CASE REPORT

Subarachnoid hemorrhage in neurofibromatosis type 1: Case report of extracranial cerebral aneurysm rupture into a meningocele

Hémorragie sous-arachnoïdienne dans la neurofibromatose de type 1 : rupture d’un anévrysme extracrânien dans un méningocèle

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Summary Described here is a case of subarachnoid hemorrhage due to rupture of an extracranial vertebral artery (V3 segment) aneurysm in a patient with neurofibromatosis type 1 (NF-1). The pathophysiology of this never-before reported complication of NF-1 is examined in the light of a focused literature review and with illustrations characteristic of this unique case, involving complex malformations of the spine and meningeal spaces, as well as of the vertebral artery wall itself. All these abnormalities are directly related to the underlying NF-1 disease.

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Introduction

von Recklinghausen’s neurofibromatosis type 1 (NF-1) is characterized by cutaneous neurofibroma and so-called ‘café-au-lait’ spots. Vascular complications are not unusual, and most usually affect the kidney, gastrointestinal tract and heart vessels. However, cerebrovascular complications are rare, while many cases of stenosis, occlusion, aneurysm and arteriovenous malformations have been reported in the literature. The present case report is of a young woman with NF-1 and subarachnoid hemorrhage caused by rupture of an extracranial vertebral artery aneurysm into a giant cervical meningocele.

Case report

A 36-year-old woman with NF-1, but only cutaneous clinical symptoms such as multiple café-au-lait spots, freckles...
and numerous neurofibromas of the skin (Fig. 1), attended the emergency ward 12 h after the acute onset of violent and unusual headache, and left cervical neck pain and stiffness, followed by photophobia and vomiting without fever. Immediate brain computed tomography (CT) was normal, but the subsequent spinal tap disclosed subarachnoid hemorrhage. Brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) showed bilateral cortical post-central subarachnoid hemorrhage with neither proximal aneurysm nor cerebral venous thrombosis. Cervical MRA disclosed a branching left extracranial vertebral aneurysm of the V3 segment (Fig. 2). MRI and cervical CT disclosed dural ectasias and spinal malformations, with severe scalloping of the adjacent vertebrae (Figs. 3 and 4a). Cervical CT and CT angiography confirmed the presence of a voluminous extracranial aneurysm, measuring $17 \times 13$ mm, of the left vertebral artery. The cervical spinal cord was distorted by dural ectasias together with spinal subluxations associated with merging of vertebrae C2 to C5, abnormal vertebral bodies and aplasia of the left posterior arches of C3 to C5 (Fig. 4a, b). There was also an anterior meningocele extending from the left C3–C4 foramina close to the aneurysm. Although it was not possible to demonstrate blood in the meningocele, its close proximity to the aneurysm together with the dural ectasia and the negative findings in the rest of the workup led to the conclusion that rupture of the aneurysm into the meningocele was the cause of the subarachnoid hemorrhage (Fig. 4c, d).

Two days later, the patient experienced acute cervical pain that radiated into the left arm along the C5–C6 dermatome pattern, and was associated with left cervical swelling. Clinical examination revealed proximal motor deficit of the left arm, with abolition of the bicipital reflex. CT scan disclosed a twofold increase in the size of the aneurysm, with thickening of the surrounding soft tissue (Fig. 4c). Conventional angiography (by Professor J. Moret, Neuroradiology Department, Adolphe...
Subarachnoid hemorrhage in neurofibromatosis type 1

Figure 4  (A) Axial CT scan of cervical spine at C2–C3 after contrast infusion (white stars = subarachnoid spaces; black lily = spinal cord; dotted arrow = incidental schwannoma; and flower = soft-tissue hematoma); (B) CT scan of cervical spine with volume-rendered imaging shows vertebral abnormalities, including wide posterior openings of the C2–C5 vertebral arches due to the meningocele; (C) cervical vertebral aneurysm, embedded in soft tissue, with the left vertebral artery (LVA) at C3–C4 level (white stars = subarachnoid spaces; white lily = spinal cord; dotted arrow = incidental schwannoma); and (D) V3 segment of LVA in close contact with the meningocele at C4 (white stars = subarachnoid spaces; white lily = spinal cord; dotted arrow = incidental schwannoma; white flow- ers = vertebral aneurysm and soft-tissue hematoma).

de Rothschild Foundation, Paris) showed dissection of the extracranial cerebral aneurysm (V3 segment). Moreover, an arteriovenous fistula of the left vertebral artery was found, arising from the V3 segment downstream of the aneurysm and draining into the spinal venous system (Fig. 5). Endovascular stenting and coil embolization were performed to prevent rebleeding, and the lesion was completely occluded while preserving vertebral artery blood flow.

