Clinical and Therapeutic Features of Neurofibromatosis in Ghana

Emmanuel J. K. Adu and Adofo Koranteng

Department of Surgery, School of Medical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
Address correspondence to Emmanuel J. K. Adu, aduemmanuel@hotmail.com

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Abstract
Introduction. Neurofibromatosis (NF) is a generalized form of benign tumors of the peripheral nerves involving the skin, subcutaneous tissue, and bone. It comprises neurofibromatosis type 1 (NF-1), neurofibromatosis type 2 (NF-2), and schwannomatosis.

Objective. To document the clinical and epidemiological features of patients with NF presenting at Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, from January 2009 to December 2013, and the outcome of management.

Patients and methods. This is a retrospective study. Data on all patients managed within the study period were retrieved from the records of the surgical outpatient department (SOPD) of KATH and theater records and analyzed.

Results. Fifteen patients underwent surgery for function impairing and disfiguring lesions, comprising five males and 10 females. Their ages ranged from three years to 55 years, with a mean age of 27.3 years. Seventeen lesions were found on the 15 patients that required surgery: 10 on the head and neck, three on the trunk, two on the upper limbs, and two on the lower limbs. Three of the lesions were neurofibromas; 14 were plexiform lesions. Fourteen patients had NF-1; only one patient had NF-2; there were no cases of schwannomatosis. Debulking was done for 12 patients; this was combined with suspension in two cases and enucleation in one case. Excision was done for five patients. Eight of the lesions recurved and the patients underwent a second debulking procedure.

Conclusion. NF causes disfigurement and functional deficits in affected patients. Surgery can achieve symptomatic relief. Early presentation is recommended for optimal results.

Keywords café au lait; neurofibromatosis; schwannomas; gliomas; surgery

1. Introduction
Neurofibromatosis (NF) is a generalized form of benign tumors of the peripheral nerves. It is derived from the fibrous element of the nerve sheath [1]. Being neuroectodermal in origin, NF may involve the skin, subcutaneous tissue, and bone [2]. It is an autosomal dominant disorder; 50% of affected patients have a positive family history [3]. The disease comprises neurofibromatosis type 1 (NF-1), neurofibromatosis type 2 (NF-2), and schwannomatosis [4].

The clinical diagnosis of NF-1 (von Recklinghausen’s disease) is based on the presence of at least two of the following: six or more café au lait spots (Figure 1), which should be more than 5 mm in greatest dimension in prepubertal patients, and more than 15 mm in postpubertal individuals; two or more neurofibromas or one plexiform neurofibroma; axillary or inguinal freckling; optic pathway glioma; two or more Lisch nodules in the iris; distinctive osseous lesion such as sphenoid wing dysplasia, thinning of long bones with or without pseudoarthrosis; a first-degree relative (parent, sibling or offspring) with NF-1 by the above criteria [5,6].

The diagnostic criteria for NF-2 are bilateral eighth nerve masses; first-degree relative with NF-2 and either unilateral eighth nerve masses or two or more of the following: neurofibroma, meningoia, glioma, schwannoma or juvenile posterior subcapsular lenticular opacity [6,7].

Patients with schwannomatosis develop multiple schwannomas affecting peripheral nerves and spinal nerve roots without vestibular schwannomas or NF-2-related tumors. It occurs in families and the predominant symptom is pain. It may be segmental with the schwannomas being restricted to one segment of the body [8].

The diagnosis of NF is clinical based on the typical diagnostic criteria above. Surgical resection or debulking is the major therapeutic option for lesions that are impairing...
Table 1: Clinical details of 15 patients with NF who were operated upon at KATH from 2009 to 2013.

