Case Report

J Chin Med Assoc
2004;67:527-532

Meningeal Hemangiopericytoma with Delayed Multiple Distant Metastases

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Key Words
epithelial membrane antigen;
immunohistochemistry;
Ki-67 antigen;
meningeal hemangiopericytoma

A 43-year-old housewife suffered from an occipital headache, and brain computed tomography (CT) showed an occipital meningeal tumor. She received a complete tumor excision and the tumor pathology was interpreted as atypical meningioma. Five years later, a subacute left neck pain with radiation to the left arm occurred. A tumor invading the second and third cervical vertebrae with compression on the dural sac was found. Angiography revealed hypervascular tumor staining supplied from the left vertebral artery. CT-guided biopsy was performed and nests of atypical spindle cells accompanied by staghorn vascular pattern were revealed histologically. Immunohistochemical studies showed positive vimentin staining but negative reactions to epithelial membrane antigen, cytokeratin low molecular weight, cytokeratin high molecular weight, CD34 and S-100 protein. Estimation of the Ki-67 proliferative (mitotic) index by using MIB-1 monoclonal antibody was 12%. Later on, a systemic survey revealed lesions in the left lung, liver and kidney. The diagnosis was revised to hemangiopericytoma. Distant metastasis is common in this tumor. However, the delayed multiple metastases without local recurrence were relatively rare. The clinical course in this patient also supported that a high mitotic activity may correlate with a poor prognosis even if the pathology is taken from the metastatic tissue, and that long-term follow-up is mandatory. Detailed immunohistochemical staining is helpful in avoiding misdiagnosis of meningioma.

Meningeal hemangiopericytoma is a rare clinical entity comprised less than 1% of intracranial neoplasm.[1,2] Anatomically, it can be found throughout the central nervous system (CNS) in vicinity of the meninges. The tumor is remarkably aggressive, exhibiting a high rate of recurrence via local invasion or distant metastasis.[3,4] Once the tumor recurs after surgical removal, a poor prognosis is very likely.[3,4] Morphologically, it is a highly cellular tumor composed of elongated or polygonal pericytes and is distinct from the atypical or malignant meningioma. Furthermore, the latter 2 tumors are characterized by displaying meningothelial architecture with varying degree of atypical or anaplastic feature which is not usually present in hemangiopericytoma.[5]

Ki-67 antigen, a nuclear protein related to cell proliferation during S, G1 and G2/M phases, has been utilized in assessing proliferation activity in tumors.[6] Of particular note, its value in providing a prognostic view of the tumor has been addressed.[7] For the investigation of meningeal hemangiopericytomas, Ki-67 proliferation index has been used; its value in predicting recurrent rate or clinical prognosis still remains controversial.[8-10] We examined proliferation potential and immunohistochemical characteristics in a patient with meningeal hemangiopericytoma, who was initially diagnosed as atypical meningioma.

CASE REPORT

A 48-year-old woman was admitted to our ward due to an intolerable neck pain with intermittent radiation pain to the left forearm for 5 months. The neck pain and tightness sensation were aggravated when she hyperextended the neck, lay flat or rotated her neck side to side. Tracing back her medical history, she had been diagnosed as having a brain tumor at the right occipital lobe 5 years before (Fig. 1A), and tumor extirpation was completed at that

Received: October 8, 2003.
Accepted: May 13, 2004.

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time at another medical center. The tumor pathology was interpreted as atypical meningioma.

On admission, her blood pressure, body temperature and heart rate were within normal limits. On neurological examination, the conscious level, muscle power and deep tendon reflex were otherwise normal. Active fasciculation at the left shoulder was noted. Also, hyperesthesia at the left third to fifth cervical dermatome was found. The sphincter function was normal. A clinical diagnosis of left cervical radiculopathies was established.

