CASE REPORT

Cervical spine arteriovenous fistula associated with hereditary haemorrhagic telangiectasia

Iain John McGurgan,¹ Roisin Lonergan,¹ Ronan Killeen,² Christopher McGuigan¹¹Department of Neurology, St Vincent's University Hospital, Dublin, Ireland²Department of Radiology, St Vincent's University Hospital, Dublin, Ireland

Correspondence to

Dr Iain John McGurgan, iainmcgurgan@gmail.com

Accepted 22 January 2017

SUMMARY

Reported is a case of a man aged 55 years who presented with progressive spastic paraparesis. Examination demonstrated multiple cutaneous telangiectases. Subsequent development of upper limb weakness, acute urinary retention and eventual respiratory compromise resulted in the requirement for intensive care unit admission and mechanical ventilation. MRI spine revealed diffuse T2 hyperintensity in the cervical cord with enhancement and cord expansion. Immunomodulatory therapy for a presumed diagnosis of transverse myelitis yielded no response, so a vascular aetiology was suspected. Spinal angiography demonstrated an arteriovenous fistula involving the upper cervical cord. Endovascular embolisation was successfully performed and a marked clinical improvement was achieved. Cervical arteriovenous fistulas can cause progressive myelopathy, subarachnoid haemorrhage and brainstem dysfunction. Management typically comprises endovascular embolisation or surgical interruption. A clinical diagnosis of hereditary haemorrhagic telangiectasia was also made in this case, and spinal arteriovenous fistula formation has been associated with this condition.

BACKGROUND

The rare occurrence of arteriovenous fistulas in the cervical spine leads to them being frequently overlooked, and the difficulty and delays encountered in their diagnosis with conventional investigations can result in life-threatening deterioration before appropriate intervention, as this report highlights. A clinical diagnosis of hereditary haemorrhagic telangiectasia (HHT) was made in this case, and classical features of this condition in the history or examination should prompt early consideration of vascular malformations as a cause of presenting neurological symptoms. Cervical arteriovenous fistulas are readily treatable with encouraging outcomes in case series and should always be included in the differential diagnosis of progressive myelopathy, subarachnoid haemorrhage or brainstem dysfunction.

CASE PRESENTATION

A left-handed Caucasian man aged 55 years presented to our hospital in September 2014 with a 3-month history of progressive bilateral lower limb weakness and unsteadiness. He had a background of long-standing alcohol dependency, generalised anxiety disorder and psoriasis, was an ex-smoker and had a family history of colorectal cancer.

His symptoms were initially restricted to the lower limbs, with progressively impaired mobility that resulted in him being unable to ascend stairs. Over time he developed intermittent symptoms of lower limb paraesthesia and a tight banding sensation around the abdomen at the level of the lower costal margin. After 3 months, he began to experience gradual onset of upper limb weakness and was admitted to a district general hospital in August after developing acute urinary retention requiring catheterisation. He described no back or neck pain, no speech or swallowing difficulties and no visual disturbance. An MR scan of the whole spine demonstrated diffuse T2 signal hyperintensity throughout the cervical cord extending contiguously from the lower medulla to C7 with evident cord expansion. The accompanying MR brain revealed only chronic microvascular ischaemic changes and there was no evidence of demyelinating disease. He was treated empirically for transverse myelitis with 1 g intravenous methylprednisolone but deteriorated immediately following 1 day of treatment, and transfer to a neuroscience centre was arranged.

On arrival, the patient was cachectic and had multiple cutaneous vascular papules and telangiectasias on the face, trunk and hands ([figure 1](#)). Cranial nerve examination was normal. Spastic hypertonicity was elicited in the lower limbs, but tone was normal in the upper limbs. Power was markedly reduced in the lower limbs (Medical Research Council (MRC) grade 3–4) and mildly reduced in the upper limbs (MRC grade 4– to 4+) in a pyramidal distribution. Deep tendon reflexes were pathologically brisk with a positive Hoffman's and Babinski's sign observed bilaterally. A bilateral C4 sensory level was detected, but vibration sense and proprioception were intact. Coordination was unimpaired and gait was not assessable because of mobility constraints. Repeat MRI ([figure 2](#)) performed on 3 September demonstrated interval inferior extension of the lesion to the level of the inferior vertebral body endplate of C7, and post-contrast imaging revealed diffuse ill-defined enhancement most marked in the superior aspect of the lesion in the lower brainstem. Flow voids were retrospectively noted on this MRI at the level of C5–C7 posteriorly. At the time of interpretation, however, the findings were deemed to be suspicious for neoplasm, with inflammatory or infectious myelitis as possible differential diagnoses. Blood tests including erythrocyte sedimentation rate, extractable nuclear antibodies, antineutrophil cytoplasmic antibodies, HIV, syphilis and lyme serology,

