

## Case Report

## Post-irradiation lumbosacral radiculopathy associated with multiple cavernous malformations of the cauda equina: Case report and review of the literature

Doniel Drazin, Ari Kappel<sup>1</sup>, Stefan Withrow, Tiffany Perry, Ray Chu, Surasak Phuphanich<sup>2</sup>

Departments of Neurosurgery, <sup>2</sup>Neurology, Cedars-Sinai Medical Center, Los Angeles, California, <sup>1</sup>School of Medicine, Stony Brook University, New York, USA

E-mail: \*Doniel Drazin - Doniel.drazin@cshs.org; Ari Kappel - ari.kappel@stonybrookmedicine.edu; Stefan Withrow - swithrow@umich.edu;

Tiffany Perry - Tiffany.perry@cshs.org; Ray Chu - ray.chu@cshs.org; Surasak Phuphanich - Surasak.Phuphanich@cshs.org

\*Corresponding author

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### Abstract

**Background:** Multiple radiation-induced cavernous malformations of the cauda equina are extremely rare. A review of the literature suggested that the post-irradiation lumbosacral radiculopathy in our patient was most likely associated with a diagnosis of multiple radiation-induced cavernous malformations of the cauda equina.

**Case Description:** A 76-year-old man with a remote history of abdominal radiation therapy presented with a 6-month history of progressively worsening right foot drop and balance impairment. Magnetic resonance imaging (MRI) revealed multiple enhancing areas of the cauda equina concerning for carcinomatous meningitis, however, cerebrospinal fluid (CSF) analysis was unrevealing. Intraoperative findings were consistent with multiple radiation-induced cavernous malformations of the cauda equina.

**Conclusions:** Multiple radiation-induced cavernous malformations of the cauda equina may mimic carcinomatous or infectious meningitis. Clinicians should be suspicious of this diagnosis when CSF and MRI findings are inconsistent with metastatic disease or infectious meningitis in patients who present with radiculopathy and a history of radiation therapy.

**Key Words:** Cauda equina, cavernous malformation, radiculopathy, radiotherapy, spine

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### INTRODUCTION

The syndrome of post-irradiation flaccid paralysis was first reported by Greenfield and Stark in 1948.<sup>[19]</sup> Since then, approximately 50 cases have been added to the literature.<sup>[2,3,13,17,22,23,27-29,33,46]</sup> The pathophysiology of this syndrome remains unclear. Some authors have endorsed radiation-induced damage to lower motor neurons,<sup>[2]</sup> whereas others have suggested alteration of vascular supply to the cauda equina nerve roots as the principal mechanism.<sup>[3,22]</sup> Of the reported cases, only 11<sup>[3,13,17,22,23,28]</sup>

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demonstrated nodular enhancements in the cauda equina on MRI, and only 5 provided histological evidence of cavernous malformation.<sup>[13,17,23,28]</sup> Here, we report the rare case of a 76-year-old man with radiation-induced radiculopathy and radiologic data consistent with multiple cavernous malformations of the cauda equina.

## CASE REPORT

A 76-year-old male was referred in 2014 with a 6-month history of progressively worsening right foot drop and balance impairment. He had a previous history of abdominal sarcoma treated with surgery, radiation, and chemotherapy in 1980. He had no neurological symptoms at that time.

Neurologic examination was normal except for 2/5 strength in the right tibialis anterior and 1/5 strength in the right extensor hallucis longus. Light touch and vibration sensations were intact. Straight leg raise test was negative, and there were no pathological reflexes. The initial MRI showed numerous small (2–3 mm), contrast-enhancing intrathecal lesions involving the cauda equina nerve roots at the levels of the L2 and L3 vertebrae [Figure 1]. Cerebrospinal fluid (CSF) analysis showed elevated protein of 273 mg/dL and glucose of 60 mg/dL with 7 RBCs/ $\mu$ L and 3 WBCs/ $\mu$ L without carcinomatous cells. Multiple CSF studies and cultures ruled out viral, fungal, and bacterial infections. Repeat CSF cytology did not show malignant cells.

