

# Craniofacial Neurofibromatosis Type 1: Clinical Features, Challenges Of Management, And A Report Of 2 Nigerian Patients

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## Abstract

**Objective:** The objective of this article is to highlight the various soft tissue and skeletal manifestations of craniofacial neurofibromatosis and the challenges involved in the surgical management of patients with complex cases. **Methodology:** An extensive literature review was conducted to highlight the clinical features of craniofacial neurofibromatosis. The notable challenges of management from the experience of the authors were highlighted and two cases of Nigerian patients are presented to demonstrate the challenges of management as it affects patients in the developing nations of Africa who often require referral abroad. **Result:** Patients with craniofacial neurofibromatosis present with varying soft tissue and skeletal features which often necessitate complex, expensive and highly technical surgical management which are often not locally available in some developing countries. In this article, the skeletal features are presented under 3 subheadings; cranial features, orbital features and orofacial features. The 2 cases presented illustrate the clinical features and the technicalities of management with emphasis on the need for a committed craniofacial team. **Conclusion:** In order to reduce the physical and financial burden in the management of complex craniofacial conditions, the need to improve facilities and expertise and to form effective craniofacial teams in the third world countries is imperative.

## INTRODUCTION

Neurofibromatosis (NF) is a generalized form of the benign tumor of the peripheral nerves derived from fibrous element of the nerve sheath. It is neuroectodermal in origin with varying involvement of the skin, subcutaneous tissue, and bone. It is an autosomal dominant inherited disorder with approximately 50% of patients having a positive family history of the disease<sup>2</sup>. There are two types; neurofibromatosis type 1 (NF-1), known as Von Recklinghausen disease which results from mutation on the long arm of Chromosome 17. It is more common, occurring with a frequency of 1 in 3000 live birth, which accounts for 96% to 97% of all cases of NF. The type 2 (NF-2) is associated with a mutation on the long arm of chromosome 22 and accounts for approximately 3% of all cases<sup>3,4</sup>. Though the disease has been found across all ethnic and racial boundaries, the prevalence among Blacks and Orientals is considerable. In a multicenter study, higher incidence rates of 12.8% and 57.4% respectively were reported among African and Asian patients<sup>4</sup>.

The incidence of head and neck involvement with neurofibromatosis ranges from 1% to 22% in the published literature<sup>5,6,7</sup>. NF-1 manifests in the craniofacial complex as varying involvement of the soft tissue and bone of the orbitocranial and jaw regions usually resulting in hemifacial deformities. Bilateral involvements have also been reported; Bloem and van der Meulen reported a case of bilateral orbito-facial involvement affecting the entire face<sup>8</sup>. Due to the extensive and destructive manifestation of craniofacial neurofibromatosis and the consequent functional and cosmetic disabilities imposed by the disease, sophisticated radio-diagnostic facilities are required for effective treatment planning. The surgical management of the disease can be highly technical because of the involvement of vital structures of the craniofacial complex. We have observed that many patients from some African and Asian countries are being referred abroad for treatment; the reasons often cited are those of inadequacy of sophisticated radio-diagnostic facilities and lack of surgical expertise for the treatment of extensive lesions.

In this article, the clinical features and challenges of

management of craniofacial neurofibromatosis are highlighted. We also report two cases of Nigerian patients with extensive lesions who were treated abroad.

## **CLINICAL FEATURES OF CRANIOFACIAL NEUROFIBROMATOSIS**

Von Recklinghausen Neurofibromatosis or NF-1 is the variant of the disease mostly associated with extensive craniofacial manifestation<sup>6</sup>. It often presents with a variety of clinical features manifested in the soft tissue and skeletal structures of the region.

### **SOFT TISSUE MANIFESTATION**

The soft tissue manifestation can involve the scalp, periorbital and intraorbital tissues, and the skin and subcutaneous tissues over the upper and lower jaws. The usual cutaneous involvement is the presence of multiple café-au-lait spots. There could be multiple nodular outgrowths over the scalp and face or an excessive and pendulous stretch of tissue hanging from the face, which on palpation, often contains a knobbly interwoven collection of fibrous, neural and vascular elements constituting plexiform neurofibromatosis. This is characteristically described as a “bag of worm”<sup>9,10</sup>. There is often a significant hemifacial hypertrophy with ipsilateral mechanical ptosis of the upper eyelid and drooping of the angle of the mouth. Sometimes the facial nerve is involved with varying degree functional deterioration<sup>11</sup>. Involvement of branches of the trigeminal nerve may be associated with pain and/or paraesthesia<sup>12</sup>. Intraoral lesions<sup>11,13,14</sup> present as discrete non-ulcerated nodules covered by normal oral mucosa usually occurring on the cheek, palate, alveolar ridge, vestibule and tongue. Some times there is simply a diffuse involvement of the oral tissues. The involvement of the tongue may result in macroglossia, and occasionally, part of the dentition may be submerged.

