Diffuse Neurofibroma Presenting with Spontaneous Intra-Tumoral Hemorrhage

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This report describes a case of diffuse neurofibroma (DNF) that presented with spontaneous intratumoral hemorrhage. A 31-year-old man with cutaneous manifestations typical of neurofibromatosis type 1 (NF1) was referred to hospital with a progressively expanding scalp swelling. Magnetic resonance imaging (MRI) showed an acute hematoma surrounded by a dense mass on the parieto-occipital scalp. Plain skull radiographs and a computed tomography (CT) scan revealed bony defects in the occipital bone around the lambdoid suture and the skull base, including the sphenoid and petrous bones. The tumor extended to the upper cervical region and infiltrated through the fascia of the musculature. The tumor and adjacent soft tissue were highly vascular, which made surgical resection difficult. We describe the clinical, radiological and pathological features of this patient and discuss the surgical methods used to avoid a life-threatening hemorrhage during surgery.

KEY WORDS : Diffuse neurofibroma · Neurofibromatosis · Hemorrhage.

Introduction

Neurofibroma is a well-known benign tumor of the peripheral nerve sheath. These tumors are categorized as localized, plexiform, or diffuse types, according to their growth patterns. Diffuse neurofibroma is an unusual neurofibroma variant in which tumor cells diffusely infiltrate the adjacent soft tissue. About 10% of these tumors are associated with NF1, which is an autosomal-dominant inherited disease with high penetrance and variable expression. Many individuals with NF1 have calvarial bone defects, especially near the lambdoid suture. However, these calvarial bone defects occur less frequently than sphenoid bone defects or dysplasia. Because life-threatening hemorrhages occasionally occur in patients with DNF, surgical excision should be planned to avoid massive hemorrhage. Our patient presented with a spontaneous intratumoral hemorrhage in a DNF that involved the scalp and upper portion of the posterior neck, and calvarial and basal skull defects were also found in the patient. We describe the clinical and radiological features of the DNF and discuss methods for surgical intervention, with emphasis on avoiding life-threatening hemorrhage.

Case Report

A 31-year-old man was admitted to our hospital with painful swelling of the parieto-occipital scalp. The swelling was rapidly increasing. The patient exhibited café-au-lait spots and numerous subcutaneous nodules that were consistent with the diagnosis of NF1. There was no family history of NF1 symptoms. Physical examination upon admission showed a huge mass-like lesion on the parieto-occipital scalp that extended to the upper cervical region, measuring 13 × 18 cm.

Before symptom onset, the patient had diffuse thick-
Fig. 2. Initial T2-weighted coronal (A) and gadolinium-enhanced coronal (B) magnetic resonance images showing a huge mass involving the left parietotemporal and suboccipital regions. Initial axial T1-weighted magnetic resonance images showing a huge mass involving the left temporal and suboccipital regions and extending to the upper cervical area (C, D, E). Initial gadolinium-enhanced axial images demonstrating peripheral enhancement of the mass and inhomogeneous enhancement of the soft tissues adjacent to the bone defect sites, including the soft tissue around the petrous bone and the upper cervical muscles (arrows) (F, G, H).

Fig. 3. Gadolinium-enhanced axial magnetic resonance images after three years showing no change in the enhancement of soft tissues and no regrowth of the tumor has occurred (A, B, C).

Enlarging of the occipital scalp and a focal mass measuring 3 × 5 cm over the scalp. About five hours before admission, the patient had painful, rapidly increasing swelling around the preexisting mass that led him to seek medical care. There was no history of head trauma.

Neurological examination and all laboratory tests were normal. There was no evidence of a tendency to bleed. Plain skull radiographs and a CT scan revealed bony defects in the occipital bone around the lambdoid suture, the skull base, and the sphenoid and petrous bones (Fig. 1). MRI revealed an acute hematoma surrounded by a dense mass on the parietooccipital scalp (Fig. 2). Administration of gadopentetate dimeglumine (Gd-DTPA) enhanced the extracranial regions adjacent to the bone defects. However, MRI revealed no abnormalities in intracranial structures. A bone scan of the skull was normal, suggesting the absence of tumor cells in the bone.

Initially, the patient was managed conservatively with bed rest, compressive dressings and close observation. The continued enlargement of the scalp swelling resulted in our undertaking surgical exploration.

In the first operation, the tumor was removed through an elliptical scalp incision. The bulk of the yellowish-white tumor was found between the galea and the pericranium. The pericranium was relatively intact. After excision of the outer surface of the tumor, an acute hematoma was identified; however, there was no active bleeding within the tumor. The tumor infiltrated subcutaneous tissue and dermis (Fig. 4). Anatomical structures such as hair, hair follicles, and other skin appendages were relatively well preserved (Fig. 4). The upper half of the mass was excised; however, massive bleeding during the operation made the resection difficult. It was estimated that 3000 cm$^3$ of blood was lost during the three-hour operation. This bleeding was reduced with suture ligatures and clamps on the surrounding subcutaneous tissue. The wound was then closed. The first postoperative course was uneventful. An angiographic examination showed the high vascularity of the affected scalp and a dilated occipital artery.
A second exploratory operation was performed two weeks later. The previous scalp incision was extended to the midcervical region and the occipital artery was ligated. Preliminary suture ligatures were then placed around the mass to prevent massive bleeding and the tumor mass was resected piece by piece. Troublesome hemorrhage occurred despite the occipital artery ligation; however, the bleeding was controlled by compression, suture ligatures and clamping the surrounding soft tissue. The tumor extended to the upper cervical region and infiltrated through the fascia of the musculature. This infiltration made complete excision of the tumor impossible. The estimated blood loss during the four-hour operation was about 1500cm³. The tumor outside the muscle fascia was removed and the wound was closed.

The final postoperative course was uneventful and the patient was discharged in good clinical condition with satisfactory cosmetic results. An MRI taken three years after the surgery showed no significant changes and no evidence of tumor regrowth (Fig. 3).

Histological examination of the resected specimen showed wavy spindle cells interspersed with Wagner-Meissner-like corpuscles (Fig. 4). The specimen was an ill-defined, infiltrative lesion that involved the entire dermis and the subcutaneous tissue, with intact skin appendages. The upper cervical specimen showed diffuse infiltration through the fascia into the muscle (Fig. 4). The intensely infiltrative character and the tactile corpuscle-like formations resembling Wagner-Meissner-like bodies provided a clear differentiation from other types of NF (Fig. 4). Numerous ectatic vessels with abnormal wall structures were observed.

**Discussion**

*DNFs* are uncommon variants of neurofibroma that have a predilection towards involving the subcutaneous tissues of the head and neck. They are usually ill defined and diffusely infiltrate the dermis and subcutaneous tissue, often extending along the connective tissue septa. Although they show an infiltrative growth pattern, normal structures such as skin appendages are relatively well preserved, as seen in our patient. The diffuse involvement of the skin and the high vascularity of the tumor make surgical excision very difficult. About 10% of these tumors are associated with NF1, which is an autosomal-dominant inherited disease with high penetration and variable expression. We discuss some characteristic features in this patient, such as skeletal involvement, possible mechanisms of intratumoral bleeding and the surgical methods used to avoid massive bleeding.

**Skeletal involvement**

Occipital and basal skull bone defects were identified in our patient. Sphenoid dysplasia is one of the typical clinical features in patients with NF1. Although it is well known that NF1 is sometimes associated with calvarial defects, most of which occur adjacent to the lambdoid suture, its precise etiology is not known.

Some authors suggest that bony defects may be attributable to erosion or resorption by the tumor. Erosion and enlargement of the internal auditory canal by vestibular schwan-
noma is well known. Abnormal vascularity may also contribute to bone resorption. Macfarlane et al. suggested that a defect in the sphenoid wing in a patient with NF1 may have been an acquired lesion. An acquired etiology would help to explain the unilateral and stereotypical nature of that bony defect. They also suggested that bony defects may be congenital malformations that are relatively small at birth and are widened by the pulsatile pressure of the brain.

In our patient, a CT scan showed that the occipital bone defect appeared to widen outwardly, perhaps by pulsatile brain pressure. The bone scan of the skull with 99m-technetium diphosphonate showed no abnormal accumulation of radiotracer at the margin of the defect. A large part of the tumor mass was over the posterior parietooccipital area; however, the bone defect was situated more inferiorly. The suboccipital bone defect was covered by muscle and was not directly compressed by the tumor. These observations indicate that erosion or compression by the tumor did not cause the bony defect. We suggest that the pulsatile pressure of cerebrospinal fluid in the brain enlarged a congenital bone dysplasia, or a defect. In infants with a skull fracture, a similar effect, called a 'growing fracture', occurs. Because anatomical structures derived from the mesoderm, such as bone, can be affected by neurofibromatosis (NF), this condition is a mesodermal dysplasia rather than simply a neurocutaneous disorder.

Tumor infiltration into the soft tissue adjacent to the bony defect was seen in MRIs after administration of Gd-DTPA to our patient (Fig. 2). Diffuse neurofibromas are poorly circumscribed, nonencapsulated tumors that involve subcutaneous tissue to the level of the fascia. In our patient, the tumor cells infiltrated muscle layer beyond the fascia (Fig. 4). MRI following administration of Gd-DTPA showed diffuse enhancement of the upper cervical muscle (Fig. 2), indicating that tumor cells had infiltrated into and interdigitated between muscle fibers. A pathology examination confirmed these observations (Fig. 4). The intense, infiltrative character of the tumor observed in our patient is extremely rare. In patients with DNF, complete removal of the tumor is rarely achieved because of its extensive and diffusely infiltrative nature.

Possible mechanism of intratumoral hemorrhage

Our patient presented with a painful swelling of the parietooccipital scalp that was rapidly increasing in size. Although DNFs are benign, they are prone to significant neovascularization. Troublesome hemorrhages often occur during tumor excision. However, a massive intratumoral hemorrhage without previous trauma is extremely rare. A few cases of spontaneous intratumoral hemorrhage have been reported; however, these were in patients with plexiform neurofibroma, not diffuse neurofibroma.

Tung et al. have suggested that progressive intratumoral hemorrhage occurs because of the inherent histopathology of the lesions combined with a lack of underlying skeletal structures. This prevents a spontaneous tamponade from bleeding. They suggested that the bleeding is likely to be propagated by a cascade of rupturing vessels, followed by more bleeding within the very friable tumor mass, causing more vessels to rupture. However, they could not identify the initial event that led to the bleeding when it occurred spontaneously.

In our patient, troublesome bleeding occurred from the grayish-white friable mass and from the normal surrounding soft tissue. Angiography showed high vascularity over the whole scalp and the upper cervical region. In the operative field, the hematoma was located at the center of the grayish-white friable mass. The cause of the bleeding was not identified. Based on clinical and anatomical features, we suggest that the cause of hemorrhage may have been an inherent histopathology. At the center of the friable mass, the newly developed deep vessels had abnormal wall structures that may have ruptured spontaneously, and the bleeding propagated by the cascade mechanism proposed by Tung et al.

Surgical treatment

Surgery is undertaken when a tumor compromises organ function or becomes cosmetically unacceptable. Surgical treatment is mandatory; in our opinion, when spontaneous, intratumoral bleeding cannot be controlled with conservative methods. Adequate provision for massive transfusions during surgery should be made, along with attempts to minimize hemorrhaging. Lin et al. proposed three ways to control bleeding: (1) hypotensive anesthesia, (2) preliminary sutures around the lesion, and (3) ligation of a limited number of feeding vessels. However, in our experience, ligation of feeder vessels does not control the hemorrhage. Suture ligatures around the lesion and clamping the surrounding soft tissue are procedures that are more effective. Although preoperative angiography and superselective embolization are essential for preventing massive bleeding, they may not produce satisfactory results because these tumors tend to revascularize quickly. Tung et al. first performed ligation of the external carotid artery during surgery in a patient with a facial neurofibroma; however, this procedure was not successful in controlling the massive bleeding. Therefore, clinicians should be aware that massive bleeding might occur during surgery, despite preoperative embolization and ligation of feeder vessels. Based on the above findings, we suggest that serial excision is the most generally accepted treatment in patients with DNF.

Complete removal of the tumor is impossible when it infiltrates the muscle layer, as in our patient. Because of the reg-
rowth of the remnant tumor, periodic follow-up examination is recommended. MRI scans of our patient taken three years after the operation showed no significant changes, suggesting that there was no growth of the remnant tumor, or further infiltration into the musculature. A longer follow-up period will be needed to investigate the fate of those tumor cells that remain between the muscle fibers.

Conclusion

We report a patient with DNF presenting with intratumoral hemorrhage. Because of the pathological characteristics of this type of tumor, such as diffuse infiltration and hypervascularity, troublesome hemorrhage may occur during surgical excision. We have described and discussed several methods that can be used to avoid a life-threatening hemorrhage.

References
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