

Spinal cavernous malformations: magnetic resonance imaging and associated findings

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INTRODUCTION We reviewed the clinical features, brain and spinal cord magnetic resonance (MR) imaging findings and associated abnormalities in six patients with spinal cavernous malformations (CMs).

METHODS Lesions were defined on gradient-recalled echo (GRE) images but measured on T2-weighted images performed on 1.5- and 3-tesla clinical scanners.

RESULTS Four patients had associated multiple cranial CMs and one patient had multiple spinal CMs. All spinal CMs were predominantly hypointense on GRE images, and most were predominantly hyperintense and surrounded by hypointense edge on T2-weighted images. Other associations included asymptomatic vertebral body and splenic haemangiomas.

CONCLUSION We conclude that intramedullary spinal CMs typically have 'mulberry' or 'popcorn' appearances similar to those of cranial CM. The presence of associated haemangioma or familial cranial CM syndrome on MR imaging may suggest the correct diagnosis without requiring invasive investigations.

Keywords: cavernomas, cavernous malformations, familial cavernomatosis, spinal cord, venous angioma
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INTRODUCTION

Cavernous malformations (CMs) of the central nervous system are angiographically occult vascular malformations defined by abnormal, enlarged vascular channels, but without interposing neural or glial tissue.⁽¹⁻⁷⁾ They may be found either in the brain or spinal cord, and there is a strong association between multiple cranial CMs and familial transmission, with several genetic mutations being described.^(4,5) Although intramedullary CMs are uncommon lesions and comprise about 5% of all spinal cord lesions, they may be associated with spinal haemorrhage, mass effect, myelopathy and significant morbidity.⁽⁸⁻¹¹⁾

With the advent of magnetic resonance (MR) imaging, the prevalence of spinal CM has been estimated to be higher than previously thought.^(7,8) Although the characteristic MR imaging features of cranial CM are well-established,^(2,6-10) the typical findings in spinal CM have not been well-described in the literature, with descriptions limited only to case reports and small series.^(7-10,12) The association of spinal CM with cranial CM as well as the differential diagnosis of intramedullary haemorrhagic lesions would also be of interest to radiologists. In this study, we retrospectively reviewed the clinical features, MR imaging findings and associated abnormalities of patients with spinal CM.

METHODS

This retrospective study was approved by the institutional review board as part of ongoing studies in the Neuroradiology digital imaging database.⁽¹³⁾ Patients with a final diagnosis

of spinal CM and who underwent spinal MR and follow-up imaging were included in the study, and all their neuroimaging and case records were reviewed. Patients with intramedullary spinal lesions, whose final diagnosis was uncertain or who had no follow-up imaging, were excluded. The MR imaging data was acquired on a 1.5-tesla imaging unit (Signa HDX; GE Medical Systems, Milwaukee, WI, USA) or 3-tesla (Achieva; Philips Medical Systems, Best, The Netherlands) clinical scanners. For the imaging studies of the spine, we used the following sequences: T1-weighted (spin echo pulse sequence; TE minimum full; TR 400 msec; matrix size 320 × 192; FOV 22 cm × 22 cm; 3.0-mm slice thickness with a 0.5-mm gap; before and after contrast injection), T2-weighted (fast-recovery fast-spin echo accelerated pulse sequence; TE 105 msec; TR 3000 msec; matrix size 384 × 256; FOV 22 cm × 22 cm; 3.0-mm slice thickness with a 0.5-mm gap) and gradient-recalled echo (fast gradient-recalled echo [GRE] pulse sequence; TE minimum full; TR 400 msec; matrix size 256 × 192; FOV 20 cm × 20 cm; 4-mm slice thickness with no gap). All computed tomography and MR imaging studies of the brain were performed using standard protocols. All images were analysed by consensus reading by two radiologists (TCCL and AH) who were not blinded to the clinical information. All brain and spine lesions were counted if they were visible on GRE images.⁽¹²⁾ The maximum diameter of the lesion was measured on either sagittal or axial planes on T2-weighted images.

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Table I. Patient demographic data, spinal MR imaging findings, associated abnormalities and clinical outcomes in patients with spinal CM.

