Intramedullary Spindle Cell Hemangioendothelioma of the Thoracic Spinal Cord
—Case Report—

Jafri Malin ABDULLAH, Samerendra Singh MUTUM*, Noor Azam NASUHA, Biswa Mohan BISWAL**, and Abdul Rahman MOHD ARIFF***

Departments of Neuroscience, *Pathology, **Nuclear Medicine, Radiotherapy & Oncology, and ***Radiology, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia

Abstract

A 28-year-old Malay man presented with progressive paraparesis over a period of 6 months. Magnetic resonance imaging of the spine revealed a thoracic intramedullary spinal cord tumor at the T-7 level with homogeneous enhancement following intravenous gadolinium administration. Laminectomy and partial decompression of the tumor was performed. Histological examination of the tumor revealed features of spindle cell hemangioendothelioma. The patient was managed with limited field radiotherapy followed by systemic interferon therapy. Good neurological improvement was seen subsequently. The patient has survived 48 months with growth restraint at the primary site, although residual neurological deficit persists. Immunotherapy should be considered as a treatment modality for intramedullary hemangioendothelioma of the spinal cord after surgery and radiotherapy.

Key words: intradural hemangioendothelioma, intramedullary hemangioendothelioma, spinal cord

Introduction

Hemangioendothelioma has been used to designate a heterogeneous group of vascular lesions ranging from benign conventional hemangioma to angiosarcoma. Four distinct entities, epithelioid hemangioendothelioma, spindle cell hemangioendothelioma, kaposiform hemangioendothelioma, and malignant endovascular papillary angioendothelioma, have been recognized.9) Spindle cell hemangioendothelioma is considered to be a vascular tumor of intermediate grade malignancy with a propensity for local recurrence after surgery but rarely metastasizes.24,27,32) Hemangioendothelioma is not uncommon in the soft tissues and has also occurred in the oral cavity, mediastinum, bone, and various superficial and deep body areas.9,16,24,27,31,33,34) However, intracranial or intraspinal involvement are infrequent.2,6,12,13,15,29,30) We describe a case of intraspinal and intramedullary spindle cell hemangioendothelioma.

Case Report

A 28-year-old Malay man presented with a 6-month history of progressive numbness of both upper and lower limbs. He became paraplegic 2 months prior to admission. He had to manually evacuate stool or use an enema every day. There was also loss of early morning erection. He had no past history of trauma, tuberculosis, backache, or neck pain.

On examination, he was conscious and alert, and all vital signs were normal. The cranial nerves were intact. Muscle tone was increased in both lower limbs compared to that of the upper limbs. Muscle power was 5/5 in both upper limbs but was 1/5 and 0/5 in the right and the left lower limbs, respectively. Both lower limbs showed hyperreflexia compared to the upper limbs. Sensation to pinprick and light touch was reduced at the level of T-7 and below. Clonus could be elicited in both legs.

Magnetic resonance (MR) imaging of the spine showed a well-defined intramedullary mass at the level of T-7. T1-weighted MR imaging showed the mass as intermediate signal intensity. T2-weighted MR imaging showed a heterogeneous area of high signal intensity on a background of high signal intensity from the syrinx. The mass was homogene-
Fig. 1 Sagittal T₁-weighted magnetic resonance image with gadolinium demonstrating a well-defined homogeneously enhanced mass in the spinal cord (arrow).

ously enhanced following intravenous gadolinium administration and measured 4 cm in length (Fig. 1). Based on the findings of a homogeneously enhanced, well-defined lesion affecting almost the whole width of the spinal cord, provisional diagnosis was ependymoma.

Removal of the primary spinal cord tumor was attempted via a T-6 to T-8 laminectomy. A well-defined intradural and intramedullary tumor was seen at the level of T-7. The tumor was very vascular, and bled on touch when excision was attempted. The tumor was partially removed piecemeal, leaving the normal spinal cord intact. Total removal could not be achieved due to gross evoked potential changes.

