10.5005/jp-journals-10031-1222

CASE REPORT

Craniofacial Plexiform Neurofibromatosis

[1]Taher A Mistry, [2]Srivalli Natarajan, [3]Gaurav Deshpande, [4]Yusuf Mistry

ABSTRACT

Multiple neurofibromatosis (NF) or von Recklinghausen's disease is an autosomal dominant disorder affecting the growth of neural tissues, caused due to the mutation of the gene located at 17q11.2 chromosome, known as neurofibromatosis type I (NF1) gene. The gene product neurofibromin serves as a tumor suppressor; hence, decreased production of this protein results in a myriad of clinical features, which include café au lait spots, multiple skin tumors, axillary and inguinal freckling, optic glioma, and Lisch nodules (pigmented hamartomas of the iris). Besides the functional troubles, it is an esthetically devastating disease. Like other genetic diseases, it has no definitive treatment and surgical corrections have a bleak prospect in improving cosmesis and only help in creating a lesser monster.

In this article, we discuss the etiopathogenesis, clinical features, and the intricacy of the surgical management of the craniofacial involvement of von Recklinghausen's disease along with two case reports.

Keywords: Craniofacial, Neurofibromatosis, Plexiform, Surgical debridement.

How to cite this article: Mistry TA, Natarajan S, Deshpande G, Mistry Y. Craniofacial Plexiform Neurofibromatosis. J Contemp Dent 2018;8(1):50-56.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Multiple NF is a genetic disease principally affecting the Schwann cells of the nerve sheath. Although this disease was first described by Smith in 1842, this pleomorphic variety of disorders is usually associated with the name of von Recklinghausen[1] who described the entity in detail.[2]

There are clinically two types of NF as reported by Gutmann et al,[3] NF1 and NF2. These two forms of the disease are caused by mutation of different genes and hence, have few common findings. Neurofibromatosis type I is often known as von Recklinghausen's disease and is the most common genetic disorder affecting humans, affecting 1 in 3,000 births. Previous studies have failed to show any sex or race predilection. It is caused by the mutation or deletion of the gene located at 17q11.2 chromosome which is known as the NF1 gene. This gene is responsible for the production of neurofibromin, a protein that acts like a tumor suppressor for Schwann cells. Alteration in the production of this protein leads to a myriad of clinical features ranging from mild lesions to severe impairments.[4] The manifestations include café au lait spots, multiple skin tumors, axillary and inguinal freckling, optic glioma, and Lisch nodules (pigmented hamartomas of the iris).[3]

Neurofibromatosis type II demonstrates a relative paucity of cutaneous findings, and has a higher incidence of meningiomas and acoustic neuromas which are frequently bilateral.[4]

Plexiform NF of the head and neck is a relatively rare condition and accounts for 3 to 7% of all cases of von Recklinghausen's disease. These are distinctly unilateral and have a more diffuse plexiform pattern of growth. They can be locally invasive and quite deep and may be associated with the erosion of the underlying facial skeleton. The facial deformity caused by plexiform NF over the face affects two mechanisms: (1) Infiltration by the tumor and (2) downward traction by neurofibromas of the adjacent unit.[5]

Herein, we describe our surgical experience in managing the facial deformities caused by craniofacial NF in the following two case reports.

CASE REPORTS

Case 1

A 27-year-old male patient reported to us with a complaint of asymmetry of the face due to a diffuse growth on the right side since early childhood, leading to drooping of the right ala and corner of the mouth. He was previously diagnosed as NF1 and had undergone two surgeries for esthetic correction in the same region. The diffuse growth had not increased in size since childhood. His father and uncle gave a positive history of a similar condition.

The patient gave a history of facial nerve weakness following the previous surgery.

On examination, we observed a diffuse growth over the right side of the face extending from the preauricular region to the midline and from the supraorbital rim to the lower border of the mandible. There was drooping of the

[1,4]Postgraduate Student, [2]Professor and Head, [3]Lecturer

[1-4]Department of Oral and Maxillofacial Surgery, Mahatma Gandhi Mission's Dental College and Hospital, Navi Mumbai Maharashtra, India

Corresponding Author: Taher A Mistry, Postgraduate Student, Department of Oral and Maxillofacial Surgery Mahatma Gandhi Mission's Dental College and Hospital, Navi Mumbai, Maharashtra, India, Phone: +917718902305, e-mail: tahermistry05@gmail.com

outer canthus of the eye, ala of the nose, and the corner of the mouth on the right side of the face. It appeared as if the lesion had dragged the alar base and the corner of the mouth downward. The overlying skin was hyperpigmented. Scars were present in the temporal and infraorbital region suggestive of previous surgery (Fig. 1).

