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Multiple Exostoses Syndrome and Basilar Artery Aneurysm: a Case Report

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Abstract

Background—Hereditary multiple exostoses (HME) is an inherited genetic condition, characterized by the formation of multiple osteochondromas, developing throughout childhood and into puberty. Vascular complications associated with HME are uncommon.

Methods—A case of a patient with HME who was admitted to hospital with subarachnoid hemorrhage (SAH), as a result of acute rupture of a basilar tip aneurysm (BTA), will be presented. Relevant literature on this topic will be systematically reviewed.

Results—We describe a rare case of a 48-year-old male patient presenting multiple exostoses in both upper and lower limbs, with no familial history of such lesions. The patient experienced an episode of loss of consciousness, followed by tonal seizures, after a short (five-day) history of headache, proved finally to be secondary to SAH due to rupture of a BTA. There was no antecedent of trauma, neck manipulation, or previous infection. Aneurysm was successfully treated with the intravascular procedure (aneurysm occlusion with coil). Progressively, the patient recovered from dysphasia and tetraparesis, almost completely, following the appropriate treatment and rehabilitation program.

In the systematic review, eight cases (including the one presented) of vertebrobasilar vascular system stroke secondary to solitary spinal osteochondroma or multiple osteochondromas were found, but only the present case was associated with basilar artery aneurysm.

Conclusion—Despite the fact that the etiopathogenesis of basal artery aneurysm presentation in a patient with osteochondromas remains unknown, medical society needs to be aware of this rare condition, as SAH may be a severe complication.

Keywords

Hereditary multiple exostoses (HME); subarachnoid hemorrhage (SAH); basilar tip aneurysm (BTA); rare vascular complication

Introduction

Hereditary multiple exostoses (HME) is an autosomal, dominant skeletal condition characterized by the formation of several benign, cartilage-capped bone tumors (exostoses or osteochondromas), arising from the metaphyseal region of long bones [1]. It constitutes one of the most common musculoskeletal disorders. The prevalence of multiple exostoses is estimated at 1:50,000 [2]. Substantially, HME is a genetically heterogeneous disorder associated with two genes, which have been identified as EXT1 (chromosome 8q23–q24) and EXT2 (11p11–p12) [3–5]. Complications occur in 4% of the cases. The main complications in hereditary exostoses

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are deformities, which include limb length discrepancies, short stature, valgus deformities of the knee and ankle [6], as well as the malignant transformation of osteochondromas [7]. Furthermore, exostoses can affect adjacent structures, such as tendons, vessels, and nerves [8]. The most common vascular complications of osteochondromas are pseudoaneurysm, claudication, acute ischemia, and phlebitis [9].

Basilar tip aneurysms (BTAs) are rare vascular lesions which can be ruptured and lead to severe subarachnoid hemorrhage (SAH) that tends to recur [10]. They compromise about 5% of all intracranial aneurysms, and they are the most common aneurysms of the vertebrobasilar vascular system [11,12]. SAH as a result of ruptured intracranial artery aneurysm constitutes approximately 5% of the strokes [13]. The hallmark of SAH is the acute onset of a headache described as "the worst headache of my life," which is referred to occur in approximately 80% of patients [10,14,15]. Noncontrast head computed tomography remains the gold standard of diagnosis of SAH [16]. However, in the suspected ruptured aneurysm, the patient should undergo computed tomography angiography of the brain, due to its high accuracy and increased sensitivity in diagnosing cerebral aneurysms [17].

To our knowledge, there are no reports in the literature with cases of HME coexisting with SAH or basilar artery aneurysm. Our aim is to present a rare case of a patient with multiple osteochondromas in the upper and lower limbs and subsequent SAH due to rupture of a basilar artery aneurysm. A systematic review of the literature on osteochondromas and stroke was undertaken.