The gross specimen consisted of multiple fragments of brownish soft tissue and bone measuring 15 mm and 50 mm, respectively, in aggregate diameter. Histological examination revealed a moderately cellular vascular lesion composed of cells with plump oval or spindled nuclei and scanty amphophilic cytoplasm with indistinct cell outlines lining small capillary lumina or ill-defined vascular clefts containing red blood cells. These cellular areas alternated with thin or thick-walled cavernous venous spaces lined by a single layer of flattened endothelial cells (Figs. 2 and 3). The spindle cells exhibited mild nuclear pleomorphism and hyperchromatism but no mitotic figures. No tumor necrosis was seen. A few

Fig. 2 Photomicrograph showing cellular areas alternating with cavernous vascular spaces (stars). HE stain, ×200.

Fig. 3 Photomicrograph showing closely packed cells with plump oval or spindled nuclei and scanty cytoplasm. The nuclei display hyperchromatism and mild pleomorphism but no mitosis. Several small capillary lumina containing red blood cells are also seen. HE stain, ×200.

Fig. 4 Photomicrograph showing positive immunohistochemical staining for CD31 in the endothelial cells lining the vascular spaces, some spindle cells, and a few large cells with vesicular nuclei. ×200.
Fig. 5 T1-weighted magnetic resonance image with gadolinium after completion of 20 fractions of radiation therapy showing the remnant of the lesion in the spinal cord (arrow).

Intramedullary Spinal Cord Hemangioendothelioma

scattered epithelioid cells with vesicular nuclei were present in the stroma. However, large stromal cells with vacuolated cytoplasm were absent. There was no associated thrombosis in the large cavernous vessels. Staining for reticulin revealed fine reticulin lining the small vascular lumina but not outlining the oval or spindle cells. Immunohistochemical staining for factor VIII-related antigen and CD31 was positive in the endothelial cells lining the vascular spaces and the few epithelioid cells, but was generally scanty in the cellular spindled areas (Fig. 4). Staining for epithelial membrane antigen and cytokeratin (AE1, AE3) were negative but for vimentin was positive. Based on these findings, the diagnosis was spindle cell hemangioendothelioma. No electron microscopy or immunohistochemical staining for cell proliferation markers was performed.

The patient was managed with radiotherapy using a total tumor dose of 55 Gy given in 29 fractions in two phases using a 6 MV linear accelerator. After radiotherapy, the motor power in both lower limbs was 3/5. Nine months later, the patient had improved subjectively and could move with support. The motor power was 4/5 in both lower limbs. He could pass urine unaided. However, he still had to use enemas to evacuate stool. There was no evidence of disease elsewhere in the body. Repeat MR imaging of the spine performed 3 months later revealed regression in the size of the tumor (Fig. 5). At subsequent follow up, the patient was offered interferon (IFN) therapy to treat the residual lesion. Treatment consisted of IFN α-2b (INTRON®; Schering-Plough, Innishannon, County Cork, Republic of Ireland) 5 million units, subcutaneous injections three times a week for 3 months. No untoward effects occurred during IFN therapy. At 48 months post-radiotherapy, he had no new neurological deficits, although residual weakness was present in both lower limbs.

Discussion

Spindle cell hemangioendothelioma was first described as a low-grade sarcoma with histological features intermediate between hemangioma and Kaposi’s sarcoma.32) This tumor is characterized by the presence of cellular spindled areas alternating with cavernous vascular spaces. In our case, no hypercellularity, marked pleomorphism, or mitotic figures indicative of malignancy were seen. Solid nests of epithelioid cells with the intracytoplasmic lumina characteristic of epithelioid hemangioendothelioma were absent. Kaposiform hemangioendothelioma is a highly cellular spindle cell tumor with glomeruloid nests. Malignant endovascular papillary angioendothelioma could be excluded as the endothelial cells lining the cavernous vascular spaces consisted of a single layer of flattened cells and showed no papillary formations.8,9) Prominent clusters of large stromal cells with vacuolated cytoplasm and intense reticulin around the cells, and arborizing blood vessels distinctive of hemangioblastoma were lacking in this tumor. The high cellularity, slit-like staghorn vascular channels, and prominent pericellular reticulin network characteristic of hemangiopericytoma were also absent.2) The lack of uniform small endothelial lined vascular channels or abundant cavernous vessels excluded conventional hemangiomia. Positivity for factor VIII-related antigen and CD31 in some but not all spindle cells may support the proposal of both endothelial and pericytic derivations for the cells.22,23)

