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Case Report

Multifocal hemangioendothelioma of the lumbar spine and response to surgical resection and radiation

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Abstract

BACKGROUND CONTEXT: Epithelioid hemangioendothelioma rarely occurs in the lumbosacral spine, with very few case reports of spinal hemangioendothelioma in the literature. There is variability in aggressiveness of these lesions without established treatment guidelines.
PURPOSE: The aim was to present a case of epithelioid hemangioendothelioma in the lumbar spine, including magnetic resonance imaging (MRI) findings, which rapidly progressed over a 2-month period as regional multifocal lumbosacral spinal lesions with epidural extension causing severe spinal canal stenosis.
STUDY DESIGN/SETTING: This was a case report in a university hospital setting.
PATIENT SAMPLE: The sample included an otherwise healthy adult male with low back pain.
METHODS: Multimodality imaging was performed to help with diagnosis and management including computed tomography, MRI, and positron emission tomography (PET). The patient was treated by embolization, L5 corpectomy and L4–S1 stabilization, and radiation therapy. The diagnosis was confirmed by tissue biopsy.
RESULTS: The patient initially presented with severe back and leg pain after a vertebroplasty for an L5 compression fracture at an outside hospital where biopsy was negative for malignancy. Magnetic resonance imaging showed diffuse abnormality of L5 with several smaller lesions in the sacrum. Due to progressive pain 2 weeks after the vertebroplasty, the patient underwent an L5 laminectomy, L4–S1 instrumented posterior fusion, and attempted partial corpectomy for stenosis. At this surgery, the L5 corpectomy was aborted owing to profound bleeding. Pathology was again negative for malignancy. Presumed to be an atypical hemangioma, the lesion was embolized before repeat surgery where the thecal sac was decompressed by partial L5 corpectomy. Biopsy at this time revealed a vascular neoplasm, with hemangioendothelioma not excluded.

Approximately 2 months after the stabilization procedure, the patient had increasing pain and bilateral lower extremity weakness. Magnetic resonance imaging was performed and demonstrated marked local progression of disease with new multifocal lesions involving L4 through S2 vertebrae and new severe spinal canal stenosis. These lesions were subsequently treated with localized radiation therapy. Magnetic resonance imaging 2 months after radiation therapy showed significant regression of the epidural tumor although a new metastatic lesion was discovered at T6 vertebra.
CONCLUSIONS: Spinal hemangioendothelioma is a rare disease and can present in variable forms, including as a multifocal regional process—which may be mistaken for infection. Additionally, there are no standard treatment protocols for this entity. We present the extensive imaging and treatment of a single case of rapidly progressive lumbar epithelioid hemangioendothelioma, which to our knowledge has not been described with this multifocal appearance in the lumbar spine.

Keywords: Epithelioid; Hemangioendothelioma; Spine; Vascular; Surgery; Radiation; Vascular tumor; Imaging; Bone neoplasm

FDA device/drug status: Not applicable.

Author disclosures: ***LK:*** Nothing to disclose. ***FS:*** Nothing to disclose. ***AS:*** Nothing to disclose.

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Introduction

Hemangioendotheliomas in the spine are a rare occurrence, reported in the literature only as case reports and small case series. The forms of spinal hemangioendotheliomas that have been described include kaposiform, epithelioid, spindle cell, and just recently, composite form [1]. Hemangioendotheliomas are reported to generally occur between 10 and 30 years of age [2]. When epithelioid hemangioendothelioma occurs in the bone, it generally behaves less aggressively than when occurring in the soft tissue and skin [3].

Epithelioid hemangioendothelioma of the bone is generally considered an intermediary between epithelioid hemangioma (considered a benign entity) and angiosarcoma. In the spectrum of vascular lesions, epithelioid hemangiomas are generally considered to have low malignant potential. Although these lesions can be asymptomatic and incidentally discovered on imaging performed for other reasons, a common presenting symptom of skeletal epithelioid hemangioma and epithelioid hemangioendothelioma is pain [4]. In one small case series, a presenting symptom common to all patients with spinal hemangioendothelioma was back pain and point tenderness over the lesion, as well as some degree of movement restriction (with paraparesis in one extreme case) and/or sensory derangements [3].

Multilevel vertebral body involvement has been noted in instances of thoracic hemangioendotheliomas [3,5]. To our knowledge, there are no documented cases of lumbosacral multifocal hemangioendothelioma. We present a case of epithelioid hemangioendothelioma with extensive multifocal involvement of the lumbosacral spine, with rapid, short-interval progression. The imaging features of such a dramatic, regional process over a short interval period of time may be mistaken for an osteomyelitis or metastatic process. The purpose of this article was to report the imaging characteristics and progression of one case of lumbosacral spinal epithelioid hemangioendothelioma.