Case/ age (yr)/ gender	Clinical presentation	MR imaging appearance					Follow-up; outcome
		Level; maximum diameter; location	T2-W images	T1-W images	GRE images	Other MR findings	
1/57/M	Seizures; multiple CMs diagnosed on brain MRI; multiple episodes of brain haemorrhage. 4 years after diagnosis, left-sided weakness and hyper-reflexia; multiple spinal CMs diagnosed on spinal MRI	C1/2; 9 mm; Rt hemicord	Hyperintense, hypointense rim	Isointense	Hypointense	Multiple cranial CMs in pons, cerebrum L2 vertebral body haemangioma	4 years; became progressively immobile and wheelchair-bound, and died after choking on food
		C2; 2 mm; Lt peripheral	Hypointense	Isointense	Hypointense		
		C5/6; 8 mm; Lt hemicord	Hyperintense, hypointense edge	Isointense	Hypointense		
		T1; 4 mm; Lt peripheral	Hyperintense	Isointense	Hypointense		
		T3; 6 mm; Lt hemicord	Hyperintense, hypointense edge	Isointense	Hypointense with hyperintense centre		
2/2/F	Cystic hygroma at birth; seizures; multiple CMs diagnosed on brain MRI; incidental spinal CM diagnosed on MRI	C2; 7 mm; Rt hemicord	Hyperintense, hypointense rim	Hyperintense	Hypointense with hyperintense centre	Multiple cranial CMs in pons, cerebrum Splenic haemangioma	9 years; became progressively immobile and required assisted ventilation, tracheostomy
3/67/F	Neck pain, bilateral lower limb weakness and imbalance; spinal MRI showed spinal CM and brain CM; brain MRI confirmed multiple CMs	C7/T1; 30 mm; holocord	Hyperintense, hypointense rim	Iso, hypointense	Hypointense with hyperintense centre	Multiple cranial CMs in cerebrum, pons C6 vertebral body haemangioma	1 year; symptoms improved and ADL independent
4/46/M	Right upper limb weakness and numbness; spinal MRI showed spinal CM and brain CM; brain MRI confirmed multiple CMs	C4/5; 9 mm; Rt peripheral	Hyperintense, hypointense rim	Hyperintense, hypointense edge	Hypointense with hyperintense centre	Multiple cranial CMs in cerebrum, pons	8 years; exacerbations of right upper limb pain and numbness, and seizures
5/37/M	Sudden onset left hand numbness; spinal CM diagnosed on spinal MRI and negative spinal angiography; brain MRI was normal	C7; 8 mm; Lt hemicord	Hyperintense, hypointense rim, with intramedullary haemorrhage and oedema	Iso, hypo, hyperintense	Hypointense	None	1 year; haematoma resolved, symptoms improved and ADL independent
6/24/F	Sudden onset right upper limb weakness and numbness; spinal CM diagnosed on spinal MRI and negative spinal angiography; brain MRI was normal	C2; 8 mm; Rt hemicord	Hyperintense, hypointense rim, with intramedullary haemorrhage and oedema	Iso, hypo, hyperintense	Hypointense with hyperintense centre	None	5 years; haematoma resolved, symptoms improved and ADL independent

M: male, F: female, CM: cavernous malformation, GRE: gradient-recalled echo, ADL: activities of daily living; Rt: right; Lt: left

RESULTS

Table I summarises the MR imaging findings, the associated abnormalities and clinical outcomes in the patients with spinal CM. Six patients (3 male and 3 female; 5 Chinese and 1 Indian) were included in the database. One patient was a two-year-old girl, while the others were adults aged 24–67 years at presentation. Two patients (Cases 1 & 2) had a known diagnosis of multiple cranial CMs detected on MR imaging, which was

presumed to be caused by familial CM syndrome (but without genetic testing) (Fig. 1a). Both patients suffered from seizures and developed progressive neurological symptoms, including weakness and hyper-reflexia. Spinal CM was subsequently diagnosed on spinal MR imaging (Figs. 1b & c). The other four patients (Cases 3–6) developed limb weakness or numbness without a prior diagnosis of cranial CM (Case 3 had a history of seizures without neuroimaging). Case 1 had four discrete spinal