A complete blood cell count, biochemistry and a tumor marker survey including alpha fetal protein, CEA and CA-125 were all within normal limits. A cervical radiograph revealed irregular widening of the left second (C2) and third (C3) cervical intervertebral foramina (Fig. 1B). Cervical computed tomography (CT) showed an extradural tumor invading the lamina and pedicles of the left C2 and C3 vertebrae, and a mild compression on the dural sac (Fig. 1C). The heterogeneously enhancing tumor displayed a distinct margin, with erosion of bony structures (Fig. 1C). No evidence of lymph node enlargement could be identified at the bilateral internal jugular and submandibular chains on both sides. A follow-up cranial CT did not find the intracranial local recurrence (data not shown). A vertebral angiography disclosed prominent hypervasular tumor staining supplied by the muscular branches of the left vertebral artery (Fig. 1D). Trans-arterial embolization was performed with gelfoam powder, but some residual tumor stainings were still identified after this procedure.

Under CT guidance, a needle aspiration biopsy was performed, and the specimen consisted of nests of atypical spindle cells intermingled with staghorn vessels (Fig. 2A), a characteristic finding of hemangiopericytoma. Immuno-

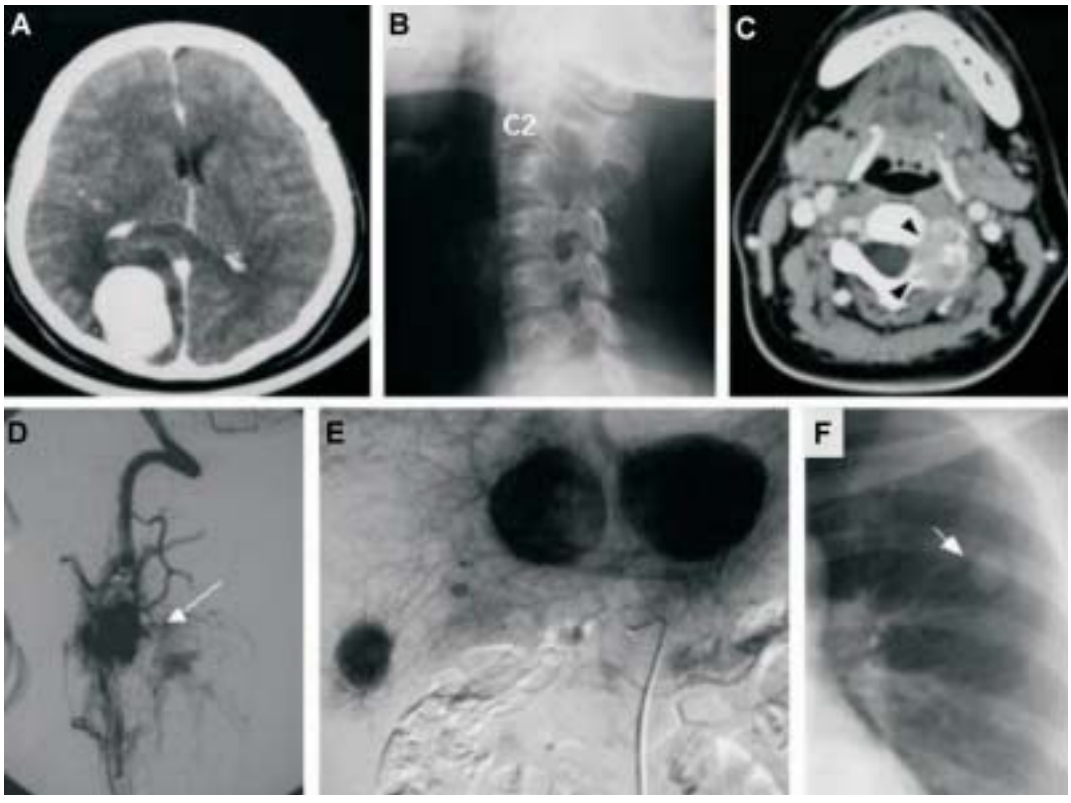

Fig. 1. Computed tomography (CT) with contrast revealed a homogeneously and intensely enhancing mass located at the right occipital region with perifocal edema (**A**). On the oblique view of the cervical radiography, widening and erosion of C2 and C3 intervertebral foramen was found (**B**). The cervical CT with constrast showed an extradural mass with erosions of the lamina and pedicles of the left C3 vertebra (arrowheads) with indentation of the dura sac (**C**). A left vertebral angiography disclosed prominent hypervasular tumor stainings supplied by the muscular branches of the left vertebral artery with early venous drainage (**D**). Multiple hepatic masses were revealed from the celiac angiography (**E**), and pulmonary mass (white arrow) in the left upper lung was found on chest X-ray (**F**).