Case report

A 67-year-old patient without significant medical history first presented to an outside hospital with back pain and was found to have a compression fracture at L5. The patient was initially treated with vertebroplasty at the outside hospital, with concomitant core needle biopsy that was negative for malignancy. Approximately 2 weeks later, the patient presented to our institution with progressive back pain and severe pain radiating down both legs. He had no lower extremity numbness or weakness, or bowel or bladder dysfunction. Noncontrast magnetic resonance imaging (MRI) revealed severe vertebral body height loss at L5 with post-vertebroplasty change. There was diffuse signal abnormality on short tau inversion recovery (STIR) images (Fig. 1) and T1 hypointensity (Fig. 2) of the L5 vertebral body with extension into the bilateral pedicles, greater on the right. The posterior margin of L5 retropulsed into the anterior epidural space causing severe central canal stenosis at L5 and S1 (Fig. 3) and severe bilateral L5 and S1 foraminal stenosis. There was relative sparing of the discs and end plates, with only mild edematous change in L4–L5 and L5–S1 intervertebral discs and adjacent paraspinal soft tissues. An additional focus of signal abnormality was noted at the S1 vertebral body. A computed tomography (CT) performed at this time confirmed the L5 fracture and severe L5 canal stenosis, as well as lytic lesions of S1 and S2 (Fig. 4).

The patient subsequently underwent an L5 laminectomy and L4–S1 stabilization and instrumented arthrodesis. L5 corpectomy was attempted but aborted secondary to excessive bleeding. Initial and permanent section pathology was negative for malignancy, demonstrating only fibroadipose tissue with large-walled vessels. Two weeks after the initial decompression, the patient underwent spinal angiography, which demonstrated a vascular lesion at L5 and S1. The lesions were subsequently embolized via the median sacral artery branches supplying L5 vertebral body with Onyx. An 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18FDG-PET/CT) and contrast-enhanced MRI lumbar spine was performed the next day. The PET-CT study demonstrated hypermetabolic activity diffusely in the L5 and S1 vertebral bodies (Fig. 5). Magnetic resonance imaging with contrast demonstrated diffuse enhancement of the L5 and S1 lesions with lesion extension to the ventral epidural space although evaluation was mildly degraded by the presence of the new spinal hardware (Fig. 6).

The patient was subsequently taken back to surgery for further decompression via partial posterior L5 corpectomy, this time with significantly decreased bleeding. Pathology of the L5 corpectomy sample (Fig. 7) demonstrated a vascular tumor with atypical epithelioid cells positive for CD31 (an endothelial marker). CD34, CD68, and Anti-Cytokeratin (CAM 5.2) analyses were negative. ERG, a transcription factor expressed in endothelial cells and used as an immunohistochemical marker, labeled some of the cells. The pathologists at our institution and an outside institution classified this lesion as a hemangioendothelioma, without further classification. A second outside pathology consult classified the lesion as an epithelioid vascular neoplasm, either epithelioid hemangioma or epithelioid hemangioendothelioma variant.

Approximately 2 months after these interventions, the patient presented to neurosurgery clinic with worsening lower extremity weakness and pain radiating to both hips and down both legs. This was associated with new weakness in bilateral feet and difficulty ambulating. He denied bowel or bladder dysfunction. On examination, he had a wide-based gait with new left 2/5 and right 3/5 dorsiflexion strength and bilateral 3/5 EHL, otherwise stable examination. Further MRI imaging at that time showed marked interval extension and progression of disease involving the majority of the L4, S1, and S2 vertebral bodies and posterior elements, as well as the posterior right iliac bone and L3 spinous process (Fig. 8). There was new extension into the anterior epidural space

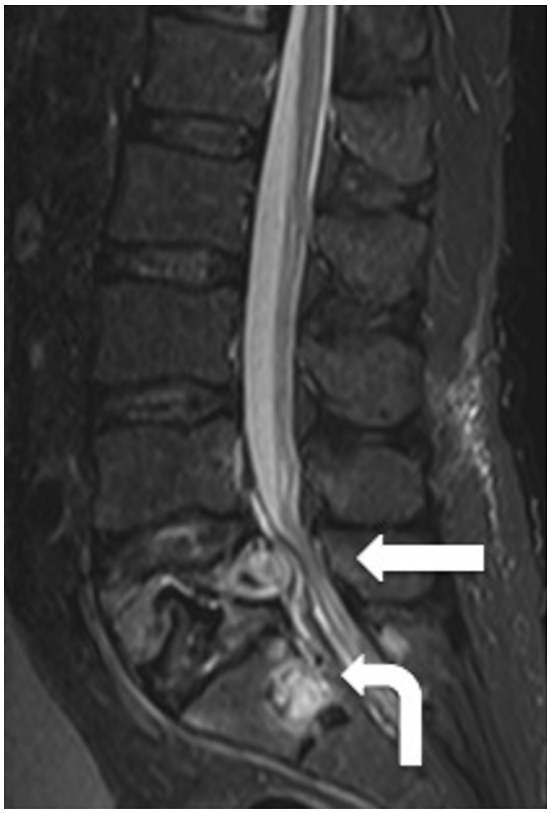

Fig. 1. Sagittal short tau inversion recovery (STIR) magnetic resonance imaging demonstrates diffuse hyperintense signal abnormality of the L5 vertebral body with loss of height and compression of the thecal sac (arrow). There is an additional lesion in S1 (bent arrow).