Soft tissue spindle cell hemangioendothelioma is clinically indolent and apparently histologically benign, but the local recurrence rate is as high as 60%.24) Aggressive behavior of a benign-looking soft tissue spindle cell hemangioendothelioma with lymph node metastasis needing amputation and radiotherapy has been described.14) Intradural extramedullary spindle cell hemangioendothelioma involving the thoracic spinal cord recurred twice despite the benign histology and was irradiated after the third excision.15) Immunohistochemical staining to identify cell proliferation markers, such as MIB-1 for Ki-67 antigen, as indicators of malignant behavior are useful in tumors of the central nervous system, particularly astrocytomas, but the implication
in vascular tumors is unclear at present.\textsuperscript{17,18,20} Electron microscopic studies could not be done in this case.

In the present case, spinal cord arteriovenous malformation (AVM) was not considered due to the absence of flow void signals suggesting enlarged arterial feeding vessels and intramedullary nidus. No evidence of recent or past intramedullary hemorrhage or evidence of gliosis or edema was found to indicate spinal cord AVM.\textsuperscript{20} Astrocytoma is expected to appear more as patchy irregular enhancement with eccentric location, usually with associated widening of the spinal cord.\textsuperscript{26}

MR imaging permits noninvasive evaluation of spinal cord anatomy and many types of spine and spinal cord pathology. However, the MR imaging findings of spinal cord hemangioendothelioma are not yet established. Complete investigation of spinal vascular lesions often remains difficult with only MR imaging, and spinal angiography remains the best method for visualizing the spinal vasculature. In most cases, MR imaging findings suggestive or diagnostic of spinal vascular malformation mandate further evaluation with spinal angiography.\textsuperscript{28}

The MR imaging findings of cavernous angioma are often characteristic and permit a relatively specific diagnosis. A rim of low signal intensity representing iron storage products is usually seen completely surrounding the lesion.\textsuperscript{27} This feature was not seen in our case and there was no evidence of multifocal disease.

Hemangioma and hemangioendothelioma are moderately radiosensitive tumors. Hemangiomas involving the skeletal system have been treated effectively with local radiotherapy for over many decades.\textsuperscript{3,30} Local radiotherapy is also useful for treating inaccessible hemangioendothelioma with good long-term local control.\textsuperscript{31} Radiotherapy is effective for such tumors involving the head and neck, intracranial sites, and liver. Intradural extramedullary spindle cell hemangioendothelioma involving the thoracic spinal cord was treated by local radiotherapy using a limited field.\textsuperscript{15} A tumor dose of 50 Gy in 28 fractions was given. The patient remained well with no evidence of recurrent tumor about 2 years after radiotherapy with good local control. Our patient was treated with local limited field radiotherapy with good growth control for 48 months after radiotherapy. Irradiation up to the therapeutic dose is very difficult in the spinal cord as the tolerance limit of the spinal cord is fixed with a LD\textsubscript{50} of 45 Gy in conventional fractionation. However, the recommended radiation dose ranges from 20 to 50 Gy.\textsuperscript{4,15}

Our patient was treated with radiotherapy because of the significant residual tumor, high vascularity, and general unpredictable behavior of hemangioendothelioma. The patient demonstrated good neurological recovery following radiotherapy and is still doing well at present. IFN therapy is a new treatment modality used for various vascular pathologies.\textsuperscript{10,11,19,21,25} Experimental studies have shown the usefulness of IFN for treating capillary hemangiomas. Successful use of IFN has been documented by various studies in childhood hemangiomas.\textsuperscript{10,11} IFN-α-2a therapy has been used with success in large infantile hemangiomas including one in the brain.\textsuperscript{31} However, the small number of reported cases of hemangioendothelioma occurring in the brain and spinal cord do not provide firm guidelines for the behavior and the management of these tumors. We used IFN-α-2b treatment for our patient because of residual disease after radiotherapy and unavailability of other treatment modalities. Following low-dose IFN therapy, our patient showed stabilization of the tumor 48 months after diagnosis.

Spindle cell hemangioendothelioma of the spinal cord is a rare entity. MR imaging shows better delineation of tumor and enables planning of decompressive surgery. Optimal tumor debulking is the primary mode of treatment. Postoperative radiotherapy with a limited field with or without IFN therapy is recommended to prevent recurrence.

References