas appear in multiple sites in about 12 percent of cases (3). Other sites for the formation of hemangioblastomas include the cervical spinal cord and cerebrum (3).

Grossly, hemangioblastomas occur as mural nodules associated with large fluid-filled cysts (4). Histopathologically, they are characterized by two major components: vacuolated stromal cells and a capillary network (1,3,4,5). The origin of the stromal cells is controversial (1,6,7). Capillary hemangioblastomas may be associated with retinal hemangioblastomas or a variety of extra-central nervous system lesions, including cysts of the liver, kidney or pancreas, renal cell
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adenomas, renal cell carcinomas, epididymal papillary cystadenomas, and pheochromocytomas (1,8,9). In this article, 2 cases of capillary hemangioblastoma diagnosed in our department of pathology are presented and the histopathological and the clinical features are discussed.

Case 1:

Thirty-eight years old male patient (1879/99) applied to a hospital with the symptom of headache and there, he was thought to have hypertension. Consequently, because of dizziness and vomiting he applied to the same hospital and this time computerized tomography (CT) revealed a cystic mural nodule localized at the midline of the cerebellar vermis, which was found to be contrast-enhancing. Recently, approximately for one month he has been complaining about having problems with his balance. In his physical examination, he was found to have retinal hemangioma and multiple cysts in his kidneys. It is known that the patient's mother, brother, grand-father, aunt and uncle died of brain tumors while the other aunt and uncle were still alive with brain tumors. After the operation, the material sent to our pathology department consisted of two hyperemic tissues of 8x5x5 mm and 3x2x2 mm. Microscopically two different components of the tumor were distinguished: vascular structures and stromal cells which had vacuolated pale cytoplasms and bizarre nuclei (Figure 1).

Fig 1. Biphasic appearance of vascular structures and stromal cells (1879/99, H&E, X40)
The endothelial cells surrounding the capillary channels were uniform. With the reticulin stain, a rich network of reticulin was observed surrounding the individual stromal cells (Figure 2).

Fig 2. Vascular structures and reticular network of the stromal cells with reticulin stain (X40)

Oil red-O stain on frozen sections showed some neutral fat in the vacuolated cells. The stromal cells expressed diffuse positivity with S-100, NSE and CD-68 stains (Figures 3,4,5). The vascular structures reacted strongly with the endothelial cell marker, Factor-VIII (Figure 6), whereas the stromal cells were negative.
Fig 3. Immunoperoxidase stain demonstrates S-100 protein positivity in the stromal cells (Avidin biotin peroxidase, X20)

Fig 4. Immunoperoxidase stain demonstrates CD 68 positivity in the stromal cells (X20)
Fig 5. Immunoperoxidase stain demonstrates S-100 positivity in the stromal cells (X20)

Fig 6. The prominence of the vascular structures with Factor-VIII (X40)
Case 2:

Thirty-six years old male patient (16652/99) applied to our hospital, with headache complaint. With the imaging techniques, a mass of 3x3x4 cm was found in the posterior fossa. In his physical examination, there was no other pathological feature. The material sent to our department of pathology consisted of a hyperemic tissue of 3,5x3x2 cm. The cut surface of the tissue was also hyperemic and multiloculated. Microscopically, numerous capillaries lined by hyperplastic endothelial cells were seen. Surrounding these capillaries, there were pleomorphic stromal cells with abundant, vacuolated and pale cytoplasms. Mitotic activity was absent. There was a rich reticulin network and again some neutral fat was seen within the cytoplasms of the stromal cells. Immunohistochemically, vimentin and S-100 protein was diffusely positive whereas EMA was negative.

Discussion

Capillary hemangioblastoma is a slowly growing tumor which usually has cystic features morphologically (10). On computerized tomography (CT), it is recognized as a contrast-enhancing nodule because of its cystic features (1,3,8). The symptoms are associated with the progressively growing cystic component of the tumor. In some cases, as a result of the erythropoietin secretion from the vascular endothelial cells of the tumor, polycythemia becomes apparent (1,3,10).