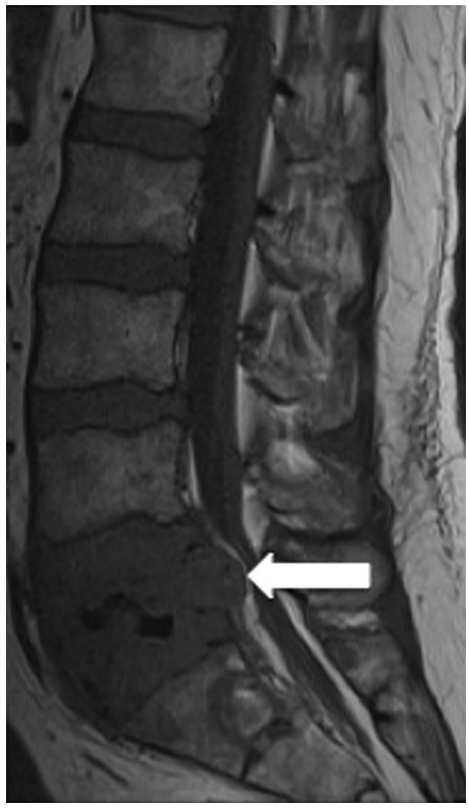

Fig. 2. Sagittal T1-weighted magnetic resonance imaging demonstrating diffuse, homogenous hypointensity of the L5 vertebral body (arrow) with additional focus of signal abnormality at S1.

from L4 to S2 resulting in increased spinal canal stenosis, with new severe stenosis at the S1 retrovertebral level (Fig. 9). There was progressive bilateral L5–S1 foraminal stenosis. The patient was admitted for further management and was started on radiation therapy to the lumbosacral region as the lesions were deemed inoperable.

On follow-up imaging, approximately 3 months after beginning radiation therapy, MRI imaging revealed marked improvement in the patient's epidural mass at L5 (Fig. 10). However, a new lesion was discovered in the T6 vertebral body (Fig. 11), consistent with disease spread. The patient's physical examination remains significant for profound loss of lower extremity dorsiflexion. Sensory loss was noted on the dorsum of both feet.

Discussion

Imaging findings

Radiographic features of epithelioid hemangioendothelioma usually include a well-circumscribed lytic lesion, with some component of sclerosis or expansion and may be difficult to differentiate from hemangioma [4]. Magnetic resonance imaging characteristics of epithelioid hemangiomas and hemangioendotheliomas are

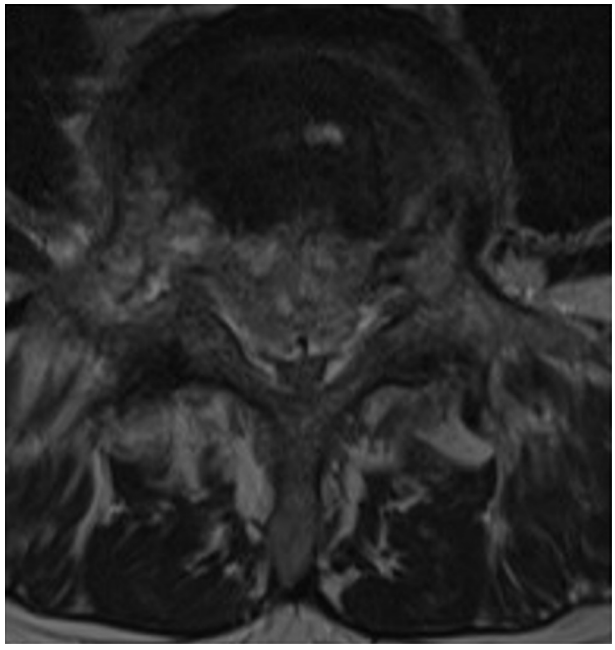

Fig. 3. Axial T2-weighted magnetic resonance imaging demonstrates retropulsion of the posterior margin of L5 into the anterior epidural space causing severe central canal stenosis at L5 and S1.