The lesion had a soft consistency, was compressible, nonfluctuant, resembling a bag of worms feel on palpation.

Intraorally, he had a similar lesion over the right buccal mucosa, which appeared to be an extension of the extraoral growth (Fig. 2).

The patient had café au lait spots and multiple neurofibromas over his torso (Fig. 3).

Corrective surgery for his facial deformity was undertaken. A Weber Ferguson incision was taken till the subcutaneous tissue to expose the neurofibromatous mass. The mass extended in the subcutaneous plane superficial to the muscular aponeurotic system, although it was not confined in one plane. There were numerous adhesions to the overlying and underlying tissues. Debulking of the lesion was done with caution to avoid injury to any significant anatomic structures. The lesion was highly vascular and multiple bleeding points were noted during the debulking of the lesion; however, hemostasis was conveniently achieved with an electrocautery (Fig. 4).

The healing was uneventful with an inconspicuous scar. There was a significant improvement in the facial esthetics. There was not only an improvement in the facial contour but also the outer canthus, alar base of the nose, and the corner of the mouth appeared to be less distorted and more symmetrical with the contralateral side. On the 3rd month follow-up, the patient did not reveal any signs of recurrence of the tumor mass (Fig. 5).

Histopathology confirmed the diagnosis of plexiform NF (Fig. 6).

Fig. 1: Preoperative picture showing gross facial deformity on the right side of the face due to the diffuse growth. There is drooping of the right ala, nostril, and angle of the mouth

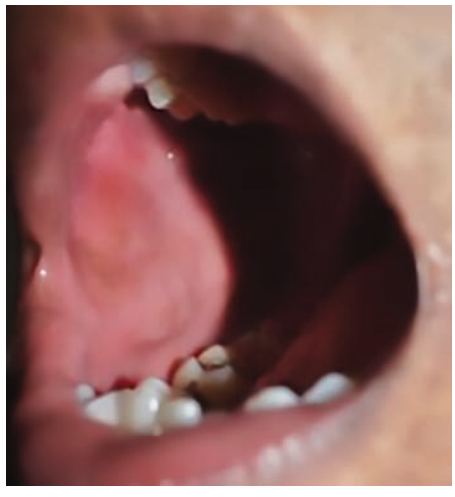

Fig. 2: Café au lait spots seen with multiple neurofibromatous lesions on the trunk

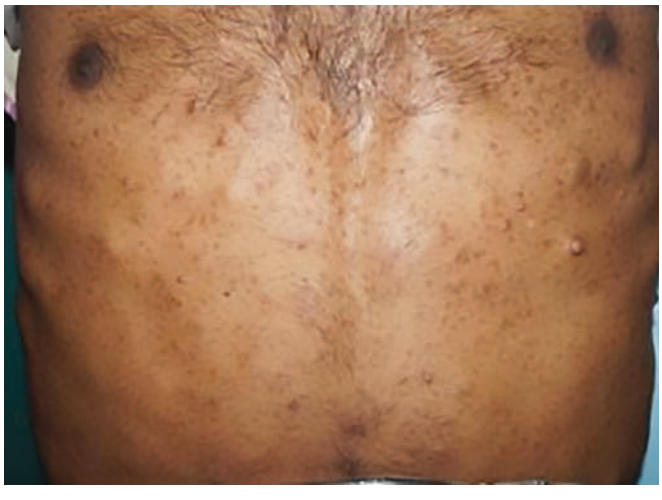

Fig. 3: Intraoral lesion seen on the right buccal mucosa. The lesion appeared to be an extension of the extraoral mass