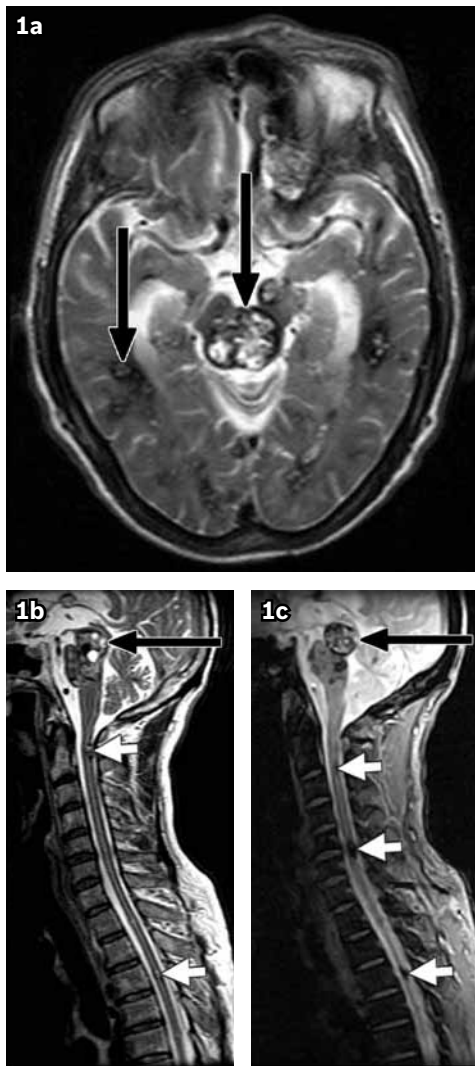


Fig. 1 Case 1: A 57-year-old man with cranial and spinal cavernous malformations (CMs). (a) Initial T2-W MR image of the brain shows multiple cranial CMs (arrows) with heterogeneously hyperintense centres and hypointense rims. Four years later, spinal MR images show multiple intramedullary spinal CMs (white arrowheads) in the cervical cord on (b) sagittal T2-W and (c) sagittal GRE images. Note the large cranial CM in the pons (arrows in b, c).

CMs (Figs. 1b & c), yielding a total of ten spinal lesions in six patients. Of these, seven were found in the cervical spinal cord, two in the thoracic cord and one at the cervicothoracic junction. The largest lesion measured 30 mm in maximum superior-inferior diameter and occupied almost the entire spinal cord, while the smaller lesions were located at the periphery of the intramedullary region or occupied less than half the cross-sectional area of the spinal cord.

On T2-weighted images, most spinal CMs were heterogeneous in signal intensity, with predominant hyperintensity surrounded by a hypointense rim or edge (Fig. 2) in eight lesions, corresponding to the typical lobulated 'mulberry-like' appearance of cranial CM.⁽¹⁴⁻¹⁷⁾ The hypointense edge was not detected in the two smallest lesions in Case 1, which were uniformly hypointense or hyperintense. The appearances were less consistent and heterogeneous on T1-weighted images. These included isointensity (in all CMs in Case 1), hyperintense, hyperintense with hypointense edge and heterogeneous intensity.

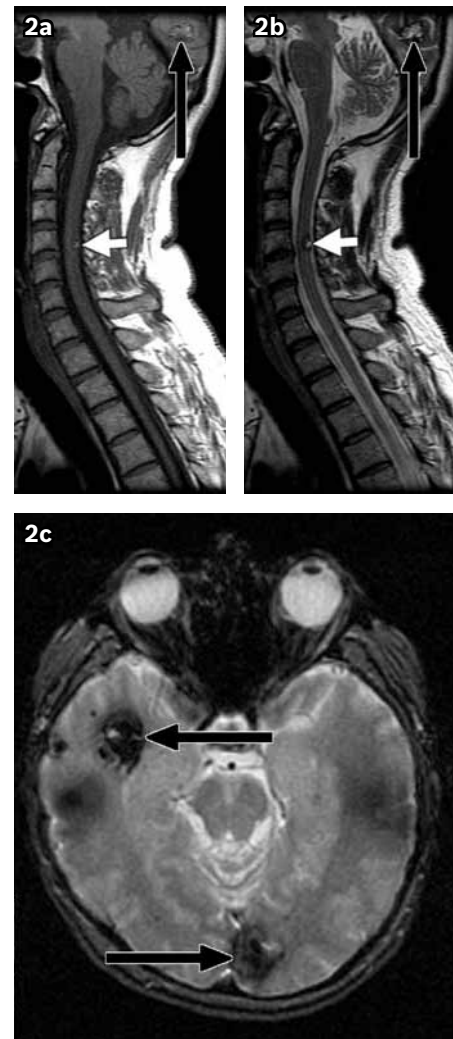


Fig. 2 Case 4: A 46-year-old man with spinal and cranial cavernous malformations (CMs). Sagittal (a) T1-W and (b) T2-W spinal MR images show a focal area of hyperintensity with hypointense rim at the C4/5 interspace (white arrowheads). A large cranial CM with similar signal intensity can be seen in the occipital lobe (arrows). (c) GRE MR image of the brain confirms the presence of multiple cranial CMs in the occipital and temporal lobes (arrows) and elsewhere.