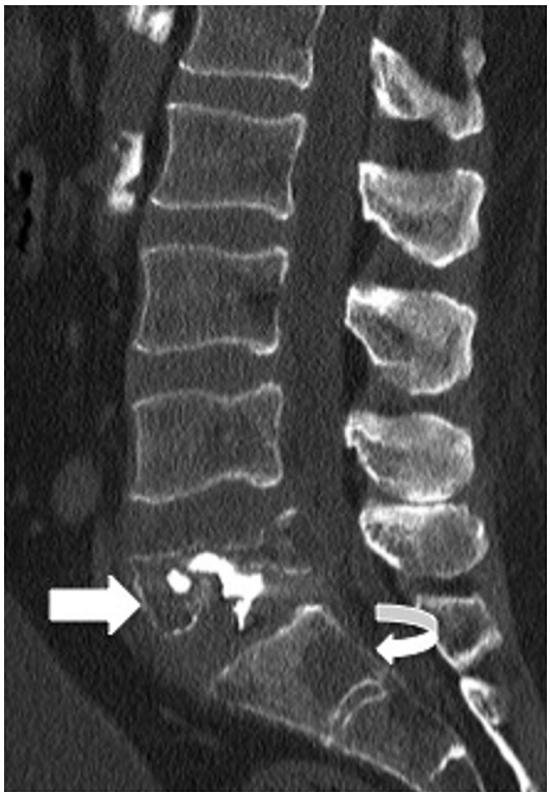

Fig. 4. Sagittal noncontrast computed tomography of the spine demonstrates a compression fracture at L5 (arrow) with cement from vertebroplasty at this level. There is also a large lytic lesion at S1 (curved arrow).

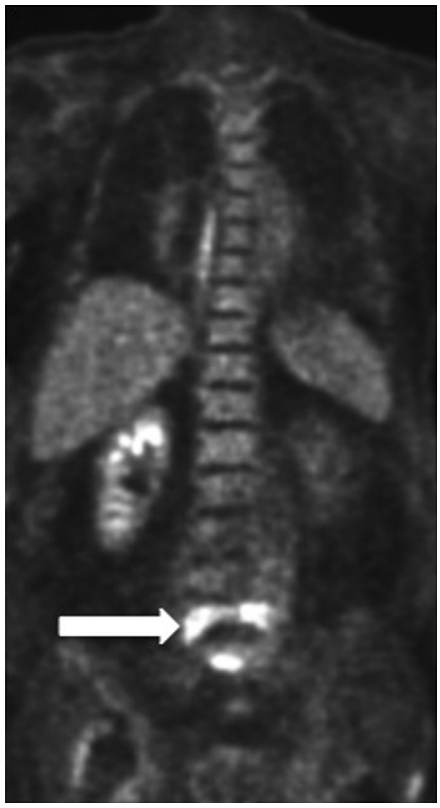

Fig. 5. Coronal 18F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) image of the spine demonstrating FDG avid lesions at L5 (arrow) and S1.

similar and include hypointense signal abnormality on T1-weighted images, and isotense to slightly hyperintense signal on T2-weighted images [5,6]. On T2-weighted images, a ''target'' appearance has also been described with a hypointense center attributed to necrosis and a hyperintense peripheral zone related to active tumor and associated edematous change within the bone marrow. After contrast administration, a peripheral rim of enhancement has been noted, correlating with areas of cellular proliferation [7].

In our case, the MRI findings revealed a destructive, aggressive process with peripheral enhancement and hypointensity on T1-weighted images with mass effect on the spinal cord. Our lesions demonstrated T1 hypointensity, with mild central T2 hyperintensity, a rim of thin T2 hypointensity, and a more peripheral rim of prominent T2 hyperintensity—in a concentric type fashion. We presume these layers represent central vascular pooling and/or necrosis, thin peripheral hemosiderin deposition, and peripheral edema and neoplastic infiltration, respectively. The end plates and discs were relatively spared. The presence of nearby ''satellite'' lesions raised concern for metastatic and neoplastic etiologies although the unusual and destructive appearance made infection a possibility as well. On CT, the lesions were lytic/lucent in nature without significant cortical destruction. The lesions were hypermetabolic on FDG-PET imaging.

Pathology

After review by several pathologists at our institution and an outside institution, hemangioendothelioma was diagnosed although the differential of an epithelioid hemangioma was added by a second outside consultation. It is not unusual to observe characteristics of both subtypes within the same pathologic specimen of bone [4]. Epithelioid hemangioma has been used to describe vascular bone lesions with pathologic features of ''angiolymphoid hyperplasia and eosinophilia,'' and with soft-tissue lesions, even characterized as ''pseudopyogenic granuloma,'' suggesting some element of a reactive process [4]. Typically, the pathologic findings of epithelioid hemangioma can include mature vessels, abundant cellular cytoplasm, and ''tombstone'' morphology of endothelial cells in which they appear to protrude intraluminally [4].

