Case Report

Pure lumbar foraminal cavernous malformation in a patient with Cowden syndrome—a case report

Ginevra Federica D'Onofrio[1,2]^, Gabriele Capo[1], Alexandre Vasiljevic[3], Cédric Y. Barrey[1,4]

[1]Department of Spine and Spinal Cord Surgery, Pierre Wertheimer Hospital, Hospices Civils de Lyon, and Claude Bernard University of Lyon 1, Lyon-Bron, France; [2]Agostino Gemelli Hospital, IRCCS, Catholic University of the Sacred Heart, Rome, Italy; [3]Department of Pathology and Neuropathology, Lyon Civils Hospitals, Lyon-Bron, France; [4]Laboratory of Biomechanics, ENSAM, Arts et Metiers ParisTech, Paris, France

Correspondence to: Ginevra Federica D'Onofrio, MD. Department of Spine and Spinal Cord Surgery, Pierre Wertheimer Hospital, Hospices Civils de Lyon, 59 Bd Pinel, 69500 Bron, Lyon, France. Email: ginevra.federica.donofrio@gmail.com.

Background: Spinal cavernous malformations (CMs) are slow flow venous vascular malformations which can occur in vertebral body, epidural space or intramedullary. Only 7 cases were described confined in foraminal space. Cowden syndrome (CS) is an autosomal dominant genodermatosis that may present and develop vascular malformations, which include CM. They were found intracranial, and rarely visceral. No association with spinal CM and CS has been reported to date.

Case Description: A 46-year-old patient with CS came to our attention with a L5 radiculopathy secondary to a slow-growing intra-foraminal mass lesion, with bony scalloping. The lesion mimicked a schwannoma at radiological imaging and intraoperative findings. *En bloc* resection with root sacrifice was performed. No excessive bleeding was observed. After surgical resection, anatomical pathology demonstrated a CM. Postoperative review of neuroimaging revealed features compatible with chronic resolved peripheral haemorrage. The patient had no intra- or post-operative complications, and an immediate relief of symptoms was observed. The follow-up spinal magnetic resonance imaging (MRI) obtained 3 months after surgery, demonstrated the total removal of the lesion.

Conclusions: CMs can be confined to foraminal space and associated with CS. They may mimic peripheral nerve sheath tumors. Diagnosis may be challenging. No pathognomonic imaging features were found. Complete resection with root sacrifice seems to be a safe and efficient technique.

Keywords: Case report; cavernous malformation (CM); intra-foraminal tumor; nerve root sacrifice; Cowden syndrome (CS)

Submitted Mar 14, 2022. Accepted for publication Jun 01, 2022.
doi: 10.21037/jss-22-21
View this article at: https://dx.doi.org/10.21037/jss-22-21

Introduction

Cavernous malformations (CMs), previously called cavernous hemangiomas, cavernous angiomas or cavernomas, are well circumscribed non-neoplastic slow flow venous vascular malformations, found in the central nervous system (CNS) and throughout the body. They are histologically composed of abnormal, dilated vascular sinusoidal channels without interposed neural tissue (1). The origin of these lesions is still unknown. Harrison *et al.* postulated that primordial vessels may lose their capacity to differentiate, resulting in a CM (2).

They rarely occur in spine, accounting for 5–12% of all spinal vascular lesions (3). Spinal CMs can develop from the intervertebral stroma, so called vertebral

^ ORCID: 0000-0001-9948-9237.

hemangioma, or may be epidural, intradural extramedullary or intramedullary. The majority of spinal CMs are confined to the vertebral bodies with or without epidural space extension, while pure epidural location is uncommon, comprising ~1–2% of spinal hemangiomas (4). The intramedullary CMs are about 3% (5), while the intradural extramedullary CMs are rarely seen, usually at level of the conus medullaris and cauda equina (6).

Despite all these malformations being histologically identical (2), vertebral and extradural lesions display rich vascularity, in contrast to intradural CMs (7), which are less vascularized.

However, all locations may cause neurological deficit through either haemorrhage and/or mass effect.