Methods

A detailed description of a patient with HME who was admitted with SAH, as a result of acute rupture of a BTA, will be presented. Initially, a systematic search was conducted in the PubMed database (https://www.ncbi.nlm.nih.gov/). The initial search terms were "osteochondroma," "hereditary multiple exostosis OR multiple exostosis," "heritable bone disease," "basilar artery aneurysm OR artery aneurysm OR pseudoaneurysm," "SAH," "vascular complication," "stroke," and "cerebral ischemia OR cerebral infraction OR cerebellar ischemia OR cerebellar infraction" (until January 2018). However, no documents were found, when we used the term "basilar" or "SAH." Moreover, ClinicalTrials.gov (https://clinicaltrials.gov/) was explored for unpublished information about the presence of basal artery aneurysm in a patient with HME until December 2017. The search was also expanded to the system for information on Gray Literature in Europe (OpenSIGLE) (http://www.opengrey.eu/) for unpublished evidence until December 2017. Furthermore, ScienceDirect.com (https://www.sciencedirect.com), ELSEVIER (https://www.elsevier.com/), Wiley Online Library (http://onlinelibrary.wiley.com), and *Journal of Vascular Surgery* (http://www.jvascsurg.org/) were used in our research, looking for books, journals, or reviews that could be associated with the presented case. Finally, computerized searches using SMJ (http://www.smj.org.sg/), ResearchGate (https://www.researchgate.net/), and Ejvesreports (http://www.ejvesreports.com) were conducted.

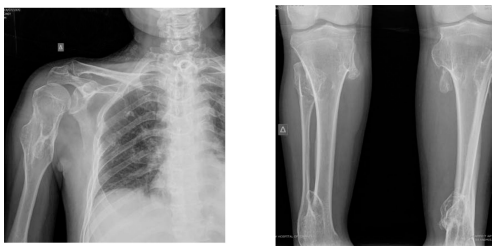

Figure 1. (A) and (B) Shoulder and tibias radiographs of the patient showing the exostoses at the metaphyseal area.

Results

Case report

A 48-year-old male with HME (Figure 1) was admitted urgently to the University Hospital of Ioannina after an episode of loss of consciousness, followed by tonal seizures. His relatives mentioned only a five-day history of headache. There was no antecedent of trauma, neck manipulation, or previous infection. Brain computed tomography and computed tomography angiography showed SAH, secondary to rupture of a BTA, with no osteochondromas found compressing the basal-vertebral arteries in the skull or in the cervical spine. Due to the progressive reduction of consciousness level (GCS 8), the patient had to be intubated within a few hours and he was admitted to the intensive care unit, for respiratory and cardiovascular support.

As an etiologic therapeutic decision, the patient was transferred to a specialized neurosurgical clinic in the University Hospital of Patras, where basal artery aneurysm embolism (intravascular stent with coil) was conducted successfully (Figure 2). The repetitive brain imaging with computed tomography revealed a reduction of brain swelling, improvement of brain ventricle

Table 1. Cases of vertebral artery complications secondary to osteochondroma

References	Age	Sex	Symptoms	Osteochon-droma	Lesion	Topography	Trauma	Treatment
Altaf *et al.*[18]	14	M	Dizziness, headache, visual field defect	Multiple	Occlusion	Right V.A.	No	Anticoagulant
George *et al*. [19]	32	M	Dizziness, neck pain, visual field defects	Multiple	Occlusion	Left V.A.	No	Surgical removal of osteochon-droma (C2 level)
Hill *et al.*[20]	41	F	Vertigo, vomiting, ataxia, neck pain	Multiple	Dissection	Right V.A.	No	i.v. heparin, oral warfarin sodium
Arauz *et al*. [21]	39	M	Vertigo, hypoesthesia, ataxia, walk disturbance	Multiple	Dissection	Left V.A.	No	Treated like a common case of dis-section
Fadili *et al*. [22]	59	M	Headache, nausea, vomiting, walk disturbance	Solitary	Occlusion	Left V.A.	No	Surgical removal of osteochon-droma(C4 level), ventriculostomy, surgical decompression of poste-rior fossa
Srikantha *et al*. [23]	23	M	Neck pain	Solitary	Occlusion	Left V.A.	No	Surgical removal of osteochon-droma(C4-C5 level)
Zhang *et al*. [24]	19	F	Vertigo, nausea, vomiting, headache, walk disturbance	Solitary	Occlusion	Left V.A.	No	Surgical removal of osteochon-droma