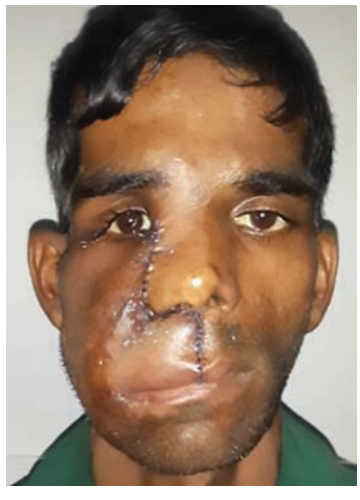

Fig. 4: Immediate postoperative picture showing the gross swelling along the operated region. Weber Ferguson incision was taken to gain access to the tumor for debulking

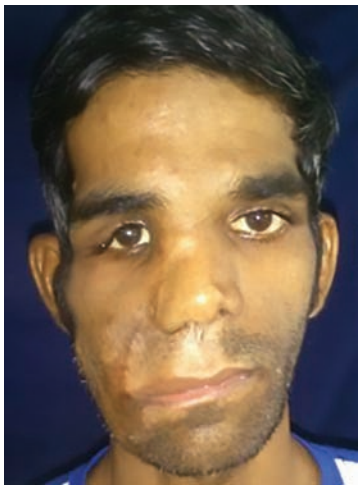

Fig. 5: Three months postoperative picture, showing significant improvement in the facial contour

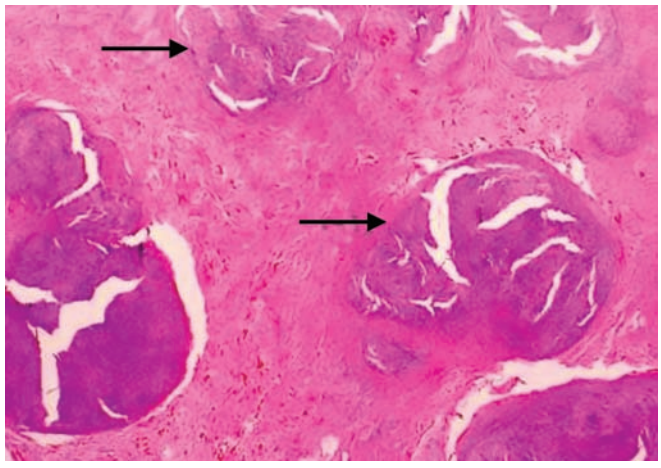

Fig. 6: Photomicrograph of case 1 showing the appearance of a plexiform neurofibroma with multiple tortuous enlargements of cutaneous peripheral nerves (black arrow) (hematoxylin and eosin staining)

Case 2

A 32-year-old male patient reported to us with a gross deformation of the left periorbital region due to an infiltrative growth of the left upper eyelid. The swelling was present since early childhood, when the patient was around 14 years old, and there was a sudden increase in the growth till the current size. The swelling had appeared to cease growing in size since last 10 years. The patient had been operated previously for debulking of the lesion and a histopathological diagnosis of neurofibroma was given. The patient did not give any history of increase in the size of the lesion after the previous surgery. He was not satisfied with the previous surgical outcome and desired further improvement in function of the eyelid and also desired some cosmetic correction for the same.

The patient did not give any family history of the disease.

On examination, the patient had a diffuse swelling involving the left upper eyelid. There was drooping of the outer canthus of the eye due to the gravitation effect of the swelling and the patient was unable to open his eye. The vision was normal with normal extraocular movements, although his eyeball was completely obstructed by the swelling. The swelling had a smooth surface, with a normal overlying skin. Some amount of eversion of the eyelid was present exposing the palpebral conjunctiva (Fig. 7).

The patient did not give any history of watering from the eyes.

The swelling was soft in consistency, compressible, and nonfluctuant. It was not tender on palpation.

The patient had numerous neurofibromas over his body and his torso showed characteristic café au lait spots (Fig. 8).