### **SKELETAL MANIFESTATION**

The skeletal manifestation is varied and can be in the form of cortical erosions from the contiguous tumor mass, dysplastic bony changes, hyperostosis or subperiosteal cysts<sup>14</sup>. The resultant deformities in the cranial, orbital and facial bone structures have been extensively described in the literature.

### **CRANIAL FEATURES**

Radiologically, there are mesodermal dysplastic changes in the sphenoid bone which include absence or hypoplasia of

the greater wing and hypoplasia and medial deviation of the lesser wing, deformity of the sella turcica and body of the sphenoid<sup>15,16,17</sup>. CT evidence of cavernous sinus enlargement has been described in up to 71% of patients<sup>16</sup>. Usually there is associated antero-posterior enlargement of the middle cranial fossa, sometimes with intracranial tumors; resulting in herniation of the temporal lobe into the orbital cavity through the bony defect created by the absence of the greater wing of the sphenoid bone<sup>21,516</sup>. When some cranial nerves are involved, usually there is enlargement of the respective exit foramina<sup>11,13</sup>. Multiple congenital calvarial defects involving the parietal, temporal and occipital bones and poor pneumatisation of the ethmoidal, sphenoidal and mastoid sinuses and erosion of the internal acoustic meatus are well documented<sup>1,819</sup>. Traditionally, most of the cranial deformities were attributed to developmental dysplasia irrespective of contiguous presence of tumor tissue<sup>20,21</sup> but recent evidence has demonstrated a close association between contiguous tumor proliferation and the dysplastic changes, hence the concept of secondary dysplasia has been suggested<sup>15</sup>.

### **ORBITAL FEATURES**

The orbital changes in neurofibromatosis type 1 have largely been attributed to the consequence of the sphenoidal dysplasia, orbital invasion and proliferation of the plexiform neurofibromatosis (PNF)<sup>15,16</sup>.

The erosion of the greater wing of the sphenoid and consequent encroachment of the content of the temporal fossa, as well as invasion of the extraocular muscles and the extraconal space with PNF results in the reduction of orbital volume causing proptosis of the globe. Sometimes there is downward displacement of the globe and expansion of the orbital rim due to PNF infiltration of the roof of the orbit. The combination of anterior displacement of the globe due to encroachment by the middle cranial fossa and downward displacement due to a mass superior to the globe results in enlargement of the orbital rim to produce the classic egg-shaped orbital deformity<sup>15</sup>. There may be complete erosion and replacement of the lateral orbital wall with tumor tissue further diminishing the orbital volume. When there is maldevelopment or narrowing of the anterior chamber angle due to direct infiltration of the globe, buphthalmos results, and this can lead to blindness or globe enucleation<sup>1,5,22</sup>. Blindness may also result from tumor infiltration of the retina with corkscrew malformation of the retinal vessels leading ultimately to retinal ischemia<sup>23</sup>. Rarely, enophthalmos and hypoglobus may occur secondary to the

widening of the inferior orbital fissure and weakening of the suspensory complex of the globe with malposition or disinsertion of the canthal ligaments<sup>924</sup>. Other ocular abnormalities include the presence of iris hamartomas (Lisch nodules) and heterotopic calcifications within the orbit<sup>1819</sup>.

## **OROFACIAL FEATURES**

The radiographic manifestations of maxillary and mandibular lesions often include radiolucencies with well-defined, poorly-defined or irregular diffuse borders<sup>26</sup>. The widening of the orbital rim often leads to hypoplasia and poor pneumatization of the ipsilateral maxilla<sup>15</sup>. There may be hypoplasia of the mandibular body and ramus, abnormal coronoid process, and zygomatic arch. Mandibular cysts have been reported and more rarely there is mandibular overgrowth with a convex outer contour and increase in the vertical height<sup>192527</sup>. When the inferior alveolar nerve is involved, there is widening of the mandibular foramen or canal<sup>113</sup>. Reported dental abnormalities include numerical aberrations, retention of molars and aplasia of the mandibular second molars in association with PNF<sup>28</sup>.