Three months after initial evaluation, the MRI was repeated and appeared stable. The patient underwent L2-L3 laminoplasty with intradural exploration for suspected leptomeningeal carcinomatosis. Intraoperative ultrasound revealed multiple hyperdensities along the cauda equina in the exposed field. The dura and arachnoid were opened under magnification, and the subarachnoid space and cauda equina were examined. Multiple small, mulberry-like nodular lesions associated with dilated vessels were discovered to be intimately involved with the cauda equina [Figure 2]. A biopsy was



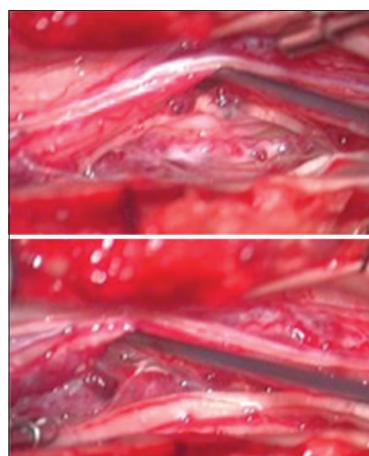
**Figure 1:** Sagittal (a) and axial (b) T1 with contrast MRI images demonstrating multiple, 2-3 mm, contrast enhancing nodules within the cauda equina

not possible due to the close association of the vascular lesions with the nerve roots. There was no evidence of tumor, infection, or arachnoiditis.

The patient was conservatively managed with bedrest, opiates and muscle relaxants and was discharged home with physical and occupational therapy. Spinal angiogram performed at three months and at two years post-operatively showed no abnormal findings. An aortogram was also performed to ensure that no other feeding vessels were identified because of the concern that his prior radiation could have induced stenosis of the vascular supply. This study was also negative. Postoperative MRI was repeated at 6 months, 9 months, and 2 years with stable appearance of the vascular malformations. His current functional status is that he still has the right foot drop and some mild distal weakness on his left.

## DISCUSSION

Our patient developed progressive flaccid right foot weakness 34 years after radiation therapy for abdominal sarcoma. Radiological data showed multiple contrast enhancing, angiographically occult nodules along the cauda equina. The absence of malignant cells in serial CSF studies made a diagnosis of leptomeningeal carcinomatosis less likely. On intraoperative exploration, the appearance of multiple mulberry-like vascular lesions associated with dilated vessels was consistent with multiple vascular malformations of the cauda equina. Because of the risk of permanent damage to the nerve roots of the cauda equina, the lesions were not biopsied and a definitive diagnosis could not be made. However, a review of the literature suggests that the diagnosis of multiple radiation-induced spinal cavernous malformations is the most likely diagnosis.



**Figure 2:** Intraoperative photograph demonstrating multiple small mulberry-like vascular malformations intimately involved with the nerve roots of the cauda equina. These vascular malformations are associated with dilated vessels, and most likely represent multiple radiation-induced cavernous malformations