Computed tomography (CT) scan of the patient showed that the lesion was extending into the temporal

Fig. 7: Preoperative picture of the patient showing the gross deformation of the upper eyelid and some portion of the exposed palpebral conjunctiva

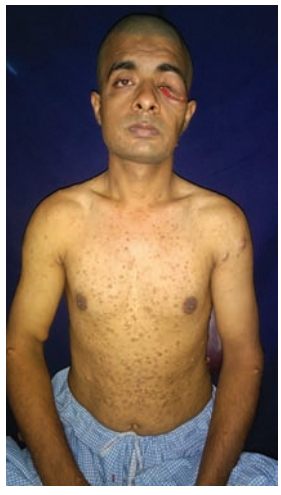

Fig. 8: Café au lait spots seen with multiple neurofibromatous lesions on the trunk

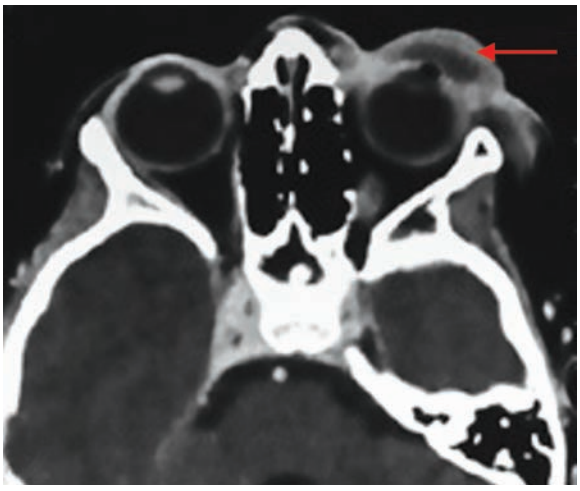

Fig. 9: The CT scan of the patient showing the lesion over the left upper eyelid and extending into the temporal region. The lesion also appears to be compressing the eyeball (red arrow showing the lesion)

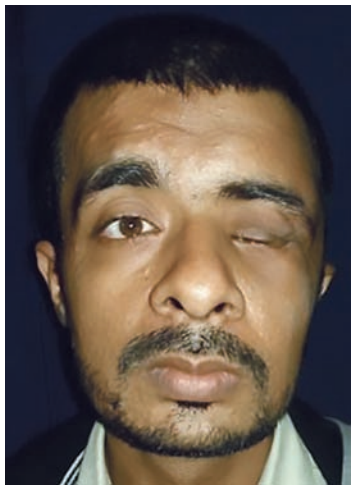

Fig. 10: Three months postoperative picture showing improved contour of the left upper eyelid

region. It also showed that the lesion was compressing the eyeball (Fig. 9).

A hemicoronal incision was taken to expose the mass. It was noted that the mass had no distinct borders and infiltrated the surrounding tissues. Debulking of the lesion was done along the inner aspect of the upper eyelid. We observed that the mass was highly vascular and bothersome hemorrhage was encountered from the edges of the tumor which was managed by electrocoagulation and other local measures.

A mucosal graft was harvested from the palatal mucosa and was used to reconstruct the inner lining of the eyelid.

On the 3rd month follow-up, the patient had an uneventful healing. The contour of the upper lip was significantly improved; however, the patient could not raise his upper eyelid due to neurological deficit. There seemed to be no signs of recurrence in the tumor mass (Fig. 10).

Histopathological report confirmed the diagnosis of plexiform NF (Fig. 11).

DISCUSSION

Neurofibromata are benign complex tumors that arise from peripheral nerve sheaths and constitute one of the main manifestations of NF1. Solitary neurofibromas may occur in any individual, but multiple NF is a characteristic autosomally dominant disorder.[1]

There are two types of NF as reported by Gutmann et al,[3] types I and II. Type I is more common of the two, occurring in almost 90% of all cases.[6] Diagnosis of NF is based on clinical findings alone. Tables 1 and 2 give the details of the diagnostic criteria for NF1 and NF2 as described by Gutmann et al.[3]

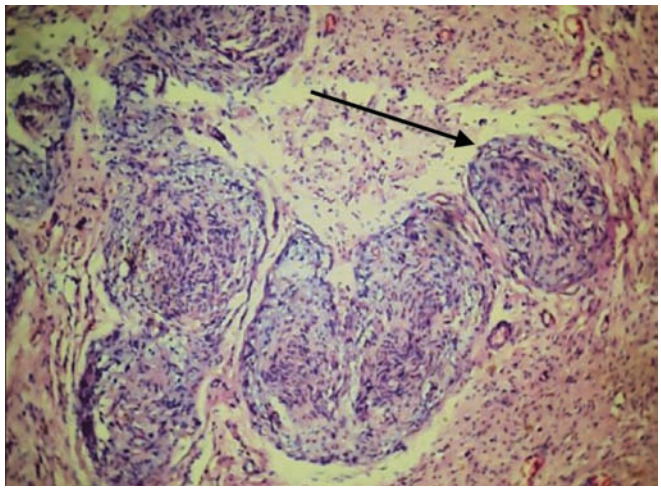

Fig. 11: Photomicrograph showing connective tissue occupied by a lesion of neural origin (black arrow) (hematoxylin and eosin staining)