## **CHALLENGES OF MANAGEMENT**

The challenges confronted in the management of craniofacial neurofibromatosis are multifarious. It includes; 1. Diagnostic challenges 2. Challenges involved in the coalition of an effective multidisciplinary team 3. Technically demanding surgical expertise 4. A long-term commitment to prolong follow-up, and management of recurrences and complications 5. Physical and psychological rehabilitation of patients

Radiological examination is most essential for the evaluation of the skeletal and soft tissue involvements which is often extensive with attendant cosmetic and functional deformities affecting vital organs. The challenges, especially in the underdeveloped parts of the world is the availability and affordability of sophisticated, modern investigational facilities and techniques e.g. computerized tomography, magnetic resonance imaging, and 3-dimensional CT imaging which are required for a comprehensive evaluation of the disease in order to effectively plan treatment and for serial monitoring of treatment progress.

The importance of a multidisciplinary team approach is underscored by the need to ensure a thorough pre-op evaluation of patients, which often involves radiologists, neurosurgeons, ophthalmologists, orthodontists, and cranio-maxillofacial surgeons. An effective synchronization of the

activities of these specialists is often difficult to achieve in places where there is no established craniofacial team. Once properly evaluated, the decision is taken whether or not to treat. Since the disease is essentially benign, the decision to treat is usually predicated on the presence of unacceptable cosmetic deformities, disturbing symptoms or significant functional aberrations. These are often very difficult to correct and require surgical expertise in craniofacial osteotomies, neurosurgical manipulations and orbital and oculoplastic surgery much of which procedures require specialized instrumentation and training, hence, should not be undertaken lightly without adequate experience.

Above all, it is important for the clinicians to realize that a venture into the management of patients with craniofacial neurofibromatosis requires a long term commitment to provide follow-up, repeated operations if necessary, management of complications and long term physical and psychological rehabilitations.

## **CASE 1**

Patient 1 is a 21-year-old Nigerian male who was referred to the Craniofacial Institute Southfield, Michigan, USA; he was sponsored by a charity organization. The patient presented with features of neurofibromatosis involving the left hemiface, the left orbit, frontal and cheek areas with associated loss of facial nerve function in the buccal and frontal branches. There were multiple facial neurofibromatoses with great excess of ptotic facial and cheek skin resulting in a pendulous overhang over the face and with significant orbital distortion. There was buphthalmos with attendant loss of vision in the left eye. MRI imaging revealed a large enhancing neurofibroma on the left, which extended into the subtemporal soft tissues. There was bone erosion and dysplasia of anterior and middle cranial fossa including the temporal bone and portions of the sphenoid as well as the sella. The underlying left brain was somewhat deformed and atrophic and there is a large arachnoid cyst present. An ovoid mass thought to represent hematoma was seen centrally within the lesion. Inferiorly, the lesion interdigitated with muscles of mastication and extended as far as the inferior margin of the mandible with extension into the pharyngeal space. Additional information provided by the CT scan was the increased height (51mm) of the anterior margin of the left orbit due to tumor infiltration. The width was deceptively normal (42,5mm) due to anterior displacement of the globe. The right orbital margin was normal in both dimension measuring 43.4mm in width and

38.4mm in height. Bilateral carotid angiography was performed for the vascular mapping of the lesion, this revealed a large hypovascular mass along the left aspect of the neck and skull resulting in displacement and distortion of the arterial system without evidence of tumor blush.

In the first surgery, a coronal flap was raised with detachment of the temporalis muscles craniotomies and orbital osteotomies were performed to gain access for tumor resection and to correct the deformity of the orbital margins. The orbital content were removed and the facial soft tissue tumor was comprehensively excised. Seven months later, a second surgery was performed for removal of the plates and screws and recontouring of the orbit. Postoperatively, the second surgery was complicated with a frontotemporal hematoma which became infected, patient also had fever and diarrhea. A possible co-existence of a gastrointestinal neurofibromatosis was ruled out. The frontotemporal abscess was drained, fever and diarrhea were controlled and the general condition of patient improved significantly. The patient subsequently received eye prosthesis to the left orbit and the general outcome was very satisfactory.

