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Neurofibromatosis Type 1 (NF-1) of the Head and Neck: Dilemmas in management

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ABSTRACT

It has been estimated that approximately 25% of all neurofibromatosis (NF) are found in the head and neck. Patients with NF type 1 of the head and neck suffer from one of the most dramatic cosmetic disabilities, which may lead to psychological troubles and social segregation. There is no known cure for NF and there is a dilemma in the management of these cases. Fifteen such patients were collected and treated at the Plastic Surgery Unit, El-Minia University Hospital, in the period from July 1997, to August 2002. We are presenting our experience in treating these cases, with a trial to establish a protocol for dealing with such cases as regards; collection and sorting them, assessment of the lesion, dealing with the complications and the plan of treatment. Difficulties encountered during surgery were discussed. Most of the patients needed revision surgery and the results were encouraging for the patients and the surgeon.

INTRODUCTION

The neurofibromatosis (NF) is the most prevalent neurological genetic disorder found in the population, affecting 1 in 3000-4000 individuals. It is an autosomal dominant disease without predilection for sex, race or color and penetrance is complete **[1-3]**. It was coined by Fredrick von Ricklinghausen in 1882, when he proposed the first systematic classification of nerve tumors **[4]**. It is a neuroectodermal syndrome that primarily affect the growth of the neural tissues (central and/or peripheral), frequently involving the trigeminal or upper cervical nerves **[3,4]**. Its major features are café-au-lait spots and multiple neurofibromas, which are benign tumors of the nerve sheath and the supporting structures of the peripheral nerves with a kind of hamartomas in the affected tissues **[1-3,5]**.

It is a progressive disease with multisystem disorders that may cause skeletal deformities, kyphoscoliosis, pseudoarthrosis, macrocephaly, hypertelorism or short stature. Headache, pruritus and also endocrinopathies as acromegally, pheochromocytoma and gynaecomastia, are common. It can arise in the retroperitoneal sites or gastrointestinal tract, causing chronic blood loss or constipation. Some oral lesions as papillomatous tumors or macroglossia may be found. It can cause serious problems as learning difficulties, behavioral problems, mental retardation, epilepsy and lack of normal social skills **[3,5,6,7]**.

In 1991, the gene causing NF-1 was found and cloned and in March 1993, the gene causing NF-2 was found on chromosome 22, but variant forms may exist. This great variability impairs our ability to understand the pathogenesis of NF **[2,7,8]**. A consensus development conference was held 1987 by the National Institute of Health, to solve the problem of terminology in NF, they established criteria for diagnosis on clinical basis **[1-3,6]**.

Identification of the gene and the development of animal model is a huge step forward and an effective treatment is now a realistic hope, though there is much more work to be done before a treatment can be found **[1,8]**.

The aim of this study was to present our experience in treating cases of NF-1 of the head and neck. Also, we threw a light on the different methods to deal with these cases, aiming at establishment of a protocol to the Unit of Plastic Surgery at El-Minia University to treat these cases

PATIENTS AND METHODS

Between July 1997 and August 2002, Twenty-one patients having NF-1 (according to the criteria of the National Institute of Health Consensus Development Conference Statement) were treat-

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ed at the Unit of Plastic Surgery, El-Minia University Hospital. They came directly to the clinic or were referred by a general practitioner or other specialists (dermatologist, pediatrician, ophthalmologist, or clinical geneticist). Full clinical data of each patient were recorded, including admission data, complete physical examination and necessary investigations. Other specialists were consulted as required, based on clinical findings.

Fifteen patients out of these twenty-one had NF-1 of the head and neck and were included in this study. The other six patients had NF in areas other than head and neck (three in the extremities, one on abdominal wall, one in the sentry and another one in the retro-peritoneal space). The patients were categorized according to the site of the center of the deformity in relation to the anatomical areas of the head and neck. An informed consent was taken from each patient or their parents. All patients were operated on under hypotensive general anesthesia. The incisions were planned to be hidden as much as we can and in respect to the boundaries of the aesthetic units of the face [9]. A follow-up protocol to re-examine each patient by multi-specialties every three months was planned.