CrossMark

To cite: McGurgan IJ, Lonergan R, Killeen R, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-218172

Figure 1 Cutaneous vascular papules (A, B) visible on the hands and face and telangiectases (C) on the trunk.

aquaporin 4 antibodies, GM1 and GQ1B ganglioside antibodies, copper and vitamin D were normal and tumour markers were negative. Antinuclear antibody was weakly positive. Cerebrospinal fluid analysis demonstrated an increased protein concentration (0.85 mg/dL); however, cell counts and glucose were normal and culture was negative. A CT scan of the thorax, abdomen and pelvis demonstrated no evidence of malignancy. A 5-day course of intravenous immunoglobulin was administered with no meaningful clinical response. He began to experience further progression of his symptoms and developed intermittent dyspnoea, with low peak flow measurements (300–360 L/m) recorded daily. Overall, the progressive but fluctuating nature of the patient's clinical course alongside refractoriness to immunosuppressive therapies suggested the possibility of a vascular aetiology.

Formal spinal angiography (figures 3 and 4) was performed on 10 September which demonstrated an arteriovenous fistula involving the upper cervical cord, located just inferior to the foramen magnum. It was supplied solely by a posterior branch of the distal right vertebral artery inferior to the origin of the posterior inferior cerebellar artery. Retrograde venous drainage was directed caudally into posterior spinal veins and rostrally into the posterior fossa. An initial diagnosis of a cervical dural arteriovenous fistula was made on the basis that there appeared to be no continuity between the feeding artery and the anterior or posterolateral spinal arteries. This would be in keeping with a dural fistula, for which the feeding vessel is a radiculomeningeal artery that does not usually supply the spinal arteries,¹ versus a perimedullary fistula on the pial surface which is supplied by the spinal arteries.² Subsequent review of the angiographic findings, however, casts doubt over this assertion. Even with superselective angiography, the exact fistula point was

difficult to define, and the possibility that the feeding vessel was in fact a posterior spinal artery (in keeping with a perimedullary fistula) is a distinct possibility.

TREATMENT

Following angiography, the patient developed severe respiratory compromise and was admitted to the intensive care unit on 11 September. Respiratory failure was attributed to diaphragmatic paralysis and tracheal intubation with mechanical ventilation was performed. A decision was made to proceed urgently with endovascular embolisation on 14 September. A 6 Fr guide catheter was placed in the right vertebral artery through a right femoral artery approach. Angiography was repeated and the feeding artery was embolised via a Magic microcatheter using 25% glubran. A single glue injection was performed and complete occlusion of the fistula was achieved with no immediate complications (figure 5).

OUTCOME AND FOLLOW-UP

Postoperatively, the patient experienced gradual improvement in power and his sensory symptoms disappeared. A repeat MR scan of the cervical spine (figure 6), performed on 14 October, revealed improvement in the appearance of the cord with a decrease in the craniocaudal extent of the lesion. Unfortunately, his functional recovery has been limited. He now permanently resides in a nursing home, requires a wheelchair for mobilisation and uses intermittent self-catheterisation, although he transfers independently and attends to shaving, showering and other self-care without difficulty. Lower limb spasticity is an ongoing issue for which he is treated with regular baclofen and attends the rehabilitation team as an outpatient. As of November 2016, we estimate his Karnofsky Performance Status score at 40%.

The finding of multiple cutaneous telangiectasias on examination raised the suspicion of the presence of HHT (also known as the Osler-Weber-Rendu syndrome) underlying this presentation. On further questioning, the patient reported a history of frequent spontaneous epistaxis since childhood. The patient's brother and father also experienced this, along with similar cutaneous lesions. A clinical diagnosis of HHT was made fulfilling all four of the Curaçao criteria, as outlined in table 1 (ie, a definite clinical diagnosis).³ Genetic testing for the most common ENG, ACVRL1 and MADH4 mutations was negative; however, panels for rarer gene mutations have been sent, the results of which are pending. Screening CT scans of the chest and abdomen performed after the diagnosis did not reveal any evidence of pulmonary or hepatic arteriovenous malformations, subsequent neuroimaging demonstrated no cerebral arteriovenous malformations and serial haemoglobin measurements and iron studies have been within normal limits.