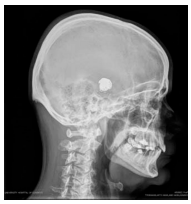

Figure 2. Lateral skull X-ray of the patient after the embolism of basal artery aneurysm with the coil in place.

extension, and reduction of blood in right occipital horn. The patient underwent tracheotomy six days later and the intraventricular tube was removed four days later.

Subsequently, the patient was transferred to the neurosurgery clinic of the University Hospital of Ioannina, where his medical condition was gradually stabilized and a tracheotomy was removed, whereas a gastrostomy tube was inserted for feeding purposes. Neurological examination revealed dysphasia, dysphagia, and tetraparesis, though without any focal deficits. He progressively became able to sit and stand on account of physiotherapy sessions he had started. Afterward, the patient was admitted to the Physical Medicine and Rehabilitation Clinic of University Hospital. His rehabilitation program included physical, occupational, and speech therapy. Removal of Foley catheter, as well as gradual closure of a sacral decubitus ulcer he had suffered from, contributed to his rehabilitation. A videofluoroscopic evaluation of swallowing was conducted and confirmed the improvement of his swallowing capacity, so the gastrostomy tube was also removed. Computed tomography brain images showed complete absorption of hemorrhagic marks. Five months since the beginning of this episode, the patient is walking independently and has returned to his normal activities.

Review of the Literature

Eight (including the one presented) cases of vertebrobasilar stroke secondary to solitary spinal osteochondroma or multiple osteochondromas were collected (Table 1). Five patients, including our own patient, had been diagnosed with HME at birth (62.5%) [18–21], while three patients presented a solitary form of osteochondroma, located on the cervical vertebrae (37.5%) [22–24].

Except for the discussed case, where the vascular damage had affected the basilar artery, in all the other cases vascular damage was described in the vertebral arteries [18–24]. Left vertebral artery was affected in five cases [19,21–24], while the right one was affected in two cases [18,20]. Angiography showed dissection in the cervical segment of the vertebral artery in two patients [20,21] who were diagnosed with multiple osteochondromas but had no exophytic lesions on the cervical bones. In the rest five patients [18,19,22–24], angiography showed a vertebral artery occlusion related to compressive osteochondroma, which arose from a cervical vertebra between C1–C5 and protruded into the transverse canal.

Both computed tomography/magnetic resonance imaging and computed tomography angiography/magnetic resonance angiography were performed to show the vascular damage in the vertebrobasilar system and the exophytic lesions on the cervical bones [18–24].

Discussion

Our aim is to present a case of SAH due to ruptured basilar artery aneurysm in a patient with HME and attempt to compare our findings with similar cases from the literature. In the literature review, seven cases of osteochondromas and vertebrobasilar stroke were found, while including our case a total of eight cases exist.

HME syndrome is an autosomal dominant disorder that mainly affects the metaphyses of the most rapidly growing ends of long bones [25]. Exostoses develop shortly after birth and continue to appear and grow throughout childhood and into puberty [26,27]. The prevalence of multiple exostoses is estimated at 1:50.000 [2]. Despite the fact that approximately 60%–70% of patients with HME have a positive family history [7,26], our patient has no family history of such lesions. Multiple osteochondromas are most commonly characterized by pain, whereas patients may also complain about their cosmetic image. Our patient, though, had no complaints about his lesions.

The prevalence of vascular compression secondary to multiple exostoses is approximately 11.3% [28]. The most commonly reported complications in a series of 97 cases were pseudoaneurysm, vascular compression, arterial thrombosis, aneurysm, and venous thrombosis [25]. 71 cases were related to sporadic osteochondromas and 26 cases were associated with HME [25]. During the growth period, osteochondromas are characterized by cartilage-capped formations, which protect the adjacent artery [29]. Later, the cap ossifies and becomes firm and rigid. Laceration of the arterial wall is caused, though, as a result of pulsation of the adjacent artery due to movement or repetitive trauma [9,21,29]. In our systematic review, two cases of patients [20,21] with HME and dissection in the cervical segment of the vertebral artery had no exophytic lesions on the cervical bones. Moreover, five cases of patients [18,19,22–24] with osteochondroma had a vertebral artery occlusion adjacent to the lesions. However, in our case, no evidence of exostoses adjacent to the basilar artery was documented. This finding is supported by two previously reported cases of vertebral artery dissection in patients with hereditary multiple osteochondromas [20,21].

Main symptoms of stroke are headache, nausea, vomiting, neck pain, vertigo, and walk disturbance, while epileptic seizure or loss of consciousness is less commonly detected. However, our patient was admitted to the hospital after an episode of loss of consciousness, followed by tonal seizures «F» and a five-day history of headache. Thus, our patient received antiepilepsy medication. Seizures may occur in approximately 20% of patients with SAH, mostly within the first 24 hours of hemorrhage [30]. In the systematic review, four patients [19,22–24] were treated with surgical removal of osteochondroma, two patients [18,20] were treated only with medications, and one patient [21] treated like a common case of dissection, in contrast to our patient who was treated for a BTA by intravascular procedure (aneurysm occlusion with coil) but the osteochondromas remained untouched.

No cases of hereditary multiple osteochondromas have been previously associated with SAH due to BTA. The specific relation between HME and stroke remains uncertain. Osteogenesis imperfecta (OI) is also an autosomal dominant condition genetically characterized by mutations in type 1 collagen, which may explain some of the disease's vascular complications such as cervical arterial dissection [21]. OI has been associated with vertebral artery lesions in two cases collected from the international literature [21,31]. The first case refers to vertebral artery dissection, whereas the second one to vertebral artery fusiform aneurysm which ruptured leading to SAH. Similar to patients with osteogenesis, genetic diathesis of connective tissue has been proposed as a possible explanation of vertebral artery dissection in patients with hereditary multiple osteochondromas [21]. There is often a tendency of arterial wall weakness in patients with cervical arterial dissection [32]. Structural or functional arterial abnormalities may be risk factors of vascular complications in patients with heritable bone diseases [32]. Abnormalities in structural proteins common to both bone and blood vessels possibly predispose the arterial wall to weakness, which may lead to dissection or aneurysm and subsequently to SAH [21]. Thus, we believe that our patient also had a predisposition of arterial wall weakness owing to HME syndrome.

Limitations of the study are the possible unrecognized cases of stroke patients with hereditary bone diseases.

Conclusion

HME associated with SAH due to ruptured BTA has not previously been subscribed. Despite the fact that the etiopathogenesis of basal artery aneurysm presentation in a patient with HME remains unknown, medical society needs to be aware of this rare condition as SAH is a severe complication.

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References

1. Pedrini E, et al. Genotype-phenotype correlation study in 529 patients with multiple hereditary exostoses: identification of "protective" and "risk" factors. *J Bone Joint Surg* 2011;93(24):2294–2302.
2. Schmale G, et al. The natural history of hereditary multiple exostoses. *J Bone Joint Surg Am* 1994;76(7):986–992.
3. Wuyts W, Van Hul W. Molecular basis of multiple exostoses: muta-

tions in the EXT1 and EXT2 genes. *Hum Mutat* 2000;15(3):220–227.