RESULTS

Fifteen patients with neurofibromatosis type-1 of the head and neck were treated in the Unit of Plastic Surgery. Nine were males and six were females (Table 1). Their age ranged from 9 to 40 years with the mean age of 21±9.52 years. Clinical data are summarized in Table (2). The most predominant lesions were in the orbito-tempro-palpebral areas and cheeks (Table 1). Five patients had associated lesions in areas other than the head or neck (Fig. 1). Three patients have undergone previous surgeries in some other centers. Clinical features and complications were not different from other large clinical studies [2,6].

Excessive bleeding was noticeable during excision of the tumors. Most of the patients needed blood transfusion and hence, all patients were operated on under hypotensive general anesthesia. Adequacy of tumor excision was never been satisfactory during the operation due to poor delineation of the tumors, especially in the neck and cheek. Post-operative massive edema was almost a constant manifestation in this series. Delay in wound healing, stretch of the scar and even unstable scars were noticed in most cases (Figs. 2 & 3). Correction of the deformity was very satisfactory in cases with pre-auricular and side of the neck lesions (Figs. 1 & 3), but to a less extent in cases with cheek and orbito-tempro-palpebral lesions.

Follow-up ranged from 1 to 48 months. Three cases were followed up to 3 years with detection of some recurrence. Revision surgery was done to improve the results of recurrence and sagging of the tissues. One patient was lost before surgery. Two other patients were lost in the early post-operative period. The overall results were satisfactory (85.72%). Three patients with fair results (21.43%), seven patients with good results as regard function and appearance (50.00%), one patient with very good results (7.14%) and another patient (7.14%) with excellent results (Table 3).

Table (1): Distribution of lesions.

Site of lesion	Six distribution		No. of patients
	M	F	
Orbito-palpebral	1	–	1
Orbito-temporal	2	1	3
Temporal	2	–	2
Pre-auricular	–	1	1
Cheek	1	1	2
Lip	1	–	1
Ear, lip and cheek	1	–	1
Side of neck	–	1	1
Side of neck and nape	–	1	1
Nape and scalp	1	–	1
Multiple of neck and chest	–	1	1
Total	9	6	15

Table (2): Patients' profile.

Patient (No)	Age (yrs)	Sex	Site & clinical features	Follow-up (months)	Outcome
1	34	F	Orbito-temporal, with nose, cheek & ear	48	Good
2	11	M	Cheek	2	Fair
3	28	F	Side of neck and nape	36	Good
4	40	M	Ear	4	Good
5	19	M	Temporal	40	Excellent
6	30	M	Orbito-temporal	1	Good
7	14	M	Lip and palpebral	–	Preliminary
8	20	F	Side of the neck	15	Good
9	30	F	Multiple in neck & chest Pre-auricular	10	Good
10	12	F	Cheek	13	Very good
11	9	F	Orbito-palpebral	1	Fair
12	14	M	Ear, lip and cheek	2	Fair
13	18	M	Nape and scalp	–	Lost
14	12	M	Temporal	–	Preliminary
15	24	M		8	Good

Table (3): Aesthetic results.

Preliminary	2	14.28%
Fair	3	21.43%
Good	7	50.00%
Very good	1	7.14%
Excellent	1	7.14%