<table>
<thead>
<tr>
<th>Number</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Site of lesion</th>
<th>Type of lesion</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>3</td>
<td>F</td>
<td>Left temple</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>2.</td>
<td>9</td>
<td>F</td>
<td>Right lower limb</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>3.</td>
<td>9</td>
<td>F</td>
<td>Left temporal scalp</td>
<td>NF-1 (plexiform, displacing left ear)</td>
<td>Debulking and suspension</td>
</tr>
<tr>
<td>4.</td>
<td>15</td>
<td>M</td>
<td>Face</td>
<td>NF-1 (plexiform)</td>
<td>Excision</td>
</tr>
<tr>
<td>5.</td>
<td>19</td>
<td>M</td>
<td>Left temporo-occipital scalp</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>6.</td>
<td>20</td>
<td>F</td>
<td>Parietal scalp</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>7.</td>
<td>22</td>
<td>M</td>
<td>Left forearm and hand</td>
<td>Neurofibromas</td>
<td>Excision biopsy</td>
</tr>
<tr>
<td>8.</td>
<td>26</td>
<td>F</td>
<td>Parietal scalp</td>
<td>NF-1 (plexiform)</td>
<td>Excision</td>
</tr>
<tr>
<td>9.</td>
<td>30</td>
<td>F</td>
<td>Right thigh and leg</td>
<td>NF-1 (plexiform on thigh; neurofibroma on calf)</td>
<td>Debulking</td>
</tr>
<tr>
<td>10.</td>
<td>30</td>
<td>F</td>
<td>Right hand</td>
<td>NF-1 (plexiform)</td>
<td>Excision</td>
</tr>
<tr>
<td>11.</td>
<td>38</td>
<td>M</td>
<td>Trunk (lateral and posterior)</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>12.</td>
<td>40</td>
<td>M</td>
<td>Right cranio-orbital half of face</td>
<td>NF-2 (plexiform lesion with propotic blind eye)</td>
<td>Debulking with enucleation</td>
</tr>
<tr>
<td>13.</td>
<td>41</td>
<td>F</td>
<td>Parietal scalp</td>
<td>NF-1 (plexiform)</td>
<td>Debulking</td>
</tr>
<tr>
<td>14.</td>
<td>53</td>
<td>F</td>
<td>Face, trunk, vulva</td>
<td>NF-1 (generalized neurofibromas; 2 plexiform lesions on vulva)</td>
<td>Excision of plexiform lesions</td>
</tr>
<tr>
<td>15.</td>
<td>55</td>
<td>F</td>
<td>Left temporo-mandibular region of face</td>
<td>NF-1 (plexiform lesion with microtia)</td>
<td>Debulking and suspension</td>
</tr>
</tbody>
</table>

function or causing severe disfigurement. Because of severe bleeding [9], occasional nerve damage, and tumor recurrence following surgery [10], most asymptomatic lesions are better left alone. Other therapeutic options include laser surgery [11], especially CO₂ laser, which can be used to remove hundreds of neurofibromas in one session to improve cosmetic appearance [12].

Though the condition is common in Ghana, there is a paucity of information in the literature about the spectrum, pattern, incidence, and management options.

The objective of the study was to document the clinical and epidemiological features of patients with NF presenting at Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, between January 2009 and December 2013, and the outcome of management.

2. Patients and methods

This is a retrospective study of patients with the features of NF managed at KATH from January 2009 to December 2013. Data on all the patients managed within the study period were retrieved from the records of the surgical outpatient department (SOPD) of KATH, and from theater records. Data collected included the name, age, and sex of the patient; the site and type of lesion; the treatment given; and the outcome.

The patients were examined clinically. The type of lesion and the site involved were recorded. A clinical photograph of the lesion was taken. Where indicated, an appropriate imaging technique such as ultrasound scan, X-rays or CT scan was done. The lesion was then classified as either NF-1, NF-2 or schwannomatosis based on the clinical criteria. NF-1 patients should have two or more of the following: six or more café au lait spots; two or more neurofibromas or one plexiform neurofibroma; freckling in the axillary or inguinal region; two or more Lisch nodules (from slit lamp examination by ophthalmologist); optic glioma (from CT scan); sphenoid wing dysplasia or thinning of long bone cortex (from CT scan and plain X-rays); a parent, sibling or offspring with NF-1 by the above criteria.

NF-2 patients should have bilateral eighth nerve masses (from CT scan or MRI) or parent, sibling or offspring with NF-2 and either unilateral eighth nerve mass or two or more of the following: neurofibroma, meningioma, glioma, schwannoma or juvenile posterior subcapsular lenticular opacity.

The indication for surgery in NF disease is disfiguring lesions especially in conspicuous locations. The aim of surgery is twofold: to achieve an acceptable aesthetic outcome, and to preserve function. Lesions requiring surgery were either excised or debulked. Excision was indicated for lesions of 3 cm diameter or less, mostly neurofibromas, where the defect could be closed directly. Debulking was indicated for larger lesions more than 3 cm diameter, mostly plexiform lesions. Surgeries on the extremities were performed under tourniquet to minimize bleeding. Lesions on the face were debulked, and the remaining tissue was suspended by anchoring it to the bony skeleton, especially the zygomatic arch, with nonabsorbable sutures to achieve symmetry. In cranio-orbital NF, preservation of the eye was indicated when vision was present.

All tissue excised at surgery were sent for histopathological examination. Only lesions confirmed as NF were entered into the study.