histochemical study for vimentin, epithelial membrane antigen (EMA), cytokeratin low molecular weight (LMW), cytokeratin high molecular weight (HMW) and S-100 protein were performed according to the immunoperoxidase method. The tumor tissue showed negative reaction to the EMA (Fig. 2B), S-100, and cytokeratins but positive immunostaining for vimentin (Fig. 2C). The immunoreactivity of CD 34 was not very evident (Fig. 2D), showing only patchy stain in the vessel wall and stroma. Using the MIB-1 monoclonal antibody immunostaining (Fig. 2E), the Ki-67 index was estimated to be 12%, suggesting an increased mitotic activity. A systemic survey for the patient revealed multiple hepatic masses (Fig. 1E) and a left upper lung nodule (Fig. 1F). For the specific tissue appearance noted in the spinal lesion, we were kindly given a chance to recheck the pathological specimen of the primary brain tumor (Fig. 2F), which was compatible with meningeal hemangiopericytoma. Therefore, a diagnosis of meningeal hemangiopericytoma with delayed multiple metastases was made. The patient received a total radiation dosage of 4320

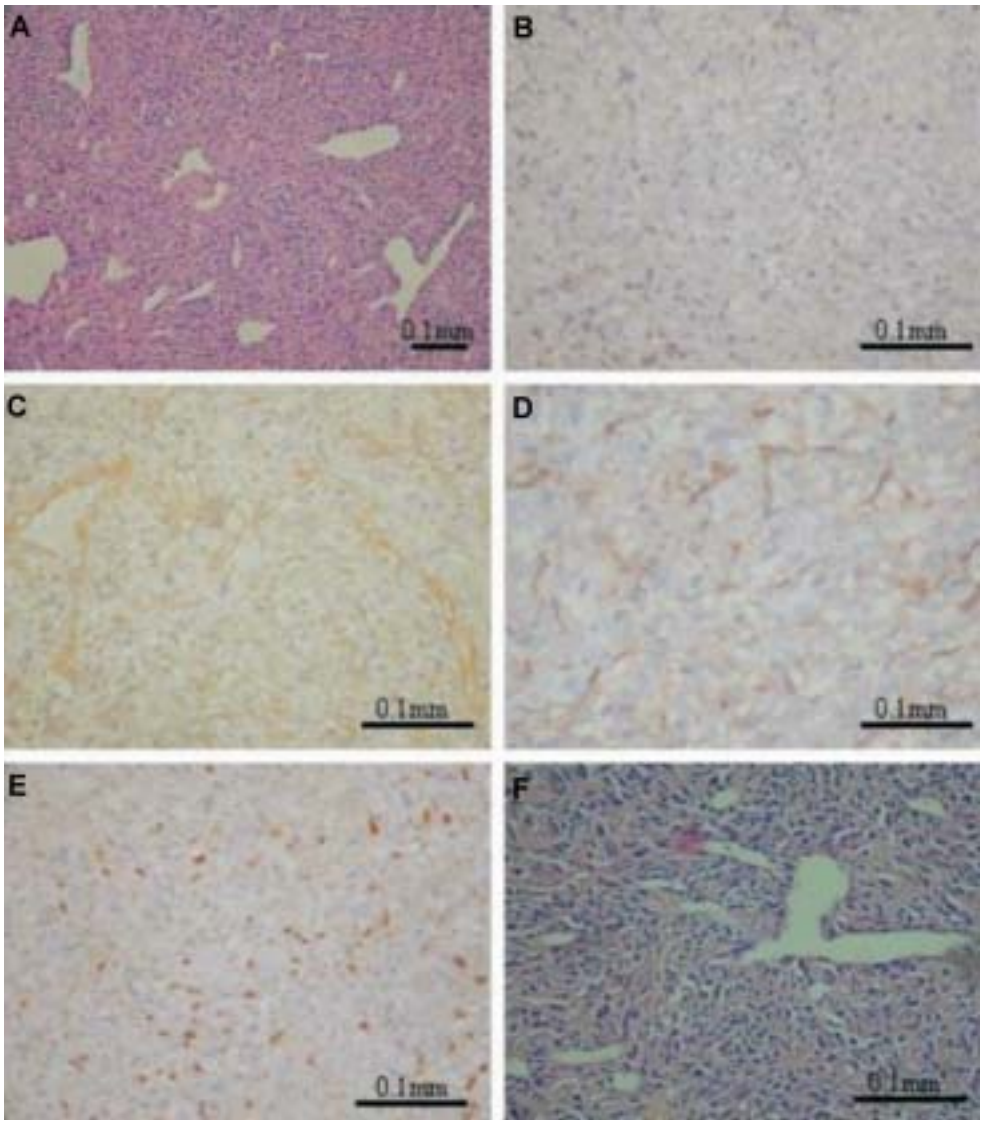

Fig. 2. Densely packed elongated or polygonal neoplastic cells are arranged around branching staghorn-like vasculatures (Hematoxylin-eosin stain) from the brain (**F**) and the cervical tumors (**A**). The immunohistochemical studies revealed negative staining for epithelial membrane antigen (**B**) and positive cytoplasmic staining for vimentin (**C**). The immunoreactivity of CD 34 showed patchy stain in the vessel wall (**D**). The median of MIB-1 immunohistochemical staining index (**E**), i.e., Ki-67 mitotic index, shows a median value of 12%. Scale bars represents 0.1 mm.