The pure (intradural-extramedullary) foraminal CMs are extremely rare and, to the best of our knowledge, only 7 cases have been reported. Among them, 5 were in the lumbar spine. These lesions represent a challenge to radiologists who may misdiagnose them as nerve sheath tumors. Establishing a correct diagnosis may help to provide proper treatment avoiding maneuvers that favor bleeding.

We present a case of a pure foraminal CM originating from the L5 nerve root, presenting in a 46-year-old female, with low back pain and right lower extremity radiculopathy, in the context of the Cowden syndrome (CS). CS is an autosomal dominant multisystem disorder with a predisposition for the development of benign hamartomas and a spectrum of malignancies. Vascular malformations also are not uncommon (8). We present the following case in accordance with the CARE reporting checklist (available at https://jss.amegroups.com/article/view/10.21037/jss-22-21/rc).

Case presentation

A 46-year-old female with CS presented with a history of intermittent radicular pain in the right L5 nerve root distribution. The pain was described as paroxysmal tingling and burning sensation. Magnetic resonance imaging (MRI) of the spine showed an intra-foraminal lesion which measured 15×15 mm in axial slides at L5-S1 level, following the L5 nerve root through the foramen on the right side. The lesion had hypointense signal on T1-weighted images (T1-WI), hypersignal on T2-weighted images (T2-WI) and demonstrated low-contrast enhancement. No intra or peri-lesion haemorrage had been described, nor CM suspected. No T1-WI fat-saturation or T2-WI gradient-echo (T2*GRE) imaging was completed. Considering the localization of lesion and the imaging appearance, a provisional diagnosis of spinal schwannomas was suggested.

Based on episodic symptoms and in the absence of neurological deficit, after discussion with the patient, we decided to repeat MRI at 6 months. Subsequently the patient postponed the follow-up visit and MRI.

She returned to our attention 4 years later with severe and persistent radicular pain with nocturnal awakenings not relieved by analgesics. No focal neurological deficit was identified on physical examination, as in the first assessment. The new conventional MRI (T1-gadolinium, T2-WI) found an increase lesion volume (17×20 mm), but not other new features were described (*Figure 1*). Scalloping of the posterior surfaces of the vertebral bodies and enlargement of intervertebral foramen was present on CT (*Figure 2*). Elective surgery was scheduled.

The patient underwent right L5 hemilaminectomy with partial L5-S1 facectomy and Y-shaped dural incision. The entire L5 root was resected, and lesion totally removed.

No precautions had been taken for approach. The lesion was intra-extradural (small component intradural), with extension along the nerve sheath. It presented firm consistency. The root was completely infiltrated by the lesion, mimicking a neurogenic tumor. Complete removal of the tumor tissue was not achievable without the sacrifice of the root. No bleeding was observed during the *en-bloc* resection.

Histological examination revealed a CM. The lesion was characterized by the presence of multiple vascular channels of varying size, lined by thick collagenous walls with adhesion to some nerve fibers (*Figure 3*).

The patient made an excellent recovery with pain improvement without postoperative complications. No post-operative neurological deficit was identified. The follow-up spinal MRI obtained 3 months after surgery demonstrated the total removal of the lesion (*Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