Table 1: Diagnostic criteria for neurofibromatosis type I

The patient should have two or more of the following:
1. Six or more café-au-lait spots more than 0.5 cm in the greatest diameter in prepubertal individuals and more than 1.5 cm in postpubertal individuals
2. Two or more neurofibromata of any type or one or more plexiform neurofibroma
3. Freckling in the axillary or inguinal regions (Crowe's sign)
4. An optic pathway tumour
5. Two or more Lisch Nodules (iris hamartomas)
6. A distinctive osseous lesion, such as sphenoid wing dysplasia or thinning of the cortex of the long bones (with or without pseudoartrosis)
7. A first-degree relative with NF1 by the above criteria

Gutmann et al[3]

Clinically, neurofibromatous lesions can be divided into two types, localized and plexiform.[4]

Localized neurofibroma arises from a single point and presents as a focal mass with well-defined margins.

Table 2: Diagnostic criteria for NF2

The patient should have the following clinical criteria:
Bilateral vestibular schwannomas (VS) or
Family history of NF2 (first-degree relative) plus
• Unilateral VS < 30 years or
• Any two of the following: meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract

Gutmann et al[3]

However, plexiform variety arises along the nerve sheath and causes significant disfigurement. Although benign, they infiltrate the surrounding tissues, making it impossible for complete excision.[6]

These lesions rarely occur at birth, and have a tendency to increase in size and number at puberty.

Oral manifestations of NF occur in around 72% of the cases.[7]

In both the cases that we have discussed, the patients fulfilled the diagnostic criteria of NF1, with plexiform neurofibromas involving the craniofacial region. There was a presence of café au lait spots, plexiform NF, and axillary freckling in both the patients; however, Lisch nodules, optic pathway tumors, and osseous lesions were not noted. One patient gave a positive history of familial presence of the disease.

Plexiform NF has a devastating effect on the esthetics of the patient. Singhal et al[5] have hypothesized two mechanisms by which these lesions cause disfigurement. First, by infiltration of the tumor into the adjacent tissues, and, secondly, by the gravitational effect and downward pull of the tumor from the adjacent subunits. They have advocated that repositioning of the medial canthal ligament, the nasal cartilage, and the corner of the mouth is often indicated along with debulking of the lesion. Local or regional flap may be also be used for reconstruction following gross excision of the mass.[8]

In our first case, the patient had no functional deficit. In spite of the corner of the mouth being dragged downward, he had no drooling of saliva. Similarly, the distortion in the outer canthus of his eye had no functional deficit. The patient's chief complaint was solely the unesthetic appearance of the lesion.

The previous surgery which he had undergone had led to an iatrogenic injury to the facial nerve. This further complicated his management.

Overzealous excision of the tumor mass in case of craniofacial NF often leads to the damage of vital structures. The neurofibromatous mass often is firmly adherent to important anatomic structures; hence, prudence is required in performing the debulking of the lesion. It is often wise to leave behind some portion of the tumor if it involves any vital structure because the aim of the surgery is to correct the contour and deformity which the lesion has caused and not to get a histologically free margin.[8]

In the second case, the lesion over the eyelid was bothersome to the patient besides the cosmetic impairment. The tumor was insidiously causing compression on the eyeball and also had extended into the temporal region. Although the patient did not complain of the lesion increasing in size, the progression of the lesion into the orbit seemed to be alarming.

Debulking of the lesion was done to remove the mass compressing the globe, and the inner lining of the eyelid was reconstructed using mucosal graft harvested from the palate; however, the patient developed neurological deficit in oculomotor nerve supplying the levator palpebrae superioris. The patient was unable to raise his upper eyelid. Moreover, the scar contracture led to a significant disfigurement of the upper eyelid. The patient also had facial nerve weakness with the temporal branch.