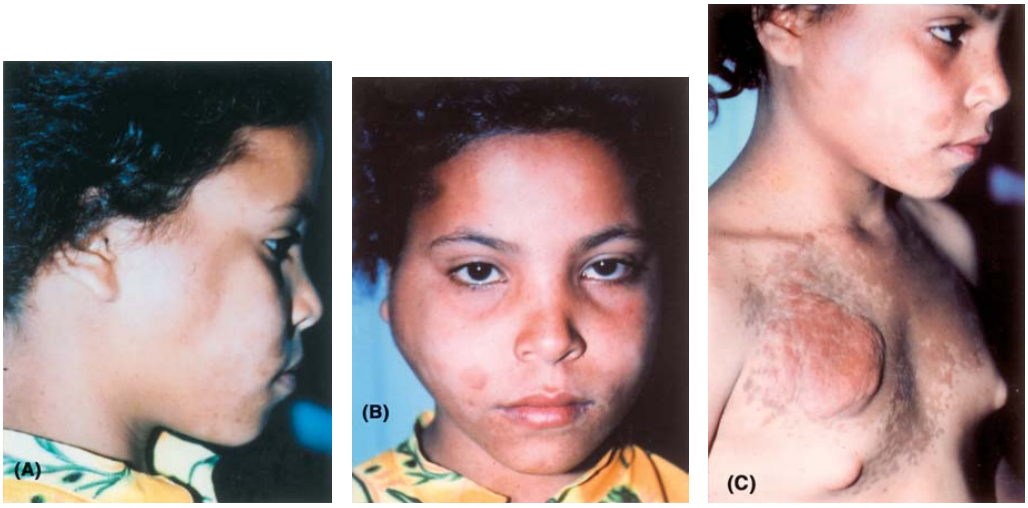

Fig. (1): Case # 10. Pre-auricular lesion with café-au-lait patches on face.

(A): Pre-operative lateral view. (B): Pre-operative front view.
(C): Eight months post-operative with good results. She is ready for removal of another lesion in the left infraclavicular area.

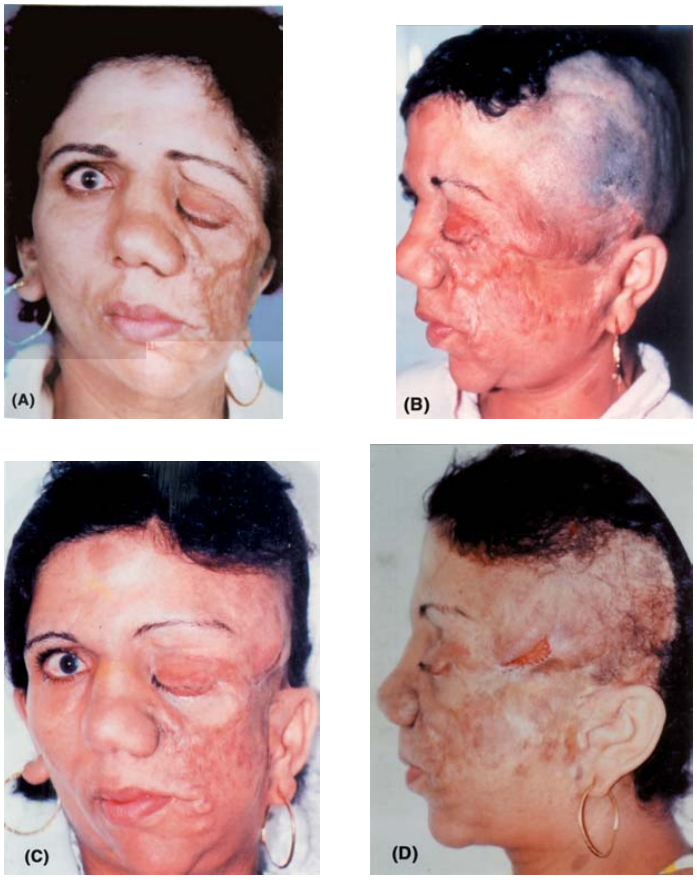

Fig. (2): Case # 1. Severe orbito-temporal lesion with affection of the side of nose, cheek and left ear.

(A): Pre-operative front view.
(B): Pre-operative side view.
(C): Post-operative front view.
(D): Post-operative lateral view. One year post-operative with acceptable results. An excision of as much as possible of the tumor with hemifacial suspension (eyebrow, upper lid and ear) was done.

Fig. (3): Case # 3. Side of the neck and nape involvement with a huge lesion. The covering skin is sagging down and thrown into folds like candle wax.

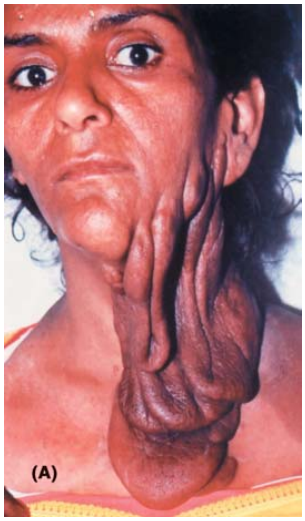

Fig. (3-A): Pre-operative front view.

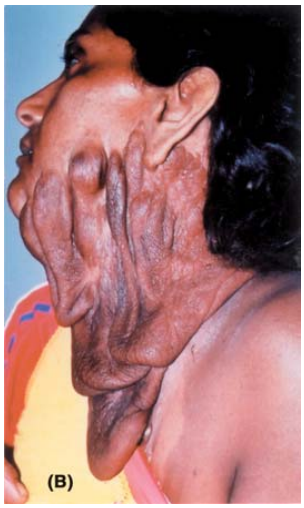

Fig. (3-B): Pre-operative lateral view.

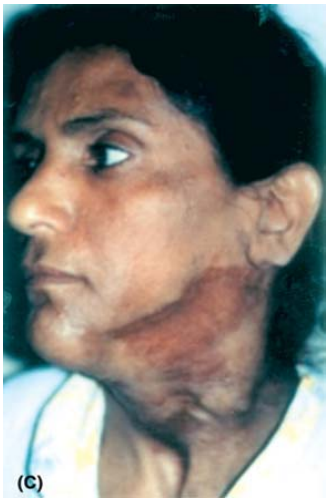

Fig. (3-C): Nine month post-operative view.

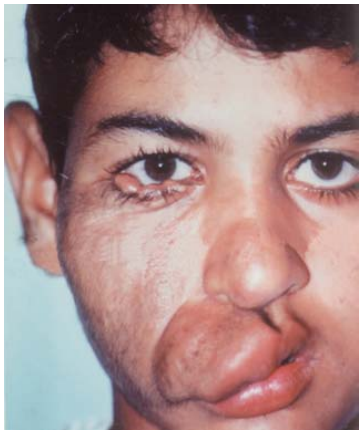

Fig. (4): Case # 7. Isolated lesion of the lip and lower lid in a boy 14 years old.

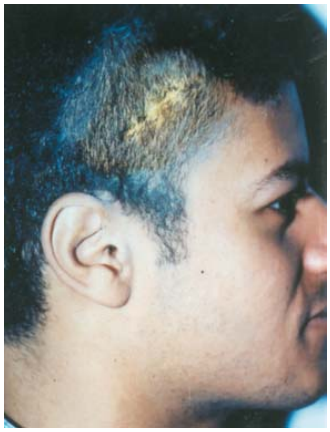

Fig. (5): Case # 5. A case of isolated temporal lesion, which was excised twice.

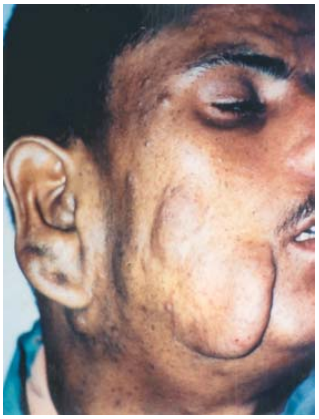

Fig. (6): Case # 13. Multiple cutaneous lesions of the ear, pre-auricular and cheek.