Figure 2 Sagittal T2-weighted (A) and T1-weighted post intravenous gadolinium (B) MRI cervical spine demonstrating expansion of the spinal cord and lower medulla. Diffuse central T2 signal hyperintensity is seen extending from the medulla to the level of the inferior vertebral body endplate of C7 with diffuse ill-defined enhancement most marked in the superior aspect of the lesion in the lower brainstem. Multiple flow voids are noted along the posterior surface of the cervical cord, particularly at the C5/C6 levels (arrows).

Figure 3 Spinal angiogram (A) performed via the right vertebral artery (*) demonstrating abnormal vessels descending through the spinal canal (arrows) supplied via the intracranial (V4) segment of the vertebral artery. Following embolisation (B), there is no evidence of the fistula, with the absence of the previously evident arteriatised veins in the cervical spinal canal.

Figure 4 Selective angiogram of the right vertebral artery (A) and later superselective angiogram of the feeder artery (B) prior to embolisation. The catheter is visible in the right vertebral artery (*) and the fistula and emissary veins are clearly demonstrated.

DISCUSSION

Spinal vascular malformations represent a rare, treatable cause of myelopathy and frequently provide a diagnostic challenge. They comprise shunting lesions including arteriovenous fistulas and malformations, as well as non-shunting lesions including cavernous angiomas and aneurysms.⁴ The aforementioned fistulas consist of a direct arteriovenous connection without an intervening nidus² and they are commonly classified according to their location relative to the dura.⁵ The angioarchitectural characteristics of arteriovenous fistulas can, however, be hard to accurately define; thus, classifying them as such can represent a challenge. The authors of one case series postulate that some previously reported cases of apparent high cervical dural fistulas may in fact have been complex forms with, for example, additional supply from the spinal arteries,¹ and perimedullary fistulas were most likely misclassified as dural fistulas in a large 2006 review.⁶

A spinal dural arteriovenous fistula, the diagnosis that was initially made in this case, is the abnormal connection between a dural branch of a radicular artery and a radiculomedullary vein along the spinal dural surface.² It is the most commonly detected malformation, accounting for 70%, and was first described by Kendell and Logue in 1977.⁷ They typically affect middle-aged men and originate predominantly in the thoracolumbar spine,

but occur at any level from the foramen magnum to the sacrum. The thoracolumbar predominance has been ascribed to anatomical differences in venous drainage patterns, with small-calibre radiculospinal veins draining the thoracolumbar cord rendering this area more susceptible to haemodynamic alterations.⁸ Perimedullary arteriovenous fistulas (also known as intradural ventral fistulas or type IV arteriovenous malformations, according to various classification systems) were first described by Djindjian *et al*, also in 1977.⁹ The age of onset varies based on the size of the fistula, with giant fistulas presenting in children and small fistulas presenting in middle-aged adults.² They tend to follow a more progressive clinical course, with major impairment occurring within 4–6 years.⁵

The mechanism underlying spinal arteriovenous fistula formation is unclear, and although some cervical dural arteriovenous fistulas have been reported following cervical spine fractures and surgical procedures, the majority are idiopathic.¹⁰ Clinical manifestations may be referable either cranially or spinally and presentations include progressive myelopathy, radiculopathy, brainstem dysfunction and subarachnoid haemorrhage. On fistula formation, arteriovenous shunting results in increased medullary venous pressure, which is transmitted in turn to the cord via the valveless coronal venous plexus and radial veins, leading to a venous hypertension-mediated myelopathy.¹¹

Figure 5 Spinal angiography anteroposterior view (A) demonstrating the presence of an abnormal tortuous vessel arising from the right vertebral artery (*) and descending emissary veins (arrows). Following embolisation (B), there is complete disappearance of these abnormal vessels.

Figure 6 Sagittal T2-weighted MRI cervical spine demonstrating an interval decrease in the size of the hyperintense lesion and the extent of cord expansion.

Venous hypertension is also suspected to be the main mechanism underlying subarachnoid haemorrhage and the rarer brainstem dysfunction in cervical arteriovenous fistulas. MR findings include T2 signal hyperintensity, mass effect and abnormal enhancement of the cord postcontrast, and less commonly flow voids in tortuous vessels along the cord (all present in the above case).⁷ Angiography (MR and formal) is also important in the initial diagnosis and in the differentiation of arteriovenous fistulas from the rarer radicular arteriovenous malformations.⁸ Difficulty in isolating feeding arteries has resulted in surgical ligation of the draining feeding vein as the primary treatment modality in many cases; however, where a single arterial supply is identified (as in this case), ligation of the artery is preferred.⁸ If the vascular anatomy permits, an initial endovascular management strategy is often effective and, if unsuccessful, surgical interruption of the shunt can be subsequently performed.