cGy to the neck and the radicular pain gradually subsided. The hepatic lesion showed regressive changes after twice selective trans-arterial embolizations with lipiodol mixed with pure alcohol followed by gelfoam powder bolus. During a 1-year follow up period, a right renal mass and multiple bony metastases were found and treated conservatively.

DISCUSSION

Meningeal hemangiopericytoma is a dura base mesenchymal tumor with sarcoma-like behavior. The biological behavior of meningeal hemangiopericytoma is usually malignant, and tends to recur at interval of years. In a review of 44 cases, Guthrie *et al* demonstrated that the recurrence rates at 1, 5, and 10 years after surgery were 15, 65, and 76%, respectively.[3] Unlike other primary intracranial tumors, extraneural metastases is frequent in patients with hemangiopericytoma, even after a complete surgical treatment.[11,12] Our patient presented with multiple extracranial metastases, suggesting significant malignancy and marked biological activity in this tumor. In the Mayo Clinic series, the average survival in patients with metastasis was 24 months.[3] Mena *et al* reported that tumors with a higher mitotic rate tended to recur faster.[4] On the other hand, researches argued that the extent of tumor removal [3,12] and the histological characteristics such as atypia, increased cellularity and mitotic activity[2,3] were unrelated to the prognosis.

Post-operative radiation therapy appeared to reduce local recurrence and improve overall survival.[3,13] Radiation therapy for the tumor was noted to be dose-dependent by observating that patients being treated with less than 45 Gy tended to experience recurrence faster.[3,13] No radiation therapy was administered after radical removal of the intracranial tumor in our patient. It should be noted that our patient developed multiple distant metastases without local recurrence 5 years after the surgery. Therefore, one of the mechanisms responsible for distant metastasis is independent of the local recurrence, according to our observation in this patient.