4. Cook A, et al. Genetic heterogeneity in families with hereditary multiple exostoses. *Am J Hum Genet* 1993;53(1):71–79.
5. Wu Y-Q, et al. Assignment of a second locus for multiple exostoses to the pericentromeric region of chromosome 11. *Hum Mol Genet* 1994;3(1):167–171.
6. Pierz KA, et al. Hereditary multiple exostoses: one center's experience and review of etiology. *Clin Orthop Relat R* 2002;401:49–59.
7. Hennekam RC. Hereditary multiple exostoses. *J Med Genet* 1991;28(4):262–266.
8. Jäger M, et al. Clinical outcome and genotype in patients with hereditary multiple exostoses. *J Orthop Res* 2007;25(12):1541–1551.
9. Vasseur M-A, Fabre O. Vascular complications of osteochondromas. *J Vasc Surg* 2000;31(3):532–538.
10. Brisman JL, et al. Cerebral aneurysms. *New Engl J Med* 2006;355(9):928–939.
11. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurgery* 1968;28(1): 14–20.
12. Greenberg MS. *Handbook of neurosurgery* 2010Greenberg Graphics
13. Barry C, et al. New therapeutic approaches to subarachnoid hemorrhage. *Expert Opin Inv Drug* 2012;21(6):845–859.
14. Feigin V, et al. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol* 2009;8(4):355–369.
15. Hop JW, et al. Case-fatality rates and functional outcome after subarachnoid hemorrhage. a systematic review. *Stroke* 1997;28(3):660–664.
16. Bederson JB, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage. a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association. *Stroke* 2009;40(3):994–1025.
17. Grasso G, et al. Management of aneurysmal subarachnoid hemorrhage: State of the art and future perspectives. *Surg Neurol Int* 2017;8:11.
18. Altaf F, et al. Osteochondroma of C1 causing vertebral artery occlusion. *Brit J Neurosurg* 2013;27(1):130–131.
19. George B, et al. Cervical osteochondroma (c2 level) with vertebral artery occlusion and second cervical nerve root irritation. *Surg Neurol* 1989;31(6):459–464.
20. Hill MD, et al. Heritable bone disease and stroke due to vertebral artery dissection. *Cerebrovasc Dis* 2001;12(1):73–74.
21. Arauz A, et al. Multiple hereditary exostoses and stroke due to vertebral artery dissection. *J Vasc Interv Neurol* 2015;8(1):46–48.
22. Fadili S, et al. Occlusion of vertebral artery due to transverse canal osteochondroma. *Clin Neuroradiol* 2014;24(4):395–397.
23. Srikantha U, et al. Spinal osteochondroma: spectrum of a rare disease. *J Neurosurg Spine* 2008;8(6):561–566.
24. Zhang Y, et al. Solitary C1 spinal osteochondroma causing vertebral artery compression and acute cerebellar infarct. *Skeletal Radiol* 2015;44(2):299–302.
25. Stieber JR, Dormans JP. Manifestations of hereditary multiple exostoses. *J Am Acad Orthop Surg* 2005;13(2):110–120.
26. Legeai-Mallet L, et al. Incomplete penetrance and expressivity skewing in hereditary multiple exostoses. *Clin Genet* 1997;52(1): 12–16.
27. Bovée JV. Multiple osteochondromas. *Orphanet J Rare Dis* 2008;3(1):3.
28. Wicklund CL, et al. Natural history study of hereditary multiple exostoses. *Am J Med Genet* 1995;55(1):43–46.
29. Matsushita M, et al. Pseudoaneurysm of the popliteal artery caused by exostosis of the femur: case report and review of the literature. *J Vasc Surg* 2000;32(1):201–204.
30. Sundaram MBM, Chow F. Seizures associated with spontaneous subarachnoid hemorrhage. *Can J Neurol Sci* 2015;13(3):229–231.
31. Kaliaperumal C, et al. Osteogenesis imperfecta presenting as aneurysmal subarachnoid hemorrhage in a 53-year-old man. *BMJ Case Rep* 2011;21:2011.
32. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. *New Engl J Med* 2001;344(12):898–906.