In this case, a unifying diagnosis of HHT was established. This is an autosomal-dominantly inherited vascular disorder

with variable penetrance and expressivity characterised by spontaneous epistaxis, telangiectasia of the skin and buccal mucosa and visceral arteriovenous malformations.¹² Multiple mutations in three major disease-causing genes (ENG encoding endoglin, ACVRL1 encoding ALK1 and MADH4 encoding SMAD4) have been identified with >80% of cases possessing mutations in ENG or ACVRL1, and two further unidentified genes have been localised to chromosomes 5 and 7.¹² The absence of a detected mutation, as in this case, does not preclude the diagnosis and molecular testing is not required for diagnostic confirmation in those with clinically definite disease. In fact, mutations are not discovered in up to 20% of HHT families.¹²

Although clinical manifestations of HHT are usually not present at birth, approximately half experience spontaneous nosebleeds by age 10 years and almost all have telangiectases beyond the third decade of life.¹³ Central nervous system involvement occurs in 10–20% of cases; however, a large proportion of neurological symptomatology is attributable to complications of pulmonary arteriovenous malformations (only one-third are due to primary cerebral or spinal vascular malformations).¹⁴ Of the reported spinal cord manifestations, the vast majority are single perimedullary fistulas, are found predominantly in children (where they may represent the first expression of the disease) and tend to respond well to endovascular embolisation.^{5 14–19} In contrast, spinal dural fistulas (which are more common in the general population) have been classically considered as acquired lesions based on the apparent lack of demonstrated associations with congenital disorders.²

Although at least one case of definite spinal dural arteriovenous fistula has been documented in a patient with HHT,¹⁷ none to the best of our knowledge have involved the cervical spine. Given the marked predominance of spinal dural arteriovenous fistulas in middle-aged men, it is probable that some unidentified factors contribute to their formation. Prothrombotic disorders, for example, are a demonstrated association of cerebral dural arteriovenous fistulas, but this does not apply to their spinal counterparts.²⁰ A clear age-related expression of the neurovascular manifestations in HHT has been described, with perimedullary arteriovenous fistulas presenting in children under the age of 5 and small arteriovenous malformations occurring in later life.²¹ This has led to the hypothesis that the development

Table 1 Clinical diagnostic criteria for hereditary haemorrhagic telangiectasia (The Curaçao Criteria)³

Criteria	Description
Epistaxis	Spontaneous and recurrent
Telangiectasia	Multiple present at characteristic sites Oral cavity Lips Nose Fingers
Visceral lesions	Arteriovenous malformations Pulmonary Hepatic Cerebral Spinal Gastrointestinal telangiectasia
Family history	First-degree relative with HHT according to these criteria
HHT diagnosis	Criteria fulfilled
Definite	3 of 4 criteria present
Suspected	2 of 4 criteria present
Unlikely	Less than 2 criteria present

Learning points

- ▶ Arteriovenous fistulas of the cervical spine may present with progressive myelopathy, subarachnoid haemorrhage or brainstem dysfunction.
- ▶ MRI spine alone may not demonstrate findings consistent with a spinal arteriovenous malformation; thus, a low threshold for performing angiography should be maintained where a vascular aetiology remains in the differential diagnosis for a progressive spastic paraparesis.
- ▶ Dural arteriovenous fistulas are the most common spinal vascular malformations and, although rare overall, are crucial to recognise, given their reversibility when treated appropriately.
- ▶ Hereditary haemorrhagic telangiectasia is an autosomal dominant disorder that has neurological manifestations in up to 20% of cases, and consistent symptoms and signs should prompt consideration of a vascular cause underlying any neurological symptoms.

of these lesions in HHT requires a revealing trigger of some sort; for example, local inflammation, trauma or hypoxia, and age-related characteristics of the blood vessels with regard to their strength or capacity for repair could predispose to vulnerability at a particular time.²¹ Therefore, whether the development of a cervical spinal arteriovenous fistula in the above case represents a true late association with HHT, or alternatively represents an incidental acquired lesion, is uncertain. In any case, given the amenability of spinal arteriovenous fistulas to embolisation or surgical treatment, they should always be suspected in patients with HHT presenting with neurological symptoms.

Acknowledgements The help of Dr Paul Brennan, consultant radiologist at Beaumont Hospital, and Dr Gerard Healy, radiology registrar at St Vincent's University Hospital, in providing the angiographic images for this case is greatly appreciated.