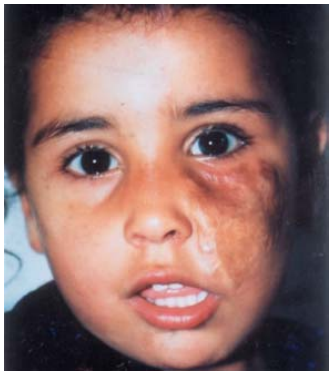

Fig. (7): Case # 11. Isolated cheek lesion in a child 9 years old.

DISCUSSION

Patients with neurofibromatosis type 1 (NF-1) of the head and neck suffer from one of the most dramatic cosmetic disabilities, especially, the numerous cutaneous neurofibromas with skin drooping or laxity, which may lead to psychological troubles, social segregation and also educational deficiency [3,7]. It has been estimated that approximately 25% of all NF are found in the head and neck with a predilection to arise as a benign deep-seated tumors and thus may interfere with functions. The cheek is a common site whether partial or total [7]. Affection of the lid eventually leads to ptosis and loss of vision in early life. Despite the presence of serious intractable complications, the priority of the patients is for cosmetic correction of the disease; therefore, the plastic surgeon and the dermatologist are frequently the first-line practitioners [3,5].

There is no known cure or even arresting of neurofibromatosis, but with identification of the causative genes for NF-1 and NF-2, research in recent years has proved hopeful for an eventual cure. Tumors are believed to arise by the loss of function of the NF-1 protein, suggesting that NF-1 gene behaves as a tumor suppressor gene. This suggested an approach to treatment using ras protein inhibitors, which are under clinical trials [1,2].

As being a progressive disease with extreme variability and multisystem disorders, there is a dilemma in the management of these cases as regards, collection of cases, sorting them, assessment of the lesion and the plan of treatment [3,7]. These patients must be monitored by a number of different specialists with one physician acting as the coordinator. The most ideal situation is a specialized multidisciplinary outpatient clinic (similar to the Cleft Lip and Palate Clinic), which deals with those patients from early ages. It provides diagnostic follow up and genetic counseling services for those patients and their families [2,6]. Diagnosis of NF did not seem to be a reason to refrain from having children, so there must be a balance between providing adequate information and causing unnecessary alarm [10,11].

Patients should have periodic screening blood work for the possibility of developing several types of leukemia, routine follow-up of blood pressure, full ophthalmic and auditory examination and skeletal survey. Annual clinical follow-up for life should be done which seems to be more beneficial than systematic investigations in those patients [2,6].

Treatment of these cases is controversial. Surgical treatment is nearly always required for functional or cosmetic reasons, or to exclude the possibility of malignant transformation (an increase in size or pain suggests possible malignant changes) and also if there is bone malformations [3,5,7,12]. However, non-progressive symptoms have to be dealt with on an individual basis. The treatment becomes more complex with elephantiasis neurofibromatosa [2,3,5].

Some authors adopt an aggressive and hopeful attitude with radical resection and reconstruction by free-tissue transfer and sometimes prosthesis especially in early ages, to prevent deformity, functional problems and subsequent recurrence [4,13]. Excision is usually done in stages in large tumors, with coverage of the defect by local or distant flaps. This is hardly feasible, because of its anatomical situation and the severe hemorrhagic problems associated with its excision, hence, others recommended conservative treatment [3,14]. We believe that each case has to be individualized concentrating on ameliorating the cosmetic disability without jeopardizing facial function and appearance. The question of the timing of operative correction remains unanswered [13], although some recommended that to be done at early ages [4].

Carbon dioxide (CO_2) laser vaporization seems to be very helpful for those small and discrete lesions. It is a simple technique under general anesthesia allowing destruction of hundreds of lesions with minimal morbidity. It also improves some symptoms as pruritus and pain [15]. We had only one case (# 9) that was treated by CO_2 laser in the dermatology department with good results. The role of radiotherapy and chemotherapy as adjuvant therapies remains unclear [7].