The patient will require additional surgical intervention to further revise the cosmetic outcome.

Use of free flaps[9] and soft tissue expansion[10] for reconstruction after excision also has been reported in literature.

Poole[11] discussed the surgical management of patients with cranio-orbital NF and stated that NF tends to infiltrate into the orbit and seldom into the cranial cavity, further complicating the surgical management of the condition. Complications of cranio-orbital NF include compression on the superior orbital fissure and optic canal, eversion of the eyelid and conjunctival damage, and blindness. Intracranial extension of the tumor can lead to a myriad of complications like increased intracranial pressure, cerebral edema, and extradural hematoma. In such cases, it is advised to perform access osteotomies over the lateral orbital rim to aid in debulking of the lesion. In our second case, the patient had NF involving the upper eyelid; fortunately, it was not involving the underlying skeletal base, and hence, we performed only soft tissue debulking for cosmetic correction.

Surgery remains the mainstay for the management of plexiform NF, and chemotherapeutic agents and radiotherapy are yet to prove their efficacy in managing plexiform neurofibroma, although both these therapeutic methods are efficacious for optic nerve gliomas and malignant peripheral nerve sheath tumors which may arise from an existing neurofibroma.[11]

Recurrence after surgical excision is subjected to much debate in previous literature. However, unanimous agreement exists that the recurrence is due to the existent growth potential of the tumor, with no evidence that excision or surgical manipulation stimulated tumor growth.[12]

Neurofibromatosis is an extremely variable condition. Clinical manifestations range from mild to severe,

varying from patient to patient. Manifestations, such as café au lait spots and cutaneous neurofibromas occur in as much as 95% of the patients, whereas Lisch nodules and optic gliomas occur in less than 5%. Moreover, there is a variability in the age of onset and exacerbations of these manifestations.[12]

Tonsgard[12] has comprehensively described various clinical manifestations of NF1. They have stated that NF1 is a progressive condition. Different complications occur at specific times and some complications worsen over time.

Café au lait spots are hyperpigmented macular round to oval lesions with fairly smooth borders. They appear at birth and tend to increase in size over the first 5 to 7 years. These lesions occur all over the body with no area-specific predilection.

Externally visible plexiform neurofibromas are apparent within the first year of life. The extent and timing of growth and the pattern of plexiform neurofibromas are unpredictable. Some case reports suggest that they stop growing after puberty.[13]

Lisch nodules are relatively rare manifestations. Onset is usually in the teenage years. They are proliferation of melanocytes and fibroblasts that appear as reddish brown spots in the iris.[14]

Optic gliomas are grade I pilocytic astrocytomas found in 15% of patients with NF1 occurring by the age of 7 years. They produce thickening of the optic nerve. Frequently bilateral and often involving the chiasma, they may extend to the optic tracts or inferiorly into the hypothalamus.[14] They may present as decreased color vision or rarely as decreased visual acuity.

One of the most serious complications of NF1 is the transformation of plexiform neurofibroma to malignant peripheral nerve sheath tumor. The overall incidence is 3% and the greatest risk period is between 15 and 40 years. They are invariably associated with pain and are often multicentric. Metastasis to the lung is prompt. Treatment is complete surgical excision with chemotherapy; however, survival beyond a year is unusual.[14]

On the contrary, neurofibromas are painless; hence, if a patient complains of significant pain, there is a possibility that the neurofibroma has undergone malignant transformation into a malignant peripheral nerve sheath tumor.[14]

Other conditions associated with NF1 include attention deficit hyperactive disorder, scoliosis, short stature, pheochromocytomas, and paraspinal plexiform neurofibromas.[14]

The first step in management is genetic counseling. Half of all the cases are familial. If a parent is affected, there is 50% risk that the offspring will be affected. Hence, they need to have some appreciation of the potential problems that NF1 presents with.[12]

The myriad of complications that NF1 presents with provide a challenge throughout the lifetime of the patient.

Tonsgard[12] has suggested the following protocol for the management of patients with NF1.