All the lesions were predominantly hypointense on GRE, with some of the larger lesions showing a hyperintense centre. After contrast media injection, no significant enhancement was detected in the spinal CM. In addition to spinal CM at C7 spinal level, Case 5 presented with extensive intramedullary haemorrhage and oedema extending from C3 to T4 (Fig. 3a). Case 6 also had intramedullary haemorrhage and oedema from C1 to C7 around the spinal CM at C2.

Four of the six patients had associated multiple cranial CMs. Cases 1 and 2 had a presumptive diagnosis of familial cranial CM with large lesions in the pons and cerebrum; spinal CM was only diagnosed later. Cases 3 and 4 initially presented with spinal symptoms, and cervical spinal imaging not only detected spinal CM but also incidental MR imaging evidence of asymptomatic cranial CM in the medulla oblongata and occipital lobe (Figs. 1a-c, 2a & b). Subsequent dedicated brain MR imaging studies revealed multiple CMs in the cerebrum and pons (Fig. 2c). In addition, associated asymptomatic lesions outside the

brain and spinal cord were detected, including vertebral body haemangiomas (Cases 1 & 3) and splenic haemangiomas (Case 2). Cases 5 and 6 had only spinal CM without cranial CM on brain MR imaging; spinal angiography performed in both patients was normal.

All patients were followed up conservatively without surgical intervention for 1–9 years. Cases 1 and 2, who had large lesions in the pons, became progressively weaker and immobile; Case 1 died after four years and Case 2 required assisted ventilation. Case 4 complained of symptomatic exacerbations, while Cases 3, 5 and 6 recovered their neurological functions and were independent in activities of daily living at the last follow-up. Repeat spinal MR imaging in Cases 5 and 6 showed resolution of intramedullary oedema and haemorrhage, with myelomalacia and residual blood products around the CM (Fig. 3b).

DISCUSSION

In our series, four (Cases 1–4) out of six patients with spinal CM had associated multiple cerebral CMs. Multiple CMs affecting the brain are often associated with the familial form of cavernomatosis, an autosomal-dominant pattern of inheritance with incomplete penetrance, first described in French and Hispanic families,^(18,19) and subsequently reported all around the world. Linkage studies have revealed genetic heterogeneity among the dominantly inherited forms, suggesting the existence of at least three loci on chromosomes 7q11-21, 7p13-15 and 3q25.2-27.^(4,5)

Although none of the patients in our series underwent genetic testing, they probably had familial CM, as multiple cranial CMs is a *sine qua non* of the condition, affecting 50%–85% of patients. Cases 1 and 2 were known to have multiple, probably familial cranial CMs, and subsequently developed symptoms that revealed spinal CM on MR imaging of the spinal cord. On the other hand, Cases 3 and 4 were not known to have cranial CM and first presented with spinal symptoms; on spinal MR imaging, the asymptomatic cranial CMs were detected, leading to the diagnosis of multiple CMs. Multiple spinal CMs, detected in Case 1 in our series, are rare, comprising only 2% of spinal cord cavernomas.⁽²⁰⁾

Two studies of 117 and 17 patients, conducted by Zevgaridis and Vishteh et al, respectively, detected only one case of multiple spinal CMs each, and these two patients also had familial CM syndrome with multiple cranial CMs.^(21,22) The MR imaging features of spinal CMs in our patients were similar to the typical descriptions of intracranial CMs in the literature.⁽¹⁴⁻¹⁷⁾ Seven of the ten spinal lesions had a well-defined, lobulated appearance, with a reticulated core of heterogeneously hyperintense signal associated with a hypointense edge or rim on T2-weighted images, the ‘mulberry’ or ‘popcorn’ appearance typical of CM.⁽¹⁴⁻¹⁷⁾ According to previous histological studies on cranial CM, extracellular and intracellular methaemoglobin and thrombosis are probably responsible for the high-intensity signal, while calcifications, fibrosis, and acute and subacute blood products are responsible for the low-signal areas within the



Fig. 3 Case 5: A 37-year-old man with spinal cavernous malformations (CMs). (a) Sagittal T2-W spinal MR image shows focal hyperintensity with hypointense edge at the C7 vertebral level (arrowhead) with surrounding spinal cord oedema. (b) Repeat sagittal T1-W MR image two months later shows myelomalacia and partial resolution of haemorrhage and oedema.

lesion.⁽⁷⁾ Two of the smallest lesions in Case 1 did not exhibit the typical appearance on T2-weighted images, and were uniformly hypointense or hyperintense. On T1-weighted images, signal intensities were less consistent, with most lesions being heterogeneously isointense. GRE, which is very sensitive to even small amounts of magnetic susceptibility caused by the presence of iron in blood products, typically detects cranial and spinal CMs as focal areas of hypointensity, with the larger lesions in our study showing a heterogeneous, predominantly hyperintense centre, presumably resulting from thrombosis, fibrosis, calcification and haemorrhage.⁽²⁾ Typical MR imaging features of spinal CM accompanied by synchronous multiple cranial CMs may be helpful for diagnosis.