Pathologic findings of epithelioid hemangioendothelioma can be distinguished from epithelioid hemangioma by immature vascular features, hyalinized matrix in the extracellular space, and a ''corded'' cellular arrangement. In epithelial hemangioendothelioma, cellular expression of vimentin, factor VIII–related antigen, CD31, and CD34 on immunohistochemical analysis have all been reported [2,8]. In our case, CD31 was positive. Epithelioid hemangioendotheliomas also tend to manifest as larger, infiltrative

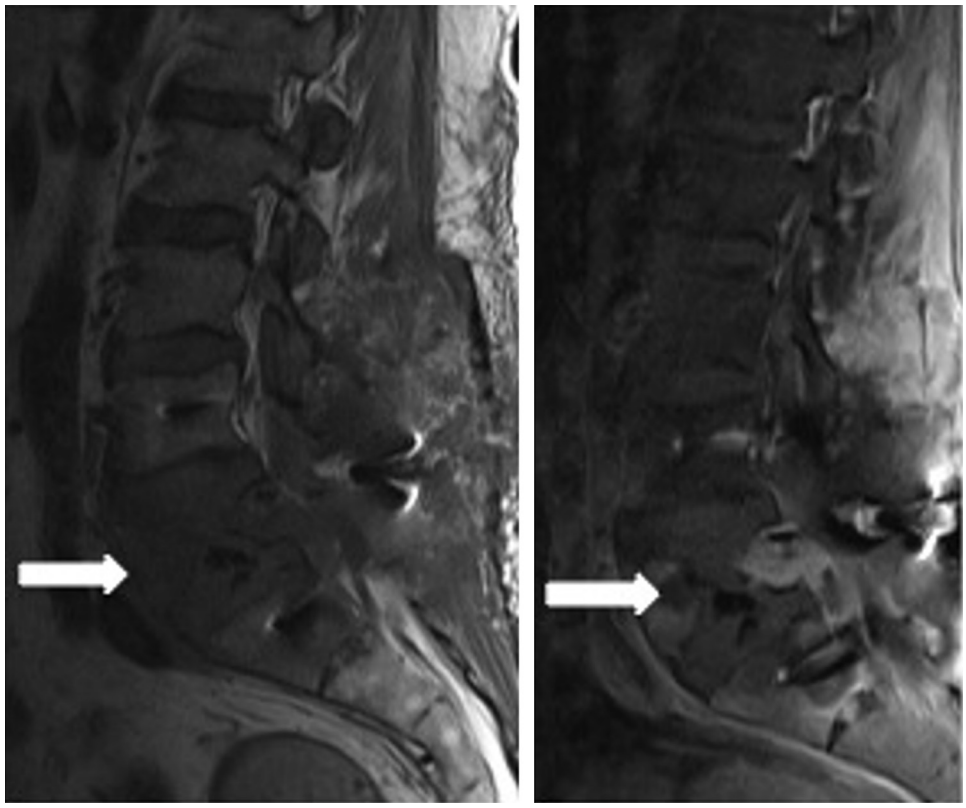

Fig. 6. (Left) Sagittal precontrast T1-weighted image demonstrates hypointense mass (arrow) at L5 extending into the ventral epidural space. (Right) Sagittal postcontrast T1-weighted image shows avid enhancement of the L5 lesion (arrow).

lesions, as opposed to the low-grade epithelioid hemangiomas. Grossly, a surgical specimen of an epithelioid hemangioendothelioma has been described as ''a rubbery red-gray tissue'' [2,5]. Even allowing for these differences, it may be difficult to definitively separate the two. To add to the confusion, the concurrent presence of epithelioid hemangioendothelioma and angiosarcoma appearing has been reported in a single cervical spine lesion [8].

Epithelioid angiosarcoma in the spine is extremely rare in the literature and can be misdiagnosed as a metastatic lesion. The presenting symptom is usually bone pain. These lesions can be extremely destructive and grossly demonstrate areas of necrosis and hemorrhage. The classic pathologic features of epithelioid angiosarcoma involve groups of atypical, large, polygonal epithelioid cells with abnormal mitosis adjacent to focal, communicating epithelioid cell–lined blood vessels [9]. The high mitotic rate in epithelioid angiosarcoma has been used to distinguish it from epithelioid hemangioendothelioma [10]. Both angiosarcoma and epithelioid hemangioendothelioma can be positive for