## **CASE 2**

Patient 2 is a 19-year-old Nigerian male who presented with features of right-sided cranio-orbito-facial neurofibromatosis of soft tissue and bone and was also referred on the sponsorship of a charity organization. There was significant deformation of the skull, orbit, and nasal architecture with skeletal enlargement of the right hemiface. There was buphthalmos of the right eye. CT and MRI imaging revealed enlargement of the right side of the face including the orbit, mandible, maxilla, alveolus and zygoma. There were bony projections into the cranium along the sagittal and mildly in the parietal suture areas. The deformed and thickened mandible and maxilla were also demonstrated on panoramic radiograph.

The surgical treatment was in two stages; at first, large frontal craniotomy was accomplished via a coronal approach. The nasal and orbital bones were osteotomized and placed in the correct position, a cranial bone graft was harvested from the parietal bone and grafted to the bridge of the nose. The floor and medial wall of the right orbit was recontoured to correct the exophthalmos. Excess skin of the scalp, neck and eyelid was removed and the right oral commissure was reconstituted. There was extensive intraoperative bleeding which was treated intraoperatively by a combination of hypotensive anaesthesia and transfusion

of packed cells, platelets, fresh frozen plasma and crystalloids. Postoperatively, the patient went into respiratory failure with pulmonary crepitations. He had positive pressure ventilatory support, continuous monitoring of arterial blood gasses and diuretics. Patient recovered fully afterward with satisfactory healing and a good postoperative outcome.

A second surgery was performed about a year later for cosmetic improvement of residual exophthalmos and facial appearance. The previous coronal incision was opened, further excision of residual neurofibromatous tissue was done, followed by orbital recontouring, medial and lateral canthopexy and face-lift.

## **DISCUSSION**

The two patients presented were referred from Nigeria based on the complexity of their craniofacial neurofibromatosis. These patients presented with extensive lesions associated with distortion of multiple cranial and facial tissues requiring adequate and judicious diagnosis and treatment planning.

Characteristic dysplastic features of craniofacial neurofibromatosis were found on CT and MRI imaging. Patient 1 had sphenoid bone defects associated with orbital deformities resulting in exophthalmos and buphthalmos which had resulted in blindness of the left eye. Patient 2 had a similar manifestation but the visual acuity of the buphthalmic eye was within acceptable limits. Calvarial defects and deformities of the jawbones are well depicted in patient 2. The skeletal and cosmetic deformity was more extensive in patient 2 in whom nasal bone grafting and face-lift had to be performed to improve final aesthetic outlook.

The disseminated nature of the tumor involving orbital, intra- and extracranial tissue as well as extensive bony distortion of the skull and jaws necessitated a team approach which was facilitated by the well-established existence of a craniofacial team at the institute headed by the senior author (ITJ). This enabled adequate radiological, ophthalmological, neurosurgical and cranio-maxillofacial assessments and comprehensive treatment planning. The surgical management which was accomplished by a neurosurgeon and the senior author (ITJ) – a craniofacial surgeon, involved a combination of craniotomies and orbital osteotomies to gain access for intraorbital tumor resection and for correction of orbital volume and the widened orbital margin. The reconstruction of the nasal skeleton was effected with a

cranial bone graft in patient 2.

Profuse intraoperative hemorrhage has been associated with operations on neurofibromatosis; this is attributed to the interwoven vascular elements within the neurofibromatous tissue<sup>29</sup>. This was the experience with patient 2 who required large volume of crystalloids and blood products to maintain hemodynamic stability intraoperatively. The patient developed respiratory failure post operatively with evidence of fluid overload. He recovered completely following adequate positive ventilatory support and diuresis with continuous monitoring of arterial blood gases until stability was achieved.

More often than not, the treatment of neurofibromatosis requires repeated surgery for several reasons. One is that it is usually impossible to excise all the tumor tissue; another is the tendency for recurrence and malignant transformation. In addition, further surgeries are often required to improve aesthetics. In these two patients, further operations were performed to recontour the orbit for orbital prosthesis and to improve the aesthetic value of the patients, which indeed does enhance psychological rehabilitation.

In conclusion, we have highlighted some essential clinical and radiological features of craniofacial neurofibromatosis based on literature reports; we have also identified the various challenges involved in the management of the disease. Finally, we have presented the cases of two patients whose management significantly illustrates the challenges often encountered in the management of the disease. In order to reduce the physical and financial burden in the management of complex craniofacial conditions like these, the need to improve facilities and expertise and to form effective craniofacial teams in the third world countries is imperative. This will facilitate the treatment of patients in their home countries.

## **CORRESPONDENCE TO**

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