We present a case of a spinal CM in the context of CS,

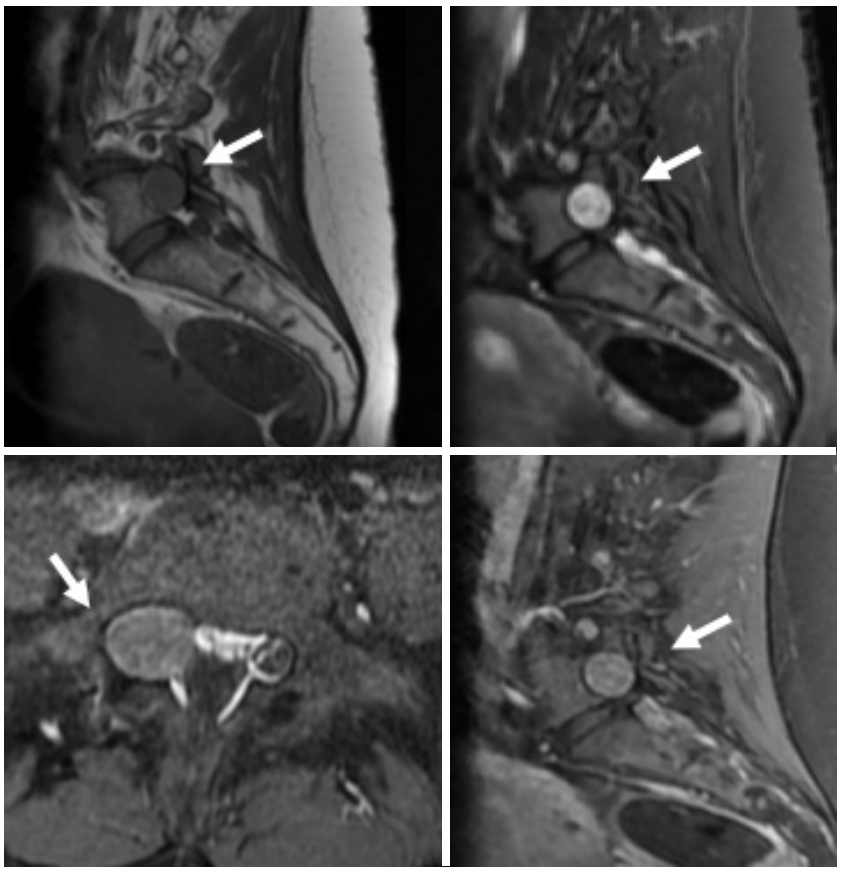

Figure 1 Preoperative MRI. Upper left: sagittal T1-WI images showing a lesion with isointensity signal (arrow). Upper right: sagittal T2-WI MRI scans demonstrating a hyperintense signal of the lesion (arrow). Lower left and lower right: T1-WI contrast-enhanced axial and T1-WI contrast-enhanced sagittal imaging demonstrating an intervertebral foramina mass at L5-S1 with homogenous enhancement (arrows). MRI, magnetic resonance imaging; T1-WI, T1-weighted images; T2-WI, T2-weighted images.

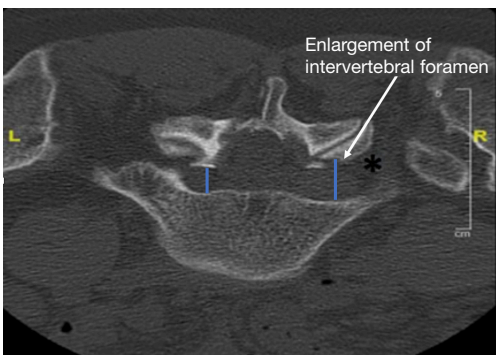

Figure 2 Preoperative axial computed tomographic image demonstrating evidence of an isodense soft-tissue into intervertebral foramen (asterisk) with enlarged right neural foramen (arrow) related to an expansile mass. Comparison between the two foramina (blue lines).

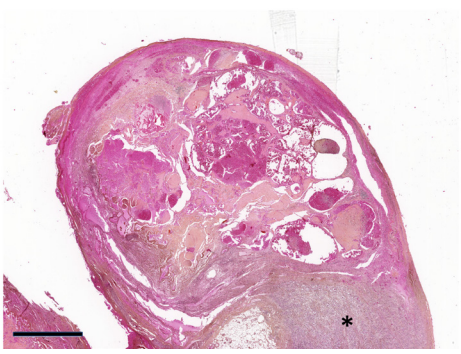

Figure 3 Histopathological aspect (hematoxylin, phloxine, saffron staining; scale bar: 2 mm): the lesion is a CM consisting of clustered multiple vascular channels of varying size. Vascular channels are lined by thick collagenous walls without intervening nervous tissue, elastic fibers, and smooth muscle cells. The vascular lesion adheres to some nerve fibers and clusters of ganglion cells (asterisk). CM, cavernous malformation.