3. Results

A total of 15 patients with NF were treated surgically for function impairing or disfiguring lesions. Their ages ranged from three years to 55 years, with a mean age of 27.3 years. It comprised five males and 10 females. The clinical details of the 15 patients are shown in Table 1.
A total of 17 lesions were found on the 15 patients that required surgery; these were distributed as follows: 10 on the head and neck, three on the trunk, and two each on the upper and lower extremities. Nine of the lesions were located on the left side of the body, four on the right, and four centrally on the scalp and trunk. Three of the lesions were neurofibromas; the remaining 14 were plexiform lesions. Fourteen patients had NF-1; only one patient had NF-2; there were no cases of schwannomatosis.

Debulking was the main surgical procedure performed for 12 patients; this was combined with suspension in two cases involving the face, and enucleation in one case involving the right cranio-orbital region (Figure 2). Excision of the lesion and direct closure of the defect was the procedure in five patients; the lesions were 3 cm or less in diameter; no recurrence of the lesions has been observed in this group of patients.

Although debulking of the plexiform neurofibromas of the scalp brought symptomatic and aesthetic relief to the patients, almost all of them recurred within six months. Eight of them have had a second debulking procedure.

After a debulking procedure for NF of the right lower limb (Figure 3), a nine-year-old girl was able to move about and perform her activities of daily living. However, symmetry with the normal left leg could not be achieved as further surgery would have compromised the blood supply of the affected limb.

### 4. Discussion

Although the lesions observed in this study appear to be concentrated on the head and neck ($N = 15$), the distribution involved almost all parts of the body: upper and lower limbs, trunk, head and neck, and perineum. NF is a disease with protean manifestations. It may involve both skeletal and soft tissues of almost all the systems of the body because of its ubiquitous nature. In West Africa, NF involvement of the extremities, especially the forearm [13,14], gluteal and pelvic regions [15], axial and peripheral skeleton [16], and the head and neck [17], have been documented. These findings indicate that the disease can mimic many conditions that clinicians should be aware of, and hence they should consider NF in the differential diagnosis of any unfamiliar medical condition.

Though several cases of neurofibromas were encountered during the study, only three of them required surgical excision, the rest being asymptomatic. The remaining 14 lesions that required excision or debulking were plexiform neurofibromas, and most of them ($N = 17$) were found on the head and neck (Table 1). The head and neck is a conspicuous region; any disfiguring lesion causes psychological embarrassment to the patients; they are therefore anxious to undergo surgery to improve their appearance. The plexiform neurofibromas can be extensive and cause neurological deficits as well as disfigurement (Figure 4). Diagnosis must be fully established before surgery is undertaken, especially for lesions on the trunk (Figure 5) and extremities, so that the necessary precautions are taken to avoid any disastrous bleeding, nerve damage, and delayed wound healing [5].
Surgery for cranio-orbital NF should be multidisciplinary, involving plastic, craniofacial, and ophthalmic surgeons, as it may involve debulking and enucleation (Figure 2).

The study revealed that 93.3% ($N = 15$) of the patients had NF-1. This finding is consistent with other series which indicate a higher prevalence of NF-1 compared to NF-2. NF-1 is known to account for 96% to 97% of all cases of NF, with NF-2 accounting for 3% [18]. There is no known ethnic group in which NF-1 does not occur or is unusually uncommon. One multicenter study reported higher incidence rates of 12.8% and 57.4%, respectively, among Blacks and Orientals [19]. NF-1 has a birth frequency of 1 in $2,500$–$3,000$, and a minimum prevalence of 1 in $4,000$–$5,000$. Fifty percent of affected patients result from new mutations [4]. The gene for NF-1 was cloned on chromosome 17q11.2 in 1990 [20].

In the current study, only one patient (6.7%, $N = 15$) had NF-2. Other studies indicate that NF-2 has a birth frequency of 1 in $25,000$ and a disease prevalence of 1 in $60,000$ [21]. The gene for NF-2 has been cloned on chromosome 22q11.2 [22].

The male-to-female ratio of the current study is 1:2. This finding is not consistent with the literature, which indicates equal sex distribution for NF disease [23]. This apparent higher female prevalence may be due to the smaller sample size which may not be representative of the general population. However, most of the NF patients presented with lesions that were causing functional or cosmetic problems (Figure 6); the study revealed that most of the lesions that were operated upon were disfiguring plexiform neurofibromas of the head and neck. Since women are more concerned about their external appearance than men, it is not surprising that more females presented for surgical treatment.

5. Conclusion
NF causes disfigurement and functional deficits in affected patients. Surgery can achieve symptomatic relief but is associated with severe hemorrhage, delayed wound healing, and a higher recurrence rate. Early presentation is recommended to achieve optimal results.

References