**Table 1: Reported cases of radiation-induced cavernous malformations of the cauda equina**

First Author (Year)	Age at Presentation (Sex)	Initial Interval (years)	Cancer	Presentation	Clinical Course	CSF	MRI	MRI Findings Localization	Histology
Bowen <sup>[3]</sup> (1996)	61 (M)	11	Testicular Seminoma	Asymmetric distal leg weakness.	Progressive	Protein 400 mg/dL, acellular	Focal enhancement of the lumbosacral roots	Cauda equina	Clusters of dilated vascular channels with thick hyalinized walls
Bowen <sup>[3]</sup> (1996)	47 (M)	10	Testicular teratoma	Initially monomelic distal leg weakness. Areflexic legs.	Progressive	Protein 300 mg/dL, acellular	Focal enhancement of the lumbosacral roots	Cauda equina	Clusters of dilated vascular channels with thick hyalinized walls
Hsia <sup>[22]</sup> (2003)	40 (M)	21	Hodgkin	Left foot drop, L5 radiculopathy, back and leg pain.	Progressive	Protein between 217 to 271 mg/dL, acellular	Nodular leptomeningeal enhancement	Conus medullaris, cauda equina	NA
Hsia <sup>[22]</sup> (2003)	52 (M)	17	Hodgkin	Asymmetric, bilateral leg weakness, wasting and hyporeflexia; intact senses	Progressive	NA	Nodular thickening and enhancement	Cauda equina	NA
Hsia <sup>[22]</sup> (2003)	50 (F)	24	Hodgkin	Asymmetric, bilateral leg weakness and hyporeflexia; intact senses	Progressive	Normal with no malignant cells	Nodular leptomeningeal enhancement	Conus medullaris, cauda equina	NA
Jabbari <sup>[23]</sup> (2004)	33 (M)	29	Wilms Tumor	Asymptomatic incidental finding	NA	NA	Multiple diffuse intradural enhancement of L1-L3	Cauda equina	Clusters of vascular caverns lined by a single layer of endothelium
Labauge <sup>[28]</sup> (2006)	52 (M)	26	Hodgkin	Asymmetric, bilateral leg weakness, wasting, fasciculations, and distal areflexia; intact senses	Progressive	NA	20 mm by 15 mm nonenhanced, intradural mass at L1 of heterogeneous intensity	Cauda equina	Closely apposed dilated vascular cavities without intervening nerve tissue
Ducray <sup>[13]</sup> (2006)	53 (M)	20	Renal Cancer	Left leg numbness, asymmetric weakness, wasting, hyporeflexia, saddle hemianesthesia and sexual dysfunction for four years	Progressive	Protein of 1.8 g/L, with 2 lymphocytes, no malignant cells	Multiple nodular enhancements of the cauda equina nerve roots	Cauda equina	Arachnoid biopsy excluded a malignant infiltration
Ducray <sup>[13]</sup> (2006)	39 (M)	13	Hodgkin	Insidious onset of right foot drop with steppage gait	Progressive	Protein: 250-330 mg/dL, 2 lymphs, no malignant cells	Diffuse, nodular enhancement on T1	Cauda equina	Spinal root cavernomas

Contd...

First Author (Year)	Age at Presentation (Sex)	Initial Presentation (years) cancer	Presentation	Clinical Course	CSF	MRI	MRI Findings Localization	Histology
Ducray <sup>[13]</sup> (2006)	71 (M)	47	Testicular Seminoma	Symmetric, distal weakness of the legs, wasting, fasciculations, areflexia	Progressive	Protein 120 mg/dL, acellular	Diffuse, nodular enhancement of the cauda equina nerve roots on T1	Cauda equina
Farid <sup>[17]</sup> (2014)	NA	NA	Testicular Cancer	Lower back pain and right lower extremity weakness	Progressive	Protein 335 mg/dL, glucose 86 mg/dL, 4 RBCs and 4 WBCs	Multiple nodular enhancement, hyperintense on T1 and iso- to hypointense on T2	Cauda equina
Drazin (2016)	76 (M)	34	Abdominal Sarcoma	Right foot drop and balance impairment for six months	Progressive	Protein 273 mg/dL, glucose 60 mg/dL with 7 RBCs and 3 WBCs	Multiple, small contrast-enhancing intrathecal lesions	NA

CSF: Cerebrospinal fluid, MRI: Magnetic resonance imaging

Intradural spinal cavernous malformations are uncommon lesions that account for only 3–13% of all space occupying spinal lesions.<sup>[25]</sup> Even more unusual is the finding of cavernous malformation of the cauda equina. A review of the literature revealed 23 reported cases of cavernous malformations in the cauda equina.<sup>[4-8,13,14,16,17,21,23,28,34-37,39-41,48]</sup> Most cavernous malformations are believed to be of congenital origin, either developing sporadically or inherited in an autosomal dominant pattern with incomplete penetrance.<sup>[44]</sup> Over the past 20 years, a growing body of literature has linked the development of cavernous malformations to radiation exposure,<sup>[9,24]</sup> however, most of these lesions occurred in the brain.<sup>[18,20,26,30,32,38,49]</sup> Only 11 reported cases of cavernous malformations of the cauda equina were related to prior radiation exposure,<sup>[13,17,23,28]</sup> and only 5 of these provided histologic confirmation.<sup>[13,17,23,28]</sup>