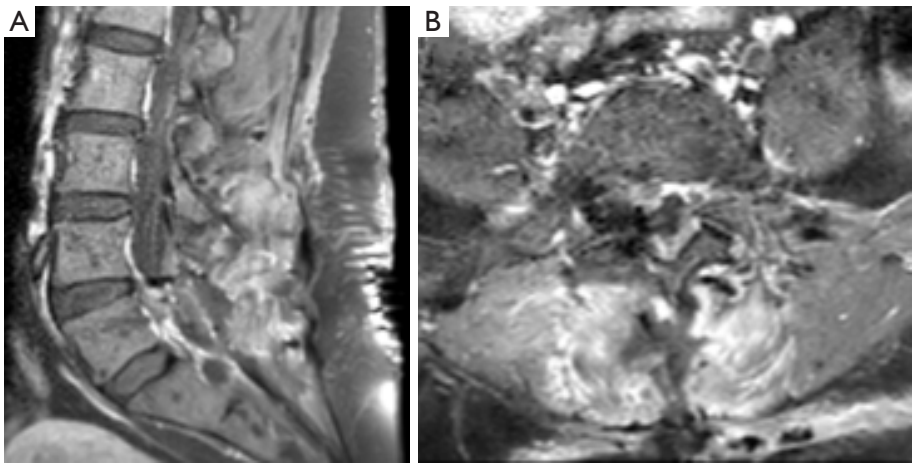

Figure 4 Post-operative MRI. (A) T1-WI contrast-enhanced axial and (B) T1-WI contrast-enhanced sagittal imaging showing the complete removal of the lesion without any residue. MRI, magnetic resonance imaging; T1-WI, T1-weighted images.

Table 1 Characteristics of the 7 patients with pure foraminal CM

Case No.	Age (years)/sex	Symptom and sign	Treatment	Histological record	Recurrence
1	73/female	Low back pain + radiculopathy	Total resection	Cavernous angiomas	No
2	19/female	Radiculopathy	Total resection	Cavernous angiomas	No
3	34/female	Low back pain	Total resection	Cavernous angiomas	No
4	36/male	Deficit triceps	Total resection	Cavernous angiomas	No
5	52/female	D3 dysesthesie nocturnal pain	Total resection	Cavernous angiomas	No
6	48/male	Leg pain	Total resection	Cavernous angiomas	No
7	62/male	Low back pain + radiculopathy	Total resection	Cavernous angiomas with capillary angioma	No

1, Oliveira; 2, Slavotinek; 3, Santoro; 4, Carlier; 5, D'Andrea; 6, Zhang; 7, Zhong. CM, cavernous malformation.

a rare autosomal dominant disease characterized by hamartomas which can involve any organ with a potential of malignant transformation (8). In literature association between vascular anomalies and CS has been described, but only 7 cases of intracranial CM associated with CS were identified (9). We are not aware of other cases of spinal CM in patients with CS.

Several cases of dorsal epidural spinal CMs with foraminal extension were reported (10,11). Conversely the pure intra-foraminal CM without epidural extension is extremely rare. A total of 7 cases were described in literature (4,10,12-16) with the first presented in 2000 by Carlier (12). We summarized these reports in *Table 1*.

Among these, five were found in lumbar spine, one in cervical and the last one in dorsal segment. Clinical presentation of the series was typically with local pain, with or without radiculopathy, progressive loss of strength and sensory disturbance (4,10,12-16). Symptoms were slowly progressive, however sudden onset were reported and may be attributed to haemorrhage or venous thrombosis with consequent enlargement of lesion (17).

The MRI features are summarized in *Table 2*. Variability from classic brain CM imaging were observed.

Typically, T2-weighted sequences portray brain CMs as areas of mixed signal intensity, with a central complicated core and a peripheral rim of decreased signal intensity (18,19). This characteristic was not found in epidural lesions (20).

