Clinico-Pathologic Presentation and Management of neurofibromatosis type 1(Von Recklinghausen's) Disease among North-Eastern Nigerians: A six year review

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SUMMARY

Objective: Neurofibromatosis type 1 is not an uncommon disorder, its prevalence is said to be around 1 in 2000-4000 live birth. It has diverse manifestations that may affect any part of the body and present to clinician of any specialty, however, little or no attention have been given to area of neurological, ophthalmological and auditory complications in these patients. This study is aimed at evaluating the clinical, histological presentation and to highlight the need of multi disciplinary approach in the management of this condition.

Methodology: The case records of patients who presented with clinical signs and request form with histologically proven neurofibromatosis were retrieved and reviewed from University of Maiduguri Teaching Hospital and Federal Medical Center Azare from January 2000-December 2005. The clinical characteristics, histological reports and complications were evaluated. Information such as the age, sex, site and histological diagnosis were extracted from the patient's case notes and histology request form.

Results: Forty seven patients fulfill the diagnostics criteria of the national institute of health consensus development conference NIHCDC. The age range was 10-65yrs, with the mean of 27.85yrs. There were 23 males and 24 females, sixteen patients had a positive family history of similar condition in a first degree relative and three are from same parents. Forty one had cutaneous fibroma (87.2%) while 6 (12.8%) were plexiform. Twenty-nine patients had café a lait lesion (61.7%), while 30(63.8%) presented with axillary and or inguinal freckling. One of the cases presented with osseous lesion and hypertension. The commonest site of neurofibroma was the trunk 16(34%), head and face 11(23%), then the lower limb 10(21.8%). Treatment modality was mainly excision of neurofibroma.

Conclusion: This study have documented that NF1 is not an uncommon disorder in this region and has no sex predilection and present commonly within the second and third decade of life when dermal neurobribroma start to occur in the skin; the trunk, head and face being the commonest area of affliction. Attention is to be paid to neurological, ophthalmological and auditory systems in the evaluation of the patients and to follow up these patients for a long time to evaluate the long term complications.

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Key words: Neurofibromatosis type 1 (NF1), Clinico-pathologic presentation and management

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INTRODUCTION

Neurofibromatosis type 1 (NF1) best term neurofibromatosis is an autosomal dominant neurogenetic disorder with diverse clinical manifestations that may require care from every type of clinician. It is a common genetic disorder affecting the nervous system which occurs 1 in every 2000-4000 live birth and occurs in all races and in every geographical location, without sex predilection[1-7]. Neurofibromatosis may results from mutation in 50% of patients; however, 50% have family history of autosomal transmission[5-7]. The gene for NF1 is located on chromosome 17 (17q11.2) [1,6]. The common presentation of NF1 is the occurrence of many neurofibroma which could range from benign manifestation to gross disfigurement fig 1. This disorder though mostly benign may be associated or complicated with other clinical conditions such as pheochromocytoma, fractures, hypertension, neuromotor dysfunction, attention deficit, hyperactivity disorder and visuo-spatial processing or present with compressive symptoms or may lead to the development of neurofibrosarcoma 3-7. Patients with NF1 have an estimated 3-15% additional risk of malignant disease in their life time.

NF1 is associated with various neurologic and endocrinologic abnormalities; these include acoustic nerve involvement, deafness, optic nerve glioma, pheochromocytoma, short stature, growth hormone abnormality and intracranial tumors[6, 8-11]. Many of these patients have below average intelligence and about 25-40% have learning disability [6, 8, 11-15.]

Several studies have documented the dermatological and histological presentation of NF1, which were conducted in north central and south western Nigeria. To date no studies was conducted in the North eastern Nigerian. This study was embarked upon to ascertain where the same clinico pathological presentation NF1 occurred in this part of the country and to emphasis of the need of multi disciplinary management of this common autosomal dominant disorder.

METHODOLOGY

Retrospectively case records of patients, who presented with clinical signs and histologically proven neurofibromatosis were retrieved, reviewed and evaluated from University of Maiduguri Teaching Hospital and Federal Medical center Azare from January 2000 to December 2005. The clinical characteristics, histological reports and complications and management of these patients were documented. Patients included in the study are those who fulfilled the national institute of health consensus development conference (NIHCDC) criteria 16. These criteria are met if a person has two or more of the followings Viz: Six or more café au lait macules over 5mm in greatest diameter prepubertal persons and over 15mm in greatest diameter in postpubertal persons; two or more neurofibromas of any type or one plexiform neurofibroma; freckling in the inguinal or the axillary regions; optic glioma; two or more Lisch nodules (irish hamartoma); a distinctive osseous lesion such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudarthrosis; a first degree relative (parent, sibling or offspring) with neurofibromatosis 1 by the above criteria.

RESULTS

Forty-seven patients had clinical and histological diagnoses of neurofibromatosis 1 from University of Maiduguri Teaching Hospital and Federal Medical Centre Azare, during the 6year study period. There were 23 males 48.9% and 24 female 51.1%. The peak age of presentation was the third decade 19 (40.4%) of life and followed by decline to the first decade as shown in Table 1. The trunk was the commonest site of neurofibroma with 16 (34%) followed by the head and face with11 (23%) fig1&2 then the lower limbs 10 (21.7%) and upper limbs 8 (17%).