Macroscopically, hemangioblastoma is a well-circumscribed tumor which has both solid and cystic components (2,3). The solid component, so called the mural nodule shows contrast enhancement on CT and prominent vascular features on angiography. Macroscopically, the tumor has a bright yellow color as a result of its lipid content (1,3,8). The histological features are rather original consisting of 2 components. These components are the capillary network lined by hyperplastic endothelial cells and the stromal cells which have pleomorphic or lobulated nuclei and lipid containing abundant, pale cytoplasms (1,3,5,8). Mitoses are usually inapparent (1,3). The origin of the stromal cells is controversial. According to most of the literature reviews, the stromal cells have both glial and vascular origin (1).

The expression of growth factors and growth factor receptors have been studied by Böhling et al. (11), and it has been found that the stromal cells express abundant epidermal growth factor receptor (EGFR) and some platelet-derived growth factor receptor-alpha (PDGF-alpha). It was concluded that the expression of highly angiogenic growth factors and their receptors might contribute to the rich vascularity of the tumor. The stromal cells reveal immunoreactivity for cytokeratin, vimentin, neuron-specific enolase (NSE), S-100 protein, glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA) and actin, but are negative with F-VIII/von Willebrand’s factor (1,3,7,8). On the other hand, the relation between angiogenesis and tissue expression of vascular endothelial growth factor (VEGF) has been studied by Vaquero J et al. (12) and it has been found that the number of intratumoral microvessels, identified by the endothelial marker CD 34, does not correlate with the degree of VEGF expression. This finding suggests that endothelial growth factors other than VEGF may regulate tumor angiogenesis in these neoplasms. Especially the immunoreactivity with vimentin, GFAP, EMA and cytokeratin is almost identical to the reactivity pattern of meningotheliomatous
meningioma and so the possibility of the stromal cells of hemangioblastoma to derive from the arachnoid cells of meningotheliomatous meningiomas by cellular degeneration has been considered (13). Also alpha-1–antitrypsin (alpha 1AT) and alpha-1-antichymotrypsin (alpha 1ACT) are occasionally observed in stromal cells. Since CD 68 is a lysosome marker as do alpha 1AT and alpha 1ACT, CD 68 positive stromal cells in our first case may indicate fibrohistiocytic differentiation according to Nemes Z (14). Although there are many different views about the histogenesis of the stromal cells, its exact origin is still not clear.

In both of our cases, hematoxylen-eosin stained sections were sufficient for the diagnosis. The histochemical and the immunohistochemical stains (NSE, S-100, GFAP, keratin, CD-68, reticulin, Factor-8 and Oil red-O stains) were applied to support the diagnosis and the staining patterns were found to be consistent with the related publications.

In the differential diagnosis of capillary hemangioblastoma, metastatic renal cell carcinoma must be considered. Renal cell carcinoma shows necrosis, mitoses and cytokeratin, vimentin and EMA immunoreactivity, which are important clues in distinction (1,3,8). It is also suggested that the AgNOR method is a useful adjunct in achieving the differential diagnosis of hemangioblastoma and renal cell carcinoma in the nervous system (15). Anaplastic astrocytoma and meningioma also show similarity to the tumor (16). In the study, in which cytologic features of hemangioblastoma are compared with meningioma, anaplastic astrocytoma and renal cell carcinoma intraoperative smears were evaluated and concluded that smears of hemangioblastomas are cellular and cohesive, the cytoplasmic borders are indistinct and the nuclei are hyperchromatic and mildly pleomorphic. Smears of meningiomas, anaplastic astrocytomas and renal cell carcinomas are more discohesive than those of hemangioblastomas. The cells of renal cell carcinoma show distinct cellular borders while in astrocytoma there is prominent cytoplasmic fibrillarity (16).

Another lesion which must be considered in the differential diagnosis is angioglioma (3,17). In angioglioma the neoplastic astroglial cells are scattered among the vascular structures and usually the glial component is prominent (17). Capillary hemangioblastomas may be multiple (1,18). Cases of hemangioblastoma in association with bilateral pheochromocytoma and von Hippel-Lindau syndrome have been reported (1,19).

As a conclusion, capillary hemangioblastomas are biologically slowly growing lesions which have cystic and solid (mural) features morphologically. The symptoms are associated with the progressively growing cystic component of the tumor. Hemangioblastomas show very good prognosis with sufficient surgical excision, but with insufficient excisions recurrences are inevitable.

References