Homogenous enhancement was observed in spinal CMs (21), in contrast to brain CMs which generally is

Table 2 Preoperative spinal MRI features of patients with pure foraminal CM

Case No.	Spinal level	T1-weighted	T2-weighted	Enhancement	Dilated foramen	Bony erosion	Form
1	L1-L2	Isointense	Hyperintense	Homogeneous enhancement	No	No	Oval
2	L4-L5	Intermediate	Hyperintense	Mild enhancement	No	No	Fusiform
3	L3-L4	Unavailable	Unavailable	Unavailable	No	No	Oval
4	C6-C7	Heterogenous and isointense	Hyperintense	Homogeneous	Yes	No	Oval
5	D3-D4	Hypo-isointense	Heterogenous hyperintense	Homogeneous	No	No	Oval
6	L4-L5	Isointense	Hyperintense	Homogeneous	No	No	Oval
7	L4-L5	Isointense	Slight hyperintense	Homogeneous	No	No	Fusiform

1, Oliveira; 2, Slavotinek; 3, Santoro; 4, Carlier; 5, D'Andrea; 6, Zhang; 7, Zhong. MRI, magnetic resonance imaging; CM, cavernous malformation.

not seen or really variable (22).

Schwannomas are lesions frequently cystic with mixed intensity on T1 and T2-weighted images. Enhancement upon contrast application is variable from intense and homogeneous in some lesions to heterogeneous in larger schwannomas with cystic degeneration (23).

In our case, the initial diagnostic hypothesis was in favor of nerve sheath tumor (24,25). Light mixed signal intensity on T2-WI was seen, but not clear "popcorn" appearance. The thin hypointense rim on T2-weighted imaging, could be compatible with chronic resolved hemorrhage or hemosiderin surrounding the lesion, but also with epidural fat or necrosis. Unfortunately, no specific susceptibility-weighted technique was done to confirm. Homogenous light contrast enhancement was observed.

Considering vascular malformation in differential diagnosis of epidural and/or foraminal lesion is important to avoid intraoperative bleeding (7,22). Internal debulking and piecemeal removal of the tumor to allow mobilization of lesion, possible in the case of schwannomas, are not advisable for CM. Indeed, the attempt to dissect the carrier root and a piecemeal resection technique could result in bleeding that makes the procedure more difficult with an increased risk of damage to nearby structures. *En bloc* resection is recommended, even for foraminal lesion invading functional root, as described by Butenschoen *et al.* (26). No severe long-term deficit was observed.

In our case, the CM was in lumbar spine, according to the most common location reported previously. Although it infiltrated a functional nerve root (L5), no postoperative deficit was observed after nerve sacrificed. Probably the function of the root was lost over time with the slow growth of the CM, and it was associated with a compensation mechanism by the other roots.

At the histological examination, clusters of ganglion cells were identified within the lesion, suggesting that the vascular malformation probably originated from peri-radicular vessels.

Follow-up MRI showed no relapse.

Conclusions

CS can be associated with spinal CM. Our case suggests considering CM in the differential diagnosis of pure foraminal lesions. *En bloc* resection with root sacrifice for foraminal CM seems to be achievable without postoperative deficit.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://jss.amegroups.com/article/view/10.21037/jss-22-21/rc