Histologically, cavernous malformations consist of dilated, thin-walled, and compact endothelial-lined channels, which are devoid of intervening neurological tissue.<sup>[1,10,45]</sup> MRI typically reveals areas of mixed signal intensity (SI) with a reticulated core and a prominent surrounding rim of decreased SI on T2-weighted MRI,<sup>[10,43]</sup> but a variety of other MRI appearances are possible and these have been described and classified by Zabramski *et al.*<sup>[50]</sup> Cavernous malformations are angiographically occult. Other angiographically occult vascular malformations include capillary telangiectasias, arteriovenous malformations (AVMs), and venous malformations. The literature suggests that cavernous malformations and small thrombosed AVMs are the most common types of angiographically occult vascular malformations.<sup>[11,12,15,31]</sup> However, data suggests that thrombosed AVMs are a rare cause.<sup>[47]</sup>

The finding of lower motor neuron signs and multiple nodular enhancements of the cauda equina nerve roots in a patient with a history of malignancy and previous radiation therapy presents a diagnostic challenge.<sup>[42]</sup> The differential diagnosis principally concerns metastatic disease, infectious meningitis, and cavernous malformations.<sup>[13,17,22]</sup> CSF studies can help delineate the etiology. The absence of malignant cells and an infectious profile on serial CSF studies makes the diagnosis of metastatic spinal tumors and meningitis unlikely. Mildly elevated protein in the CSF may be present, however, an otherwise normal CSF study points toward the diagnosis of radiation-induced cavernous malformations.<sup>[13]</sup> Other vascular malformations including capillary telangiectasias and AVMs have not been reported. In similar cases of post-irradiation radiculopathy where histologic analysis was available, the definitive diagnosis of multiple cavernous malformations was made [Table 1].<sup>[13,17,28]</sup>

In 1996, Bowen *et al.*<sup>[3]</sup> reported two cases of post-irradiation lumbosacral radiculopathy associated

with gadolinium enhancement of the cauda equina. In this study, histologic examination of fibrosed cauda equina nerve roots revealed clusters of abnormally dilated vascular channels with hyalinized walls. The authors did not use the term "cavernous malformation" to describe these lesions, however, the characteristic histologic features were consistent with this vascular lesion,<sup>[45]</sup> and were similar to the lesions in other studies with histologically proven cavernous malformations.<sup>[13]</sup>

In 2006, Ducray *et al.*<sup>[13]</sup> reported three cases of progressive, radiation-induced lumbosacral radiculopathy, in which each case had multiple nodular enhancements of the cauda equina nerve roots on MRI. Two of these lesions were histologically proven to be cavernous malformations. Jabbour *et al.*<sup>[23]</sup> presented the only case of radiation-induced cavernous malformations of the cauda equina in an asymptomatic patient.

The development of progressive radiculopathy 34 years after lumbar radiation exposure in our patient is consistent with prior cases of post-irradiation lumbosacral radiculopathy with multiple spinal cavernous malformations.<sup>[13,17,28]</sup> The pathophysiology of this disorder may be related to changes in the blood flow caused by multiple cavernous malformations coating the cauda equina, or the presence of these lesions may represent an epiphénoménon not responsible for nerve damage.<sup>[13]</sup> Further research may elucidate the mechanisms by which cavernous malformations develop in patients with a history of radiation therapy, and the pathophysiology of lumbosacral radiculopathy in patients with multiple cavernous malformations of the cauda equina.

## CONCLUSION

Multiple radiation-induced cavernous malformations of the cauda equina may mimic carcinomatous or infectious meningitis. Cavernous malformations of the cauda equina are uncommon lesions, but are the most likely vascular malformation in the setting of post-irradiation radiculopathy. Clinicians should be suspicious of this diagnosis when CSF and MRI findings are inconsistent with metastatic disease or infectious meningitis in patients who present with lumbosacral radiculopathy and a history of radiation therapy. Preoperative diagnosis may prevent unnecessary biopsy and/or treatment.

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## Conflicts of interest

There are no conflicts of interest.

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