Discussion

NF-1 is a heterogeneous genetic disease of autosomal-dominant inheritance and variable expression. Its incidence is about one in every 3000 births. The NF-1 gene encodes a protein called “neurofibromin-1”, a tumor-suppressing protein found at various sites in the body, but especially in nerve cells, Schwann cells and oligodendrocytes. The present patient presented with the typical cutaneous manifestations of NF-1, including multiple café-au-lait spots and numerous neurofibromas of the skin, but had never before experienced any other symptoms. However, imaging of her spine and cervical arteries revealed major bone and meningeal abnormalities due to meningocele and dural ectasias.

Central and peripheral nervous system manifestations and neuroradiological abnormalities are numerous and well described [1]. However, meningoceles have seldom been described in the literature [2–7] and appear to be rare in neurofibromatosis, although it is possible that they are simply underdiagnosed. Meningoceles are caused by abnormal fibrovascular proliferation, resulting in benign distention of the meninges. Spinal meningoceles are most often located at the thoracic and lumbosacral levels [1], whereas cervical locations are extremely rare [4]. Myelography, when performed, can reveal multiple diverticular dilatations of the cerebrospinal fluid (CSF) spaces. Dural ectasias can extend through the vertebral foramina, resulting in visible enlargement on X-ray films and spine CT. When superficial, they may present as a neck tumor [2] and be mistaken for neurofibroma. Imaging is essential to distinguish between the different causes of subcutaneous and deep masses (neoplasia, neurofibroma, meningocele, vascular causes). The main problem related to dural ectasia is compression of the adjacent structures, including lungs, aorta, oesopha- gus, trachea and medulla [5,7], and the phenomenon of ‘scalloping’ due to erosion of adjacent bones [3]. Indeed, bony modifications can be major, as in our patient here, who had a severely deformed cervical spinal cord secondary to vertebral erosions. Surgical treatment is indicated
only if the meningocele is symptomatic. Many treatment options may be proposed, such as ligation, resection and wrapping. The technique known as ‘cystopleural shunt’ has also been described in a pediatric case report [8]. In addition, NF-1 is known to be associated with cerebrovascular manifestations. These appear to be mainly stenoses or occlusions such as moyamoya syndrome, aneurysms and, more rarely, arteriovenous malformations or fistulas [9].

Aneurysms more frequently involve the aorta, kidneys, and gastrointestinal and coronary arteries, although cases of cerebral aneurysm have been reported, most usually affecting the intracranial internal carotid artery. Their pathophysiology remains unclear, although the proposed hypotheses include hypertension, which is frequently associated with NF-1, and specific vascular abnormalities, which are the more likely candidates. Some authors have found histological abnormalities in the arterial walls of NF-1 patients: Sobata et al. [10] described concentric intimal proliferation with partial fragmentation of the internal elastic lamina, while Uranishi et al. [11] reported intimal hyperplasia, thinning of the media and fragmentation of the elastic internal lamina. Those abnormalities could be related to neurofibromin dysfunction, as its inactivation leads to excess cell growth.

A review of the literature revealed 13 cases of extracranial vertebral artery aneurysm complicating NF-1 [12], and a few other published cases [13—15]. Clinical presentations may vary, depending on whether the aneurysm has ruptured or not. Weakness in the upper limbs due to direct compression of the brachial plexus has been described. Aneurysm can also be revealed by a neck mass with vascular bruits, or by neck pain related to subcutaneous hemorrhage, cervical radiculopathy, central neurological deficit related to cerebral infarction, dyspnea and pain due to hemothorax. However, none of these cases was associated with subarachnoid hemorrhage. In most cases, aneurysms were treated with a fair outcome. Two main treatment strategies were used: occlusion of the aneurysm using a detachable balloon or coils, or direct surgery.

The unique characteristic of the present case described here is that the aneurysm was responsible for subarachnoid hemorrhage, despite its extracranial cervical location, and this was because of the close proximity of vertebral and meningeal ectasias. To our knowledge, no such or similar case has even been previously reported in the international literature.

In conclusion, our present case illustrates the diagnostic difficulties and complications that arise in the evolution of NF-1. Anatomical abnormalities may be extreme, and different lesions can yield the same clinical picture, which highlights the usefulness of accurate systematic imaging protocols in patients with NF-1.

Conflict of interest statement
None.

References