In terms of treatment options, differentiation of the benign meningioma from meningeal hemangiopericytoma is of great importance. Although the CT and magnetic resonance imaging give no clear distinction between these two, there are some clues deserving our attention. Lytic but not hyperostotic bony change has been linked to meningeal hemangiopericytoma.[3,5] In our patient, the extradural tumor at the cervical spine was compatible with this radiological finding. Moreover, angiography may offer important information as the tumor frequently demonstrates 'corkscrew' vascular configuration with long-lasting venous staining and early venous drainage, which are less commonly encountered in the ordinary meningioma.[3,5,14,15] Angiographic findings in our patient included multiple feeding vessels coming from the left vertebral artery and prolonged tumor staining with early venous drainage that were in agreement with previous reports.[3,5,14,15]

In our patient, the primary occipital tumor had been recognized as an atypical meningioma at the beginning that could be avoided with the help of immunohistochemical study. Immunostaining for meningeal hemangiopericytoma used to show vimentin reactivity but not EMA, whereas for meningioma used to be immunoreactive for both.[16,18] These findings suggest that meningioma comes from both epithelial and mesenchymal origin while meningeal hemangiopericytoma is purely from mesenchymal tissue.[16,18] Besides, hemangiopericytoma also shows negative reaction to cytokeratin LMW, cytokeratin HMW and S-100 protein, an antigenic profile that is quite different from subtypes of meningiomas such as meningotheliomatous, fibroblastic, papillary, transitional, angiomatous, and anaplastic forms.[17,18] CD34, a transmembrane glycoprotein, had been proposed to be a sensitive marker for solitary fibrous tumor (SFT)[19] and could be used to differentiate SFT and hemangiopericytoma. It would stain diffusely in the SFT but only appear patchy or weakly staining in the hemangiopericytoma. The clinical presentation in these 2 tumors also differs in addition to the immunohistochemical staining. The SFT was relatively benign and did not recur unless resection was not complete.[20]

Immunostaining with monoclonal antibody Ki-67, a nuclear antigen present throughout the cell cycle, provides a reliable method in evaluating the mitotic activity of neoplastic cells.[6] The mitotic reaction has been reported to be quite variable in meningeal hemangiopericytoma, with labeling indices for Ki-67 (MIB-1) ranged from 0.2% to 39%.[7-10] Demirtas *et al*

reported that Ki-67 indices in benign meningiomas ranged between 0% and 13.6% (mean 1.83%), but in malignant cases they were between 1% and 20% (mean 7.2%).[21] Such observation is compatible with our result with a labeling index of 12%. Although a correlation with prognosis or recurrence and mitotic activity remains controversial,[2-4,8-10,21] the presence of prominent mitotic activity has been linked to a highly active biological behavior.[4,8,10] Probst-Cousin and colleagues observed a trend leading to longer survival as patients' tumor with Ki-67 labeling indices less than 5%.[8] While most recurrent tumor demonstrated little change with regard to the basic morphology,[2] Hara *et al* found that recurrent meningeal haemangiopericytoma appeared to manifest a different rate of growth as suggested by increased Ki-67 mitotic index.[10] In our patients, the Ki-67 index was not assessed for the primary tumor; an increased index in the spinal lesion may hint a poor prognosis as multiple metastases happened to her at the same time.

In view of the propensity for relapse in meningeal hemangiopericytoma such as 5 years later in our patient, a long-term clinical follow-up is still mandatory. In conjunction with the conventional histological study, immunohistochemical investigation including vimentin, EMA, cytokeratin and S-100 protein may offer additional help in the differential diagnosis. Mitotic activity assessed by Ki-67 for the tumor, either from primary or secondary site, may provide prognostic prediction in patients with meningeal hemangiopericytoma.