Contributors IJMG, RL and CMG managed the patient and contributed to the writing of the paper. RK provided and annotated the figures and critically revised the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Onda K, Yoshida Y, Watanabe K, *et al.* High cervical arteriovenous fistulas fed by dural and spinal arteries and draining into a single medullary vein: report of 3 cases. *J Neurosurg Spine* 2014;20:256–64.
- Jahan R, Vinuela F. Vascular anatomy, pathophysiology, and classification of vascular malformations of the spinal cord. *Seminars Cerebrovasc Dis Stroke* 2002;2:186–200.
- Shovlin CL, Guttmacher AE, Buscarini E, *et al.* Diagnostic criteria for hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). *Am J Med Genet* 2000;91:66–7.
- Morris JM. Imaging of dural arteriovenous fistula. *Radiol Clin North Am* 2012;50:823–39.
- Rodesch G, Lasjaunias P. Spinal cord arteriovenous shunts: from imaging to management. *Eur J Radiol* 2003;46:221–32.
- van Dijk JM, Terbrugge KG. Re: Terao T, Taniguchi M, Ide K, *et al.* Cervical dural arteriovenous fistula presenting with brain stem dysfunction: case report and review. *Spine* 2006;31:E722–7. *Spine* 2007;32:1930.
- Gilbertson JR, Miller GM, Goldman MS, *et al.* Spinal dural arteriovenous fistulas: MR and myelographic findings. *AJNR Am J Neuroradiol* 1995;16:2049–57.
- Kim DJ, Willinsky R, Geibprasert S, *et al.* Angiographic characteristics and treatment of cervical spinal dural arteriovenous shunts. *AJNR Am J Neuroradiol* 2010;31:1512–15.
- Spetzler RF, Detwiler PW, Riina HA, *et al.* Modified classification of spinal cord vascular lesions. *J Neurosurg* 2002;96(2 Suppl):145–56.
- Drazin D, Jeswani S, Shirzadi A, *et al.* Anterior spinal artery syndrome in a patient with vasospasm secondary to a ruptured cervical dural arteriovenous fistula. *J Neuroimaging* 2014;24:88–91.
- Aviv RI, Shad A, Tomlinson G, *et al.* Cervical dural arteriovenous fistulae manifesting as subarachnoid hemorrhage: report of two cases and literature review. *AJNR Am J Neuroradiol* 2004;25:854–8.
- Govani FS, Shovlin CL. Hereditary haemorrhagic telangiectasia: a clinical and scientific review. *Eur J Hum Genet* 2009;17:860–71.
- McDonald J, Woodechak-Donahue W, VanSant Webb C, *et al.* Hereditary hemorrhagic telangiectasia: genetics and molecular diagnostics in a new era. *Front Genet* 2015;6:1.
- Krings T, Chng SM, Ozanne A, *et al.* Hereditary hemorrhagic telangiectasia in children: endovascular treatment of neurovascular malformations: results in 31 patients. *Neuroradiology* 2005;47:946–54.
- Brinjikji W, Iyer VN, Sorenson T, *et al.* Cerebrovascular manifestations of hereditary hemorrhagic telangiectasia. *Stroke* 2015;46:3329–37.
- Calhoun AR, Bollo RJ, Garber ST, *et al.* Spinal arteriovenous fistulas in children with hereditary hemorrhagic telangiectasia. *J Neurosurg Pediatr* 2012;9:654–9.
- Ling JC, Agid R, Nakano S, *et al.* Metachronous multiplicity of spinal cord arteriovenous fistula and spinal dural AVF in a patient with hereditary haemorrhagic telangiectasia. *Intervent Neuroradiol* 2005;11:79–82.
- Mandzia JL, terBrugge KG, Faughnan ME, *et al.* Spinal cord arteriovenous malformations in two patients with hereditary hemorrhagic telangiectasia. *Childs Nerv Syst* 1999;15:80–3.
- Mont'Alverne F, Musacchio M, Tolentino V, *et al.* Giant spinal perimedullary fistula in hereditary haemorrhagic telangiectasia: diagnosis, endovascular treatment and review of the literature. *Neuroradiology* 2003;45:830–6.
- Jellema K, Tijssen C, Fijnheer R, *et al.* Spinal dural arteriovenous fistulas are not associated with prothrombotic factors. *Stroke* 2004;35:2069–71.
- Krings T, Ozanne A, Chng SM, *et al.* Neurovascular phenotypes in hereditary haemorrhagic telangiectasia patients according to age. Review of 50 consecutive patients aged 1 day–60 years. *Neuroradiology* 2005;47:711–20. <http://dx.doi.org/10.1007/s00234-005-1390-8>

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow