CASE REPORT

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MANAGEMENT ISSUES IN MASSIVE PEDIATRIC FACIAL PLEXIFORM NEUROFIBROMA WITH NEUROFIBROMATOSIS TYPE 1

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Abstract: *Background.* Plexiform neurofibroma is a relatively common but potentially devastating manifestation of neurofibromatosis type 1 (NF1). Surgical management is the mainstay of therapy, but within the head and neck region it is limited by the infiltrating nature of these tumors, inherent operative morbidity, and high rate of regrowth.

Method. We describe a case of a 7-year-old girl with neurofibromatosis type 1 and a massive facial plexiform neurofibroma with the aim of emphasizing the treatment and timing issues involved in the management of this difficult problem. A MEDLINE search (1966 through December 2000) was carried out, and pertinent literature on the subject was reviewed.

Result. The patient described in this case report was carefully observed for a period of 6 years from diagnosis before surgical excision of the tumor was undertaken with an uneventful recovery.

Conclusion. Surgical management remains the mainstay of treatment for these locally invasive tumors, but functional disturbances are almost inevitable in resecting substantial tumors involving the head and neck region. The indication and timing of surgery in pediatric patients therefore needs to be carefully weighed against the physical and psychologic consequences of treatment. © 2002 John Wiley & Sons, Inc. *Head Neck* **24:** 207–211, 2002.

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Neurofibromatosis 1 (von Recklinghausen's disease) and neurofibromatosis 2 (bilateral acoustic neurofibromatosis) are autosomal dominant disorders in which affected individuals are at an increased risk for developing both benign and malignant tumors. Associated features of NF1 include loss of vision, learning disabilities, hypertension, and skeletal malformations. NF2 patients commonly experience cataract formation and hearing loss.[1]

Plexiform neurofibromas (PNs) are one of several types of neurofibromas that occur in von Recklinghausen's neurofibromatosis. They are characterized histologically by a proliferation of Schwann cells in the nerve sheath across the length of a nerve, involving multiple fascicles and multiple nerves. These convoluted masses are classically described by a ''bag of worms'' appearance.[2] PNs are locally invasive, nonmetastasizing, and generally categorized by location. Tumors of the head, neck, and face are most

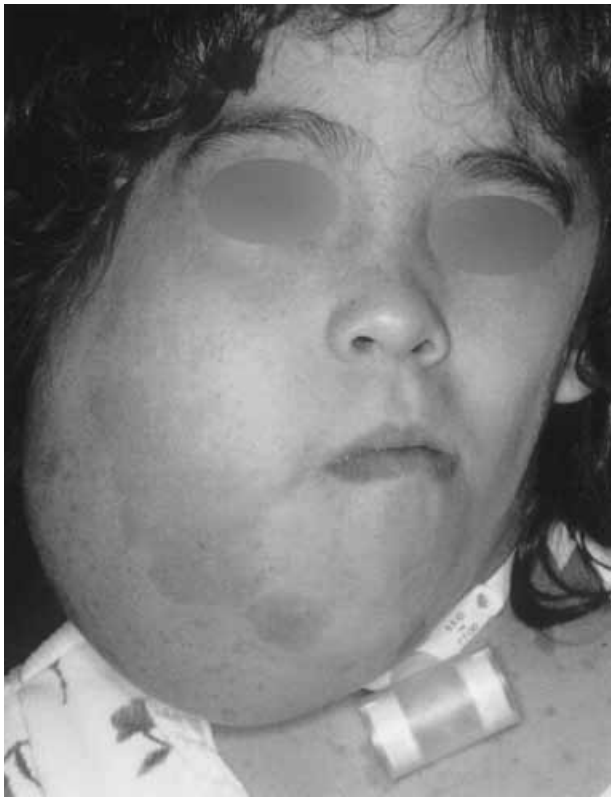

FIGURE 1. Clinical appearance of the child at age 7 demonstrated a significant increase in size of the tumor over the preceding year.

common, followed by lesions of the spine, extremities, mediastinum, and abdomen.[3]

Surgical management of facial plexiform neurofibromas in pediatric patients is especially challenging because of the infiltrating nature of these tumors, inherent operative morbidity, and tendency for regrowth.[4] The primary aim of this report is to describe a case of massive, facial plexiform neurofibroma in a 7-year-old girl with neurofibromatosis type 1, with specific emphasis on discussing the type of treatment and its timing in the management of this difficult problem.

CASE HISTORY

The patient is a 7-year-old girl with neurofibromatosis type 1 followed by our service since the age of 14 months. She was diagnosed with NF1 at the age of 12 months when she was seen by her primary care physician with axillary freckling and numerous café-au-lait spots on the trunk. In addition, her mother had noted mild, right-sided facial swelling since the age of 2 months. MRI of the lesion showed a large, right-sided

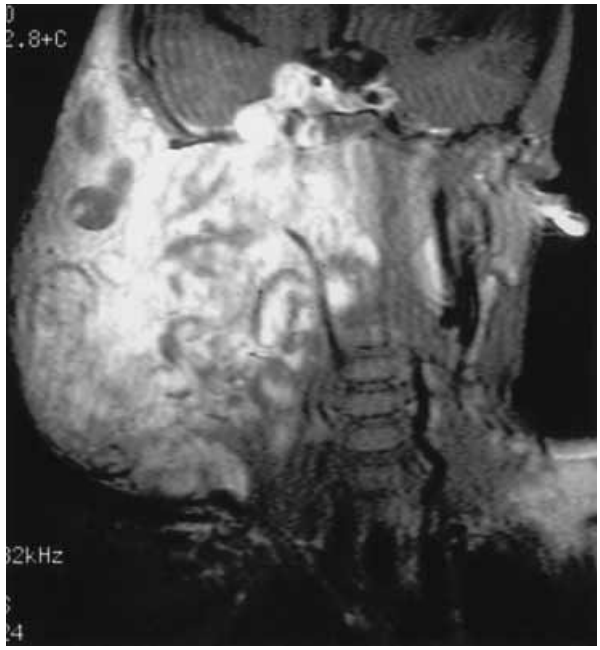

FIGURE 2. MRI showing extensive involvement of right side of the face and the middle cranial fossa at the skull base by the tumor.

plexiform neurofibroma with intracranial extension, and these findings were corroborated by tissue biopsy.

On referral to our service, the benefits of surgical excision at that age were considered against the risks involved, and a plan was made to closely follow tumor growth with serial imaging anticipating subtotal tumor resection for cosmesis when the child reached approximately school age.

At age 14 months, the patient began to exhibit a failure to thrive with respiratory distress and decreased feeding. MRI confirmed parapharyngeal extension of tumor. A tracheostomy tube was placed with marked improvement in breathing, eating, and growth.

From ages 2 to 6 years, the tumor grew proportionately with the child's growth and was carefully monitored by serial MRI scans at yearly intervals. She met developmental milestones appropriately and began regular schooling. However, by age 7 she had started experiencing headaches, right-sided facial pain, dysarthria, and difficulty clearing secretions. Physical examination revealed significant gross enlargement of tumor size over the past year (Fig. 1). An MRI at this time (Fig. 2) confirmed rapid growth of tumor and showed infiltration into the masticator and deep parotid spaces, the pterygomaxillary fossa, infratemporal fossa, and parapharyngeal

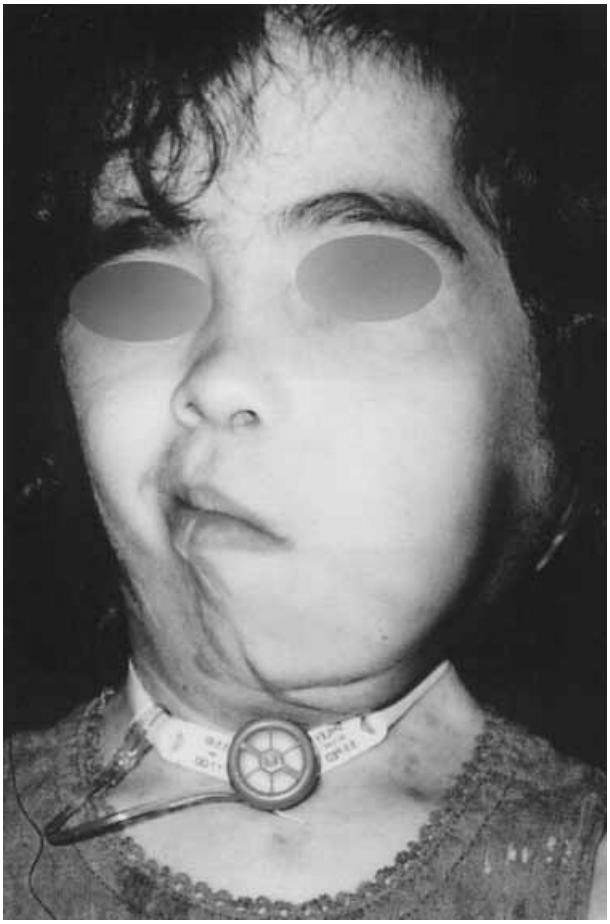

FIGURE 3. External appearance of the patient 6 months after surgical resection and reconstruction.

space. There was also extension into the middle cranial fossa at the skull base.

In view of the recent spurt in growth of the tumor and exacerbation of symptoms, a decision was made to offer surgical excision as an option to the parents. A subtotal resection was performed with the combined efforts of the head and neck, pediatric, and plastic surgery teams. Dissection was extraordinarily tedious because of the microvascularity of the tumor and loss of all identifiable tissue planes. The bulk of the mass was resected, with residual tumor persisting in the parapharyngeal space and the middle fossa skull base. Although preoperative planning included consultation with the neurosurgical team, a decision was made not to pursue the intracranial component through a craniofacial approach, because total removal of the tumor in the neck was going to be impossible in any case. Gross and histologic examination of the mass confirmed plexiform neurofibroma. Several neurovascular

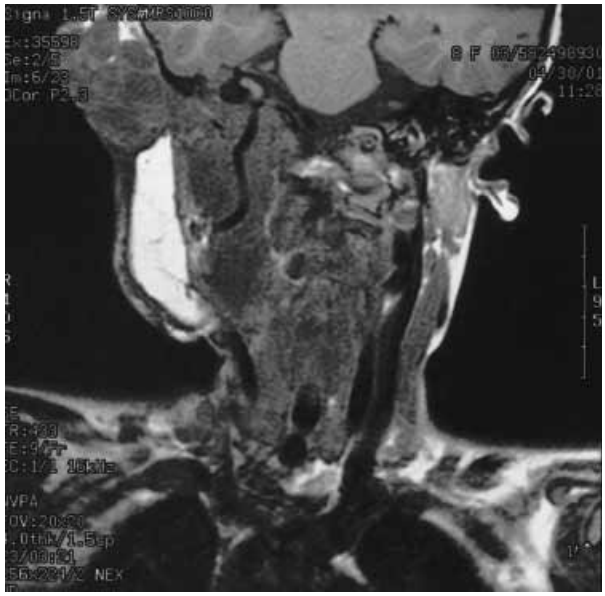

FIGURE 4. Postoperative MRI scan in the coronal view shows a healthy rectus abdominis flap and the extent of residual disease.

structures had to be sacrificed during tumor resection: the right external carotid artery; cranial nerves XI, XII; lower branches of cranial nerve VII; and the right lingual nerve.

The plastic surgery team repaired the surgical defect with a rectus free flap tissue transfer. Her postoperative course was uncomplicated, and she was discharged from hospital without event. Six months after surgery, the patient is doing well and has rejoined her second-grade class (Fig. 3). A postoperative MRI scan shows a healthy rectus flap and demonstrates the extent of residual disease (Fig. 4).

DISCUSSION

Neurofibromatosis is the most common neurocutaneous syndrome (phakomatosis). It is divided into two genetic variants, types 1 and 2. NF1, or von Recklinghausen disease, occurs in 1 in 4000 births. It is autosomal dominant with 70% to 80% penetrance. However, up to 50% of cases of NF1 result from spontaneous mutation. The genetic defect has been linked to chromosome 17 that codes for the tumor suppressor protein, neurofibromin.[5,6]

NF2, also referred to as bilateral acoustic neurofibromatosis, is less common (1 in 50,000 live births) and has been traced to chromosome 22. The hallmark of both diseases is an increased risk for the development of both benign and malignant tumors. The National Institutes of Health

Table 1. Diagnostic criteria for neurofibromatosis 1 (NF1)

The patient should have 2 or more of the following:
1. Six or more café-au-lait spots
   - 1.5 cm or larger in postpubertal individuals
   - 0.5 cm or larger in prepubertal individuals
2. Two or more neurofibromas of any type
   or one or more plexiform neurofibroma
3. Freckling in the axilla or groin
4. Optic glioma
5. Two or more Lisch nodules (benign iris hamartomas)
6. A distinctive bony lesion
   - Dysplasia of the sphenoid bone
   - Dysplasia or thinning of long bone cortex
7. A first-degree relative with NF-1

Source: References 7.

have outlined specific diagnostic criteria for NF1 and NF2.[7] (Tables 1 and 2).

PN is a common and often devastating manifestation of NF1. In fact, it is the most common peripheral neoplasm of the disease, whereas the most common central lesion is optic glioma. Generally considered pathognomonic for NF1, the prevalence of PN in NF1 is approximately 27% detected on physical examination and 44% on full-body imaging studies.[8,9]

PNs are generally categorized by location. Lesions of the head, neck, and face are most common and lead to cosmetic disfigurement and potential blindness. Spinal PNs, also referred to as ''dumbbell lesions,'' may cause cord compression syndromes. In the extremities, PNs cause local destruction and venous stasis. Finally, in the mediastinum or abdomen, lesions may result in cardiopulmonary compromise and bowel/bladder dysfunction.[3]

A significant number of plexiform neurofibromas are seen in a manner similar to the case described—soft tissue swellings first noticed during infancy or early childhood. From clinical observation, it seems that PNs undergo rapid growth during three characteristic time periods, specifically (1) infancy, (2) puberty, and (3) pregnancy. As a result, it has been speculated that growth of PNs are modulated, at least in part, by hormonal changes.[3]

As for diagnosis, high-signal weighted MRI is the imaging modality of choice. On scans, PNs exhibit variable morphology, but commonly display central areas of low-signal density. Tissue biopsy confirms the diagnosis.

Although most of these tumors are benign, PNs have the potential for malignant change. There exists a 3% to 4% risk of transformation into malignant peripheral nerve sheath tumors (MPNSTs).[10] Once diagnosed, MPNSTs have a 5-year survival of 20% to 50%.[11] Prognosis for MPNSTs is poor for two reasons: first, diagnosis is difficult because they often exist as a small focus within a large, benign PN, making incisional biopsy an unreliable method of detection; second, once diagnosed, wide surgical excision is the only reliable treatment, and there is a scarcity of effective adjuvant therapies.

Surgery is the only effective option currently available for the treatment of PN. However, success of surgical intervention is limited by the infiltrating nature of the tumors, resulting in a high rate of tumor regrowth. As such, the physician is faced with the task of identifying optimal candidates for surgery. Outcomes of PN resections were reviewed in a retrospective study performed at the Children's Hospital of Philadelphia over a 20-year period.[12] Of 121 patients who underwent resection, only 54% of patients were free from recurrence of tumor at 10-year follow-up. In addition, the investigators identified three prognostic factors for recurrence of disease. Tumors of the head/neck/face were twice as likely to recur compared with PNs of other locations (60% versus 29%). The age of the patient at surgical resection seemed to influence outcome: tumors resected before age 10 years recurred in 60% of cases compared with only 30% recurrence in patients older than the age of 10 years. Finally, as expected, subtotal resections recurred more frequently than total resections of tumor (45% versus 20%).

As in the case of the patient described herein, efforts were made to postpone surgical resection of her tumor to school-age to reduce operative morbidity and minimize her likelihood of undergoing multiple procedures. Aside from managing her airway with a tracheostomy tube placed at age 14 months, she remained relatively asymp-

Table 2. Diagnostic criteria for neurofibromatosis 2 (NF2)

Individuals with the following clinical features have confirmed NF2:

Bilateral vestibular schwannomas (VS)
or
Family history of NF2 (first-degree family relative)
plus
1. Unilateral VS < 30 years or
2. Any two of the following: meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract

Source: References 7.

tomatic for several years. Tumor growth was monitored with yearly physical examination and high-signal MRI. A decision was made to operate at age 7 only after she began complaining of facial discomfort, headaches, and swallowing difficulties. In addition, surgery for cosmetic improvement was appropriate as she entered school. The benefits of surgical resection need to weighed carefully against its risks, specifically deficits that almost certainly arise from interruption of major neurovascular structures.

PN remains a devastating manifestation of von Recklinghausen neurofibromatosis. Because surgical management remains the mainstay of treatment for these locally invasive tumors, guidelines for identification of candidates for surgery have to be clearly established. From our experience, it seems prudent to delay surgery as long as it is feasible for otherwise asymptomatic pediatric patients with facial plexiform neurofibromas. Careful surveillance for obstruction of physiologic passages such as the upper aerodigestive tract must be undertaken and the surgical treatment timed accordingly. Major surgical procedures have the potential to cure, but this has to be weighed against the functional disturbances that are almost inevitable in resecting substantial tumors in the head and neck region. Clearly, these limitations of surgery necessitate the development of additional therapies. Current research will hopefully offer new insights into this rare, debilitating, and difficult-to-manage disease and eventually improve treatment results.

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