Pre-operative investigations should assess the extent of the tumor and the risk of abnormal bleeding. Pre-operative angiography, MR angiography and highly selective embolisation are recommended when available; especially with large facial tumors 24-48 hours prior to surgery [47]. We used Doppler to ligate the occipital

vessels before excision of a tumor in the nape and scalp (case # 14). Contrast-enhanced CT, three-dimensional CT, and contrast-enhanced MRI scanning to identify the osseous and soft tissue planes surrounding the lesion are mentioned in literature to be useful tools for operative planning [3,4,13].

There is a risk between 2-15% of malignant transformation, which can occur in deeper lesions at any age [7]. The majority are soft tissue sarcomas, but the most important is the development of malignant peripheral nerve sheath tumors (MPNST) which affect NF patient more than the general population and become centrally situated, large and of high histologic grade [12,16]. Also, benign and malignant NF may occur simultaneously [7,12]. It is documented that surgery does not accelerate growth of the already slowly and irregularly growing tumor, neither it causes its degeneration or malignant transformation [3,17]. Pathological specimens from lesions after second or third operative intervention in this series did not show any signs of malignant transformation.

Many operative technical problems are recorded; the most difficult is the intractable hemorrhage. These are non-encapsulated tumors that mingle with surrounding dermal and other tissues, with inconspicuous thin walled abnormal feeding vessels, especially in the face; thus, moderate to severe bleeding is a recognized feature at operation. We used hypotensive anesthesia for all patients and even hypothermia [7,18].

Skin overlying plexiform NF is thick and extremely friable with no tensile strength. The dermis is involved in fibromyxomatous change with no definite line of demarcation [5]. In this study, there were problems in wound healing in the form of widened or unstable scars, or delayed healing (cases # 1,3,4,6 and 15) (Figs. 2,3 & 5). The superficial muscles are involved with skeletal deformities leading to loss of functions, which are almost incurable (case # 12) [14]. Affection of the lips causes macrocheilia and consequent macrostomia (case # 7, Fig. 4).

The maxilla and mandible, if affected, are hugely enlarged with osteoma-like projections. There is also asymmetry of the face with bad prognathism and malalignment of the teeth (case # 1, Fig. 2) [5,14]. Bone graft resorption after NF correction is a problem and the use of alloplastic material to establish a stable reconstruction was recommended [4,13]. Wide resection of tumors of the middle third of the face often results in complex three-dimensional defects and facial paralysis either due to removal of the facial nerve within the tumoral tissue or to extensive resection of the facial muscles might occur (case # 6). These cases might need functional muscle transplantation (we did not do any in this series) [4,19]. In the orbito-temporal lesion; the temporal lobe might prolaps into the orbit (cases # 1 and 6) [13]. Post-operative edema tends to be severe and long-lasting [4,7,13]. We found this to be almost a constant feature in this series. Subsequent operations are often necessary to keep pace with the growth of the tumors and patients must be prepared psychologically for that. We had nine cases that needed revision surgery once or twice. We had a case of temporal NF which presented for the first time in the middle age. The patient came early and the lesion was removed twice. He was followed-up for three years with excellent results (case # 5, Fig. 5). Another case with pre-auricular lesion that came early (12 years old) and was removed with very good results. Despite an increasing level of experience with this disease, patient undergoes multiple procedures with sub-optimal functional and aesthetic outcomes. Most authors have been discouraged by their results [13,17,20]. We found the same as others, that most of those patients were so gentle and cooperative but psychological support is mandatory for them [3,17].

Conclusion:

Neurofibromatosis is a progressive disease with extreme variability and multisystem disorders. There is a dilemma in the management of these cases which must be followed in a specialized multidisciplinary outpatient clinic. However, surgical resection, incomplete and imperfect as it may be, is often extremely useful in improving the appearance, comfort and quality of life of these unfortunate patients. Prolonged follow-up with routine checks every 6-12 months is advisable.

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