Several studies have noted the co-existence of spinal and cranial CMs. In a large series of 67 patients with spinal CM, the prevalence of cranial CM was found to be 42%, with 43% of these being the sporadic or nonfamilial form of the disease.⁽¹⁰⁾ Cases 1–4 had the characteristic multiple cranial and spinal CMs, as well as other asymptomatic lesions (probably haemangiomas, but not biopsy proven) in the spleen and vertebral bodies in the spine, features that support the diagnosis of familial CM.^(22,23) In such patients, it may be possible to avoid invasive confirmatory procedures such as spinal angiography and surgical excision.⁽¹²⁾ Conversely, Cases 5 and 6 had spinal CM with intramedullary haemorrhage, but MR imaging of the brain revealed no associated cranial CM, and a differential diagnosis of spinal arteriovenous malformation, haemorrhagic neoplasm (ependymoma, astrocytoma, haemangioblastoma, metastasis) haemorrhagic infection or transverse myelitis could not be excluded on imaging alone. Unless it is surgically resected, spinal

CM is often a diagnosis of exclusion, after spinal angiography has ruled out arteriovenous shunts and follow-up imaging has ruled out aggressive neoplasia. Hence, Cases 3 and 4 illustrate the importance of a systematic radiological review of the brain posterior fossa, which is included in cervical spinal MR imaging study, and subsequently a full brain MR imaging study to detect cranial CM.

Our study was limited by a small sample size and the lack of histopathological confirmation of spinal CM. Since most spinal cavernomas are detected incidentally on MR imaging, the sampling bias may explain the predominance of cervical cord spinal CM in our patients, compared to the more common thoracic location described by other authors.^(7,9,12) In this study, none of our patients underwent surgical resection, although the risk of haemorrhage in spinal CM, estimated at 1.4%–4.5% per year, is higher than that of cranial CM.^(24,25) Hence, some authors have advocated surgical excision of spinal CM⁽²⁶⁾ and proposed a prognostic classification of cranial CM based on their natural history and clinical outcomes.⁽²⁷⁾ In our small series, there were no patients who suffered repeated spinal CM haemorrhage on follow-up. However, Cases 1 and 2, who had extensive cranial CM, especially involving the pons, had poor outcomes and became progressively incapacitated, suggesting that clinical outcome may depend on the characteristics of cranial as well as spinal CMs.^(2, 28)

In conclusion, spinal CMs have typical features on MR imaging, and the ‘mulberry’ or ‘popcorn’ appearance of these lesions should be recognised. These characteristic imaging findings, together with imaging detection of similar-appearing multiple cranial CMs and haemangiomas elsewhere in the body, may be helpful to suggest a familial syndrome that may obviate the need for more invasive investigations.