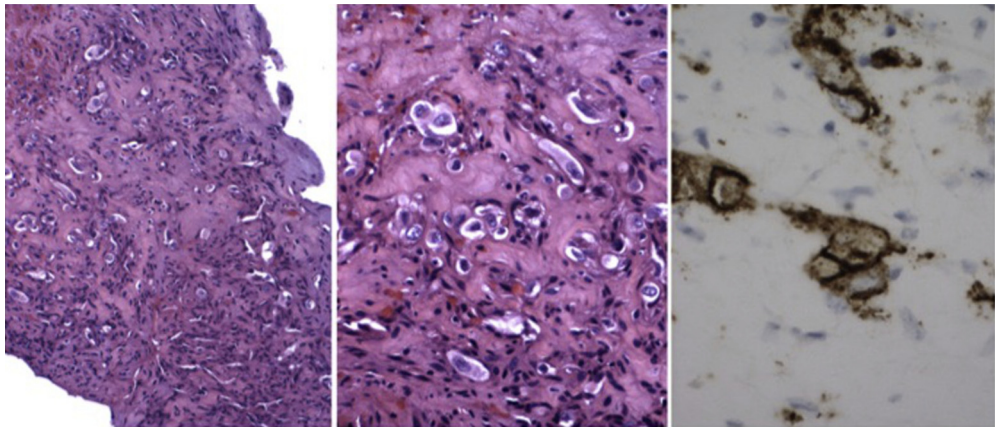

Fig. 7. The vascular L5 tumor magnified at 100x (Left) and at 200x (Middle) stained with hematoxylin and eosin demonstrating atypical epithelioid cells. The cells stain positively with CD31 (endothelial marker) at 400x (Right).

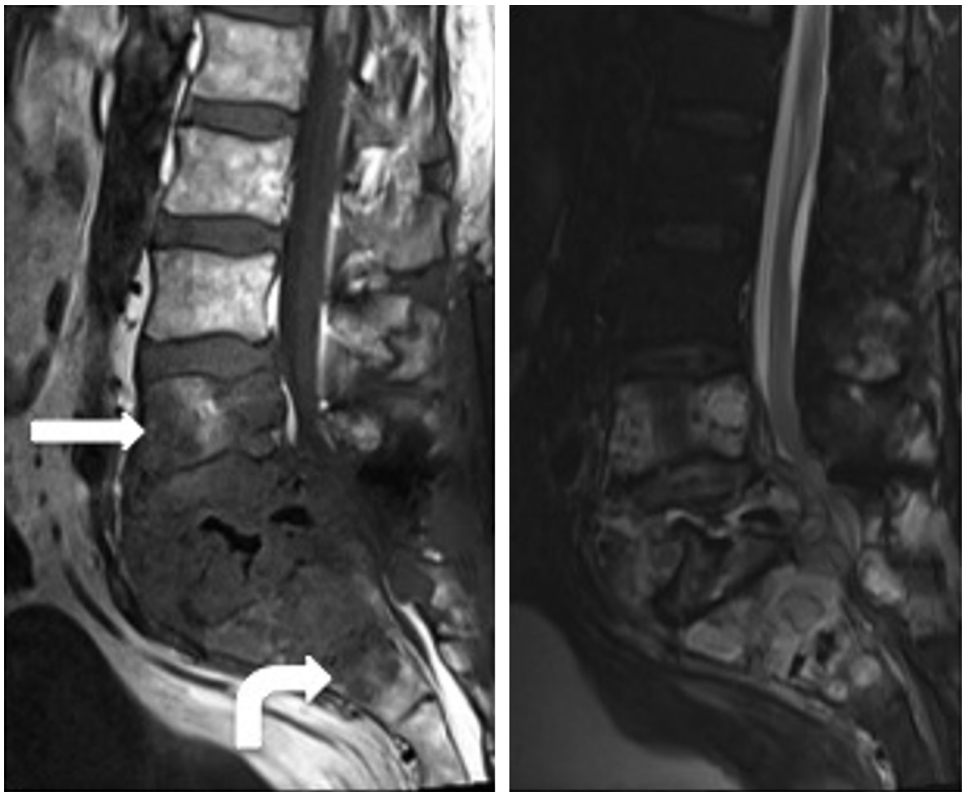

Fig. 8. (Left) Sagittal noncontrast T1 images demonstrate extensive hypointense lesion infiltrating L4 (arrow) through S2 (bent arrow). (Right) Sagittal STIR magnetic resonance imaging demonstrates diffuse signal abnormality throughout L4–S2 and involvement of the spinous process of L3.

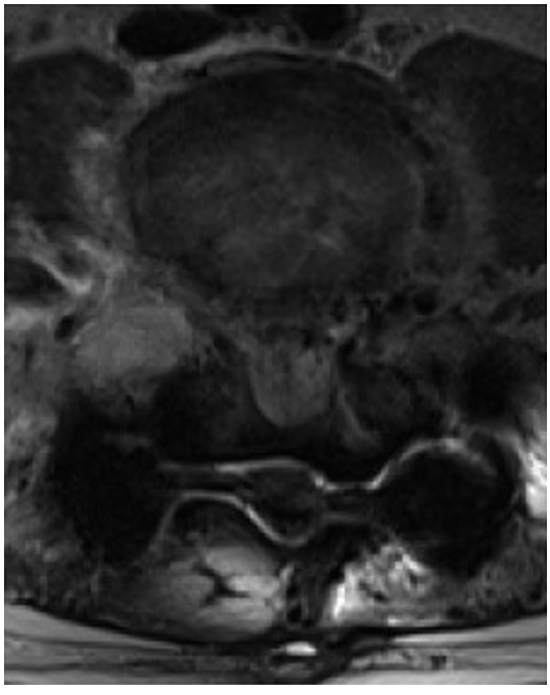

Fig. 9. Axial T2 magnetic resonance imaging demonstrates lesion extension into the ventral epidural space causing severe central canal stenosis at L5 and S1.