Peer Review File: Available at https://jss.amegroups.com/article/view/10.21037/jss-22-21/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jss.amegroups.com/article/view/10.21037/jss-22-21/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Yang T, Wu L, Yang C, et al. Cavernous angiomas of the cauda equina: clinical characteristics and surgical outcomes. Neurol Med Chir (Tokyo) 2014;54:914-23.
2. Harrison MJ, Eisenberg MB, Ullman JS, et al. Symptomatic cavernous malformations affecting the spine and spinal cord. Neurosurgery 1995;37:195-204; discussion 204-5.
3. Clark AJ, Wang DD, Lawton MT. Spinal cavernous malformations. Handb Clin Neurol 2017;143:303-8.
4. Slavotinek JP, Fowler S, Sage MR, et al. Extradural cavernous haemangioma simulating a disc protrusion. Australas Radiol 1999;43:111-2.
5. Er U, Yigitkanli K, Simsek S, et al. Spinal intradural extramedullary cavernous angioma: case report and review of the literature. Spinal Cord 2007;45:632-6.
6. Nowak DA, Widenka DC. Spinal intradural capillary haemangioma: a review. Eur Spine J 2001;10:464-72.
7. Padovani R, Acciarri N, Giulioni M, et al. Cavernous angiomas of the spinal district: surgical treatment of 11 patients. Eur Spine J 1997;6:298-303.
8. Mester J, Eng C. Cowden syndrome: recognizing and managing a not-so-rare hereditary cancer syndrome. J Surg Oncol 2015;111:125-30.
9. McLean A, Alalade AF, Golash A, et al. De Novo Cavernoma Formation in a Patient With Cowden Syndrome and Lhermitte-Duclos Disease. World Neurosurg 2020;143:308-14.
10. Zhong W, Huang S, Chen H, et al. Pure spinal epidural cavernous hemangioma. Acta Neurochir (Wien) 2012;154:739-45.
11. Feng J, Xu YK, Li L, et al. MRI diagnosis and preoperative evaluation for pure epidural cavernous hemangiomas. Neuroradiology 2009;51:741-7.
12. Carlier R, Engerand S, Lamer S, et al. Foraminal epidural extra osseous cavernous hemangioma of the cervical spine: a case report. Spine (Phila Pa 1976) 2000;25:629-31.
13. Oliveira E, Lavrador JP, Teixeira J, et al. A purely extradural lumbar nerve root cavernoma mimicking acute myeloid leukemia recurrence: Case report and literature review. Surg Neurol Int 2016;7:S908-10.
14. Santoro A, Piccirilli M, Bristot R, et al. Extradural spinal cavernous angiomas: report of seven cases. Neurosurg Rev 2005;28:313-9.
15. D'Andrea G, Ramundo OE, Trillò G, et al. Dorsal oraminal extraosseous epidural cavernous hemangioma. Neurosurg Rev 2003;26:292-6.
16. Zhang L, Qiao G, Shang A, et al. Clinical features and long-term surgical outcomes of pure spinal epidural cavernous hemangioma-report of 23 cases. Acta Neurochir (Wien) 2020;162:2915-21.
17. Isla A, Alvarez F, Morales C, et al. Spinal epidural hemangiomas. J Neurosurg Sci 1993;37:39-42.
18. Brunereau L, Labauge P, Tournier-Lasserve E, et al. Familial form of intracranial cavernous angioma: MR imaging findings in 51 families. French Society of Neurosurgery. Radiology 2000;214:209-16.
19. Zevgaridis D, Büttner A, Weis S, et al. Spinal epidural cavernous hemangiomas. Report of three cases and review of the literature. J Neurosurg 1998;88:903-8.
20. Ondřej B, Vladimír B. Cavernomas of the CNS: Basic Science to Clinical Practice. Cham: Springer, 2020.
21. Hatiboglu MA, Iplikcioglu AC, Ozcan D. Epidural spinal cavernous hemangioma. Neurol Med Chir (Tokyo) 2006;46:455-8.
22. Talacchi A, Spinnato S, Alessandrini F, et al. Radiologic and surgical aspects of pure spinal epidural cavernous angiomas. Report on 5 cases and review of the literature.

Surg Neurol 1999;52:198-203.
23. Abul-Kasim K, Thurnher MM, McKeever P, et al. Intradural spinal tumors: current classification and MRI features. Neuroradiology 2008;50:301-14.
24. Cossandi C, Fanti A, Gerosa A, et al. Rare Case of Dumbbell-Shaped Spinal Cavernous Hemangioma and Literature Review. World Neurosurg 2018;120:181-4.
25. Mushtaq R, Porrino J, Moses SA, et al. Neural Foraminal Lesions: An Imaging Overview. PM R 2018;10:880-5.
26. Butenschoen VM, Kögl N, Meyer B, et al. A Case Series of Surgically Treated Spinal Dumbbell Tumors of Critical Parent Nerve Roots: To Cut or Not to Cut? Oper Neurosurg (Hagerstown) 2021;20:260-7.

Cite this article as: D'Onofrio GF, Capo G, Vasiljevic A, Barrey CY. Pure lumbar foraminal cavernous malformation in a patient with Cowden syndrome—a case report. J Spine Surg 2022;8(3):390-396. doi: 10.21037/jss-22-21