REFERENCES

1. Pitkethly DT, Hardman JM, Kempe LG, Earle KM. Angioblastic meningiomas: clinicopathologic study of 81 cases. *J Neurosurg* 1970;32:539-44.
2. Jellinger K, Slowik F. Histological subtypes and prognostic problems in meningiomas. *J Neurol* 1975;208:279-98.
3. Guthrie BL, Ebersold MJ, Scheithauer BW, Shaw EG. Meningeal hemangiopericytoma: histopathological features, treatment, and long-term follow-up of 44 cases. *Neurosurgery* 1989;25:514-22.
4. Mena H, Ribas JL, Pezeshkpour GH, Cowan DN, Parisi JE. Hemangiopericytoma of the central nervous system: a review of 94 cases. *Hum Pathol* 1991;22:84-91.
5 Jaaskelainen J, Servo A, Haltia M, Wahlstrom T, Valtonen S. Intracranial hemangiopericytoma: radiology, surgery, radiotherapy, and outcome in 21 patients. *Surg Neurol* 1985;23: 227-36.
6. Gerdes J, Schwab U, Lemke H, Stein H. Production of a mouse monoclonal antibody reactive with a human nuclear antigen associated with cell proliferation. *Int J Cancer* 1983; 31:13-20.
7. Boker DK, Stark HJ. The proliferation rate of intracranial tumors as defined by the monoclonal antibody KI 67: Application of the method to paraffin-embedded specimens. *Neurosurg Rev* 1988;11:267-72.
8. Probst-Cousin S, Bergmann M, Schroder R, Kuchelmeister K, Schmid KW, Ernestus RJ, Janus J. Ki-67 and biological behaviour in meningeal haemangiopericytomas. *Histopathology* 1996;29:57-61.
9. Vuorinen V, Sallinen P, Haapasalo H, Visakorpi T, Kallio M, Jaaskelainen J. Outcome of 31 intracranial haemangiopericytomas: poor predictive value of cell proliferation indices. *Acta Neurochir (Wien)* 1996;138:1399-408.
10. Hara M, Aoyagi M, Nagashima G, Wakimoto H, Mikami T, Yamamoto S, *et al*. Recurrence in meningeal hemangiopericytomas. *Surg Neurol* 1998;50:586-91.
11. Horten BC, Urich H, Rubinstein LJ, Montague SR. The angioblastic meningioma: a reappraisal of the nosological problem: light-, electron-microscopic, tissue, and organ culture observations. *J Neurol Sci* 1977;31:387-410.
12. Schroder R, Firsching R, Kochanek S. Hemangiopericytoma of meninges. II. General and clinical data. *Zentralbl Neurochir* 1986;47:191-9.
13. Bastin KT, Mehta MP. Meningeal hemangiopericytoma: defining the role for radiation therapy. *J Neurooncol* 1992;14: 277-87.
14. Marc JA, Takei Y, Schechter MM, Hoffman JC. Intracranial hemangiopericytomas: angiography, pathology and differential diagnosis. *Am J Roentgenol Radium Ther Nucl Med* 1975; 125:823-32.
15. Servo A, Jaaskelainen J, Wahlstrom T, Haltia M. Diagnosis of intracranial haemangiopericytomas with angiography and CT scanning. *Neuroradiology* 1985;27:38-43.
16. Theunissen PH, Debets-Te Baerts M, Blaauw G. Histogenesis of intracranial haemangiopericytoma and haemangioblastoma. An immunohistochemical study. *Acta Neuropathol (Berl)* 1990;80:68-71.
17. Iwaki T, Fukui M, Takeshita I, Tsuneyoshi M, Tateishi J. Hemangiopericytoma of the meninges: a clinicopathologic and immunohistochemical study. *Clin Neuropathol* 1988;7: 93-9.
18. Winek RR, Scheithauer BW, Wick MR. Meningioma, menin-

geal hemangiopericytoma (angioblastic meningioma), peripheral hemangiopericytoma, and acoustic schwannoma: a comparative immunohistochemical study. *Am J Surg Pathol* 1989; 13:251-61.
19. Alston SR, Francel PC, Jane JA, Jr. Solitary fibrous tumor of the spinal cord. *Am J Surg Pathol* 1997;21:477-83.
20. Brunori A, Cerasoli S, Donati R, Giangaspero F, Chiappetta F. Solitary fibrous tumor of the meninges: 2 new cases and review of the literature. *Surg Neurol* 1999;51:636-40.
21. Demirtas E, Ersahin Y, Yilmaz F, Mutluer S, Veral A. Intracranial meningeal tumours in childhood: a clinicopathologic study including MIB-1 immunohistochemistry. *Pathol Res Pract* 2000;196:151-8.