CD31 and factor VIII–related antigen on immunohistochemistry analysis [9]. Because of these overlapping immunohistochemistry features, a more specific marker, friend leukemia integration 1 has been found to assist in the diagnosis of epithelioid angiosarcoma [10].

Treatment

The first published case of a vertebral epithelioid hemangioendothelioma was reported in a 31-year-old woman with back pain and without neurologic deficit [5]. Tenderness to palpation localized to the level of L2, and a lytic, destructive L2 vertebral body lesion was incidentally discovered on radiographs. Magnetic resonance imaging revealed an enhancing mass with T1 hypointensity and mild T2 hyperintensity. Percutaneous needle biopsy was nonspecific. Preoperative angiography confirmed the vascular nature of the lesion, and gelfoam embolization was performed to minimize intraoperative bleeding. L2 corpectomy was performed, and interestingly, the vertebral end plates were not involved. L1–L3 interbody fusion with autologous graft was performed, and the patient was asymptomatic at 9-month follow-up [5].

A case series of eight patients with spinal hemangioendothelioma and average 5-year follow-up reported using therapeutic measures including external beam irradiation, surgical resection or laminectomy without irradiation, and

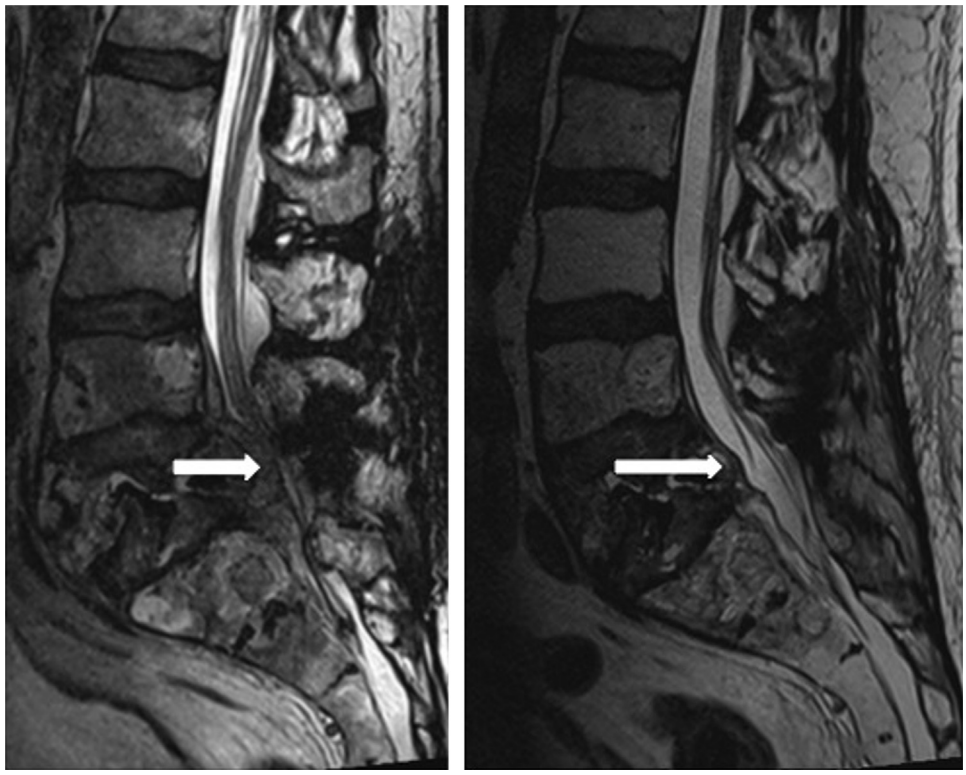

Fig. 10. (Left) Sagittal T2-weighted images demonstrate the ventral epidural extension of tumor at L5 and S1 with severe central canal stenosis before radiation (arrow). (Right) Sagittal T2-weighted image 3 months after starting radiation therapy demonstrates significant improvement of epidural mass and resolution of central canal stenosis (arrow).