Age-specific assessment:

Age 0 to 8 years:

- Careful physical examination looking for long bone bowing, limb asymmetry, and scoliosis.
- Blood pressure check; eye examination by pediatric ophthalmologist.
- Assess developmental, language, and learning.

Age 8 to 15 years:

- Careful physical examination looking for scoliosis, limb asymmetry, and neurofibromas.
- Review school performance looking for learning disabilities and attention deficit; discuss NF and the effect of puberty on NF, and ask about socialization and self-esteem.

Age 16 to 21 years:

- Careful physical examination looking for neurofibromas. Obtain imaging studies to evaluate any complaints of pain.
- Review school performance, discuss NF, and ask about socialization, and self-esteem.
- Discuss inheritance of NF1, and risk for pregnancy.
- Discuss the effects of puberty, pregnancy, and birth control pills on NF.

Age >21 years:

- Careful physical examination and blood pressure check.
- Imaging studies to evaluate any complaint of pain.
- Discuss cutaneous neurofibromas, pain, and the risk of cancer.
- Discuss socialization, and career/jobs.

CONCLUSION

The surgical management of patient with craniofacial plexiform NF presents with various complexities. Infiltration into the surrounding tissues, high vascularity of the lesion, secondary deformities, and reconstruction provide an intricate challenge to the surgeon when trying to excise the tumor.

In both of our cases, debulking of the lesion was done in an attempt to improve the cosmetic appearance, and although some residual deformity did exist, it was a definitive improvement to the existing deformity.

REFERENCES

1. von Recklinghausen, F. Uber die multiplen fibrome der haut und ihre beziehung zu den multiplen neuromen. Berlin: Hirschwald; 1882.
2. Venner B. Multiple neurofibromatosis. Aust N Z J Surg 1955 Nov;23(2):110-117.
3. Gutmann DH, Aylsworth A, Carey JC, Korf B, Marks J, Pyeritz RE, Rubenstein A, Viskochil D. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. JAMA 1997 Jul;278(1):51-57.
4. Friedman, JM.; Gutmann, DH.; MacCollin, M.; Riccardi, VM. Neurofibromatosis: phenotype, natural history and pathogenesis. 3rd ed. Baltimore (MD): Johns Hopkins University Press; 1999.
5. Singhal D, Chen YC, Tsai YJ, Yu CC, Chen HC, Chen YR, Chen PK. Craniofacial neurofibromatosis: treatment of the midface deformity. J Craniomaxillofac Surg 2014 Jul;42(5): 595-600.
6. Gorlin, RJ.; Cohen, MM.; Levin, LF. Syndromes of the head and neck. Oxford: Oxford University Press; 1990. pp. 353-416.
7. D'Ambrosio JA, Langlais RP, Young RS. Jaw and skull changes in neurofibromatosis. Oral Surg Oral Med Oral Pathol 1988 Sep;66(3):391-396.
8. Singhal D, Chen YC, Chen YR, Chen PK, Tsai YJ. Soft tissue management of orbitotemporal neurofibromatosis. J Craniofac Surg 2013 Jan;24(1):269-272.
9. Singhal D, Chen YC, Fanzio PM, Lin CH, Chuang DC, Chen YR, Chen PK. Role of free flaps in the management of craniofacial neurofibromatosis: soft tissue coverage and attempted facial reanimation. J Oral Maxillofac Surg 2012 Dec;70(12):2916-2922.
10. Singhal D, Chen YC, Seselgyte R, Chen PK, Chen YR. Craniofacial neurofibromatosis and tissue expansion: long-term results. J Plast Reconstr Aesthet Surg 2012 Jul;65(7): 956-959.
11. Poole MD. Experiences in the surgical treatment of craniorbital neurofibromatosis. Br J Plast Surg 1989 Mar;42(2): 155-162.
12. Tonsgard JH. Clinical manifestations and management of neurofibromatosis type 1. Semin Pediatr Neurol 2006 Mar;13(1):2-7.
13. Cunha KS, Barboza EP, Dias EP, Oliveira FM. Neurofibromatosis type I with periodontal manifestation. A case report and literature review. Br Dent J 2004 Apr;196(8):457-460.
14. Listernick R, Charrow J, Greenwald MJ, Esterly NB. Optic gliomas in children with neurofibromatosis type 1. J Pediatr 1989 May;114(5):788-792.