REFERENCES

- Russell DS, Rubenstein LJ. Pathology of Tumors of the Nervous System. 5th ed. Baltimore: Williams & Wilkins, 1989: 730-6.
- Rivera PP, Willinsky RA, Porter PJ. Intracranial cavernous malformations. *Neuroimaging Clin N Am* 2003; 13:27-40.
- Del Curling O Jr, Kelly DL Jr, Elster AD, Craven TE. An analysis of the natural history of cavernous angiomas. *J Neurosurg* 1991; 75:702-8.
- Dubovsky J, Zabramski JM, Kurth J, et al. A gene responsible for cavernous malformations of the brain maps to chromosome 7q. *Hum Mol Genet* 1995; 4:453-8.
- Marchuk DA, Gallione CJ, Morrison LA, et al. A locus for cerebral cavernous malformations maps to chromosome 7q in two families. *Genomics* 1995; 28:311-4.
- Rigamonti D, Drayer BP, Johnson PC, et al. The MRI appearance of cavernous malformations (angiomas). *J Neurosurg* 1987; 67:518-24.
- Deutsch H, Jallo GI, Faktorovich A, Epstein F. Spinal intramedullary cavernoma: clinical presentation and surgical outcome. *J Neurosurg* 2000; 93:65-70.
- Cantore G, Delfini R, Cervoni L, Innocenzi G, Orlando ER. Intramedullary cavernous angiomas of the spinal cord: report of six cases. *Surg Neurol* 1995; 43:448-52.
- Labauge P, Bouly S, Parker F, et al; French Study Group of Spinal Cord Cavernomas. Outcome in 53 patients with spinal cord cavernomas. *Surg Neurol* 2008; 70:176-81.
- Cohen-Gadol AA, Jacob JT, Edwards DA, Krauss WE. Coexistence of intracranial and spinal cavernous malformations: a study of prevalence and natural history. *J Neurosurg* 2006; 104:376-81.
- Ogilvy CS, Louis DN, Ojemann RG. Intramedullary cavernous angiomas of the spinal cord: clinical presentation, pathological features, and surgical management. *Neurosurgery* 1992; 31:219-30.
- Gross BA, Du R, Popp AJ, Day AL. Intramedullary spinal cord cavernous malformations. *Neurosurg Focus* 2010; 29:E14.
- Yang GL, Tan YF, Loh SC, Lim CC. Neuroradiology imaging database: using picture archive and communication systems for brain tumour research. *Singapore Med J* 2007; 48:342-6.
- Anson JA, Spetzler RF. Surgical resection of intramedullary spinal cord cavernous malformations. *J Neurosurg* 1993; 78:446-51.
- McCormick PC, Michelsen WJ, Post KD, Carmel PW, Stein BM. Cavernous malformations of the spinal cord. *Neurosurgery* 1988; 23:459-63.
- Barnwell SL, Dowd CF, Davis RL, et al. Cryptic vascular malformations of the spinal cord: diagnosis by magnetic resonance imaging and outcome of surgery. *J Neurosurg* 1990; 72:403-7.
- Akbostanci MC, Yiğit A, Ulkatan S. Cavernous angioma presenting with hemidystonia. *Clin Neurol Neurosurg* 1998; 100:234-7.
- Hayman LA, Evans RA, Ferrell RE, et al. Familial cavernous angiomas: natural history and genetic study over a 5-year period. *Am J Med Genet* 1982; 11:147-60.
- Rigamonti D, Hadley MN, Drayer BP, et al. Cerebral cavernous malformations. Incidence and familial occurrence. *N Engl J Med* 1988; 319:343-7.
- Labauge P, Laberge S, Brunereau L, Levy C, Tournier-Lasserre E. Hereditary cerebral cavernous angiomas: clinical and genetic features in 57 French families. *Société Française de Neurochirurgie. Lancet* 1998; 352:1892-7.
- Zevgaridis D, Medele RJ, Hamburger C, Steiger HJ, Reulen HJ. Cavernous haemangiomas of the spinal cord. A review of 117 cases. *Acta Neurochir (Wien)* 1999; 141:237-45.
- Vishthek AG, Sankhla S, Anson JA, Zabramski JM, Spetzler RF. Surgical resection of intramedullary spinal cord cavernous malformations: delayed complications, long-term outcomes, and association with cryptic venous malformations. *Neurosurgery* 1997; 41:1094-101.
- Abdulrauf SI, Kaynar MY, Awad IA. A comparison of the clinical profile of cavernous malformations with and without associated venous malformations. *Neurosurgery* 1999; 44:41-7.
- Santoro A, Piccirilli M, Brunetto GM, Delfini R, Cantore G. Intramedullary cavernous angioma of the spinal cord in a pediatric patient, with multiple cavernomas, familial occurrence and partial spontaneous regression: case report and review of the literature. *Childs Nerv Syst* 2007; 23:1319-26.
- Sandalcioglu IE, Wiedemayer H, Gasser T, et al. Intramedullary spinal cord cavernous malformations: clinical features and risk of hemorrhage. *Neurosurg Rev* 2003; 26:253-6.
- Kim LJ, Lanzino G, Spetzler RF, et al. Surgical management of spinal cord cavernous malformations: the Barrow Neurological Institute experience. *J Neurosurg* 2003; 98:A234-5.
- Zabramski JM, Wascher TM, Spetzler RF, et al. The natural history of familial cavernous malformations: results of an ongoing study. *J Neurosurg* 1994; 80:422-32.
- Porter PJ, Willinsky RA, Harper W, Wallace MC. Cerebral cavernous malformations: natural history and prognosis after clinical deterioration with or without hemorrhage. *J Neurosurg* 1997; 87:190-7.