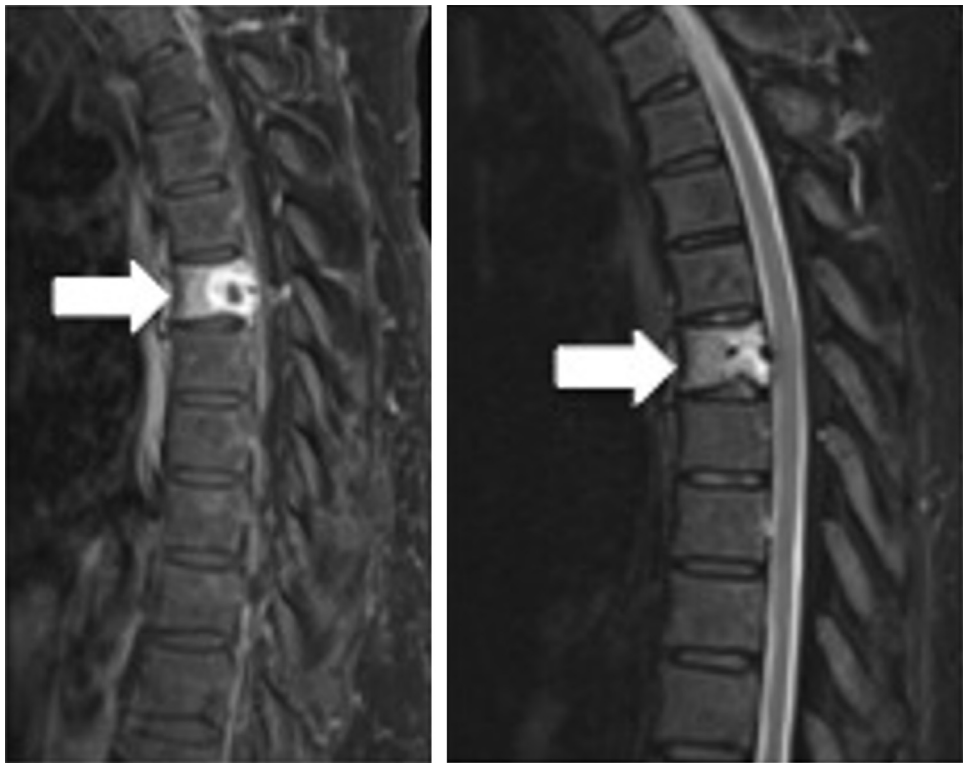

Fig. 11. (Left) On follow-up examination 3 months after beginning radiation therapy, there is a new lesion at T6 with similar, avid enhancement on post-contrast T1-weighted image (arrow) as the lumbar lesions. (Right) STIR magnetic resonance imaging image shows signal abnormality at T6 lesion, consistent with disease progression.

surgical resection or laminectomy with external beam irradiation [3]. Given the vascular nature of these lesions and the potential for significant intraoperative bleeding, presurgical selective embolization was performed [3]. In our case, L5 corpectomy was stopped secondary to excessive intraoperative bleeding, prompting angiography and embolization before a second attempt. A reported advantage to preoperative angiography, in addition to potential embolization, is for the identification of the origin of the feeder artery [5,8].

After surgery, our patient's disease rapidly increased locally, culminating in a large ventral epidural mass causing new severe central canal stenosis within 2 months. It is unclear to what extent vertebroplasty and/or surgical intervention precipitated this event. Such aggressive spread after vertebroplasty or surgical manipulation is not well documented in the literature. We postulate that growth factors may have been induced by mechanical manipulation during surgery resulting in endothelial damage and associated inflammatory changes as potentially promoting this vasoproliferative lesion. Given the aggressive behavior of the tumor, the ideal treatment should start with percutaneous diagnostic biopsy, embolization, and then en bloc resection to avoid violation of the tumor capsule that may lead to metastatic spread of the tumor.

In another case report, before a hemicorpectomy to address an epithelioid hemangioendothelioma at L2, the bilateral segmental arteries of L2 were embolized with polyvinyl alcohol particles [2]. In a case series, it was noted that the single patient receiving external beam irradiation alone was the only patient found to develop metastatic disease on follow-up [3]. Those who underwent stabilization procedures as part of their therapy generally did not develop subsequent pain although one patient developed a radiation-induced sarcoma [3].

In our case, the epidural component of the patient's extensive lumbar lesions markedly improved with radiation therapy. The radiosensitivity of endothelial hemangioendotheliomas has most recently been described in a single-center retrospective study of 14 patients with osseous hemangioendotheliomas, the majority of which (10 of 14) were treated with radiation therapy alone due to inoperable disease. In this study, 100% local control was achieved with an overall 10-year survival of 73% [11]. Another case report describes a patient with lumbar hemangioendothelioma treated with adjuvant chemotherapy (four cycles of paclitaxel and epirubicin) without evidence of recurrence or metastasis at 3-year follow-up [2].

Our case demonstrates that the imaging findings and pathology of this rare vascular spinal tumor may not be so straightforward. To our knowledge, there are no similar reports of the literature of this type of regional multifocal spread of hemangioendothelioma in the lumbosacral spine with metastatic spread to the thoracic spine. The potential rapid progression and local metastasis of an epithelioid hemangioendothelioma should be recognized to better guide follow-up and therapeutic measures. Given the lack of an established algorithm for treatment, our case adds to the few case reports and series, which describe success with preoperative embolization and spinal stabilization, for the benefit of symptom relief and enabling radiation therapy given the radiosensitivity of this tumor.

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