Forty-one (87.2%) of the patients presented with cutaneous and sub cutaneous neurofibroma while 6 (12.8%) had plexifrom neurofibroma. Sixteen of the patients had a first degree relative with similar disorder with three cases of the same parents (siblings) fig 3. Café au lait spot and axillary/inguinal freckling were present among 61.7% and 63.4% of patients respectively. One of the patients a 60 year old had documented osseous lesion, hypertension. None of these patients had CT scan or ophthalmological examinations performed or assessed for cognitive dysfunction. Twenty seven (57.5%) cases fall within the grade 1 staging while 31.9%, 6.4% and 2.9% were in grade 2, 3 and 4 NIH staging of Neurofibromatosis. The main treatment was surgical excision of the lesions fig 4.

Table 1: Age, sex distribution of neurofibromatosis

Age in years	Male	Female	Total
10-19yrs	8	4	12
20-29yrs	8	11	19
30-39yrs	3	5	8
40-49yrs	2	2	4
50-59yrs	1	1	2
>60yrs	1	1	2
Total	**23**	**24**	**47**

Table 2: Diagnostics criteria for neurofibromatosis

	Male	Female	Total
Café au lait 6 or more	12	17	29
Axillary or inguinal freckling crowe sign	9	21	30
Dermal fibroma 2 or more	21	20	41
Plexiform neurobrima	2	4	6
First degree relative with NF1	5	11	16
Optic nerve	-	-	-
Two or more lisch nodules	-	-	-
Osseous lesion	-	1	1

Table 3: Site of lesions in males and females

Site	Male	Female	Total
Head + face	4	7	11(23.4%)
Neck	3	1	4(8.5%)
Trunk + Abdomen	7	9	16(34%)
Perineal region	1	2	3(6.4%)
Upper Limb	5	3	8(17%)
Lower Limb	6	4	10(21.3%)
Multiple site	2	4	6(12.8%)

Table 4 Age distribution and grading of neurofibromatosis

Age in years	Grade 1	Grade 2	Grade 3	Grade 4	Total
10-19	10	2	0	0	12
20-29	9	7	2	1	19
30-39	7	1	0	0	8
40-49	1	3	0	0	4
50-59	0	1	1	0	2
>60	0	1	0	1	2
	27	**15**	**3**	**2**	**47**

Fig 1:

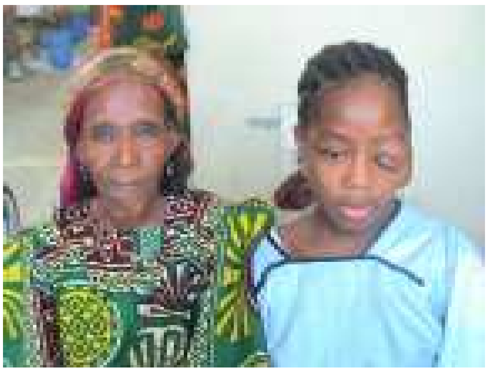

Fig 2:

Fig 3:

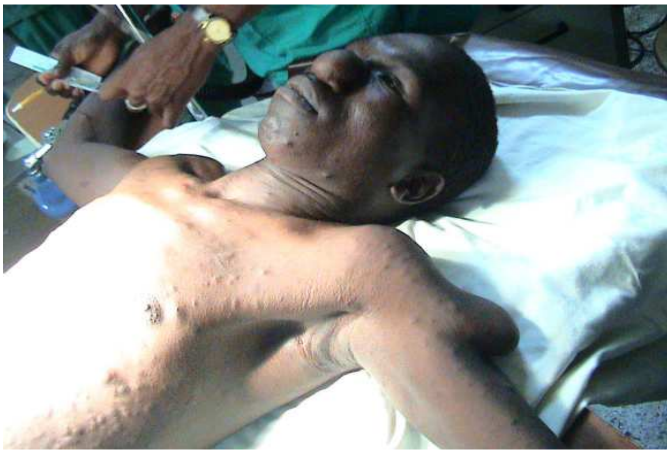

Fig 4:

DISCUSSION

In the six year period forty- seven histological proven neurofibromatoses were seen, 24 and 23 were females and males respectively with no gender predilection. This conformed to the general presentation of neurofibromatosis that NF1 occurs equally in both sexes[1-6] but differ from studies in North central[17] and south western Nigeria18 which shows male predominance. The commonest age of presentation was second and third decade, which represent 30% of cases and about 24% presented within the first decade; thus, majority of our patients presented a decade later than in the western population[6,7] and a decade earlier than a similar survey in western Nigeria, this could probably be due to the higher proportion of females in this study compared to that in western Nigeria, as female become conscious of their physical appearance at an earlier age than males.

Sixteen of the 47 cases have a first degree relative with similar condition; 3 of the cases were a woman with 2 of her daughters. Dermal fibroma was the commonest type with 41 of the cases presenting with cutaneous and subcutaneous fibroma while 6 (12.8%) cases had the plexiform type. Axillary or/ inguinal freckling were common signs after derma fibroma, which concur with similar studies as the occur in about 70% of cases of Neurofibromatosis type 1 , however this study differ from that of Odebode *et al*[17] where none of their patients had axillary or groin freckles. None of our patients had documented optic glioma or Lisch's nodules as none complaints of visual symptoms nor did they have Computerized Tomography scan or referred to ophthalmologist/neurologist for examination. Our experience was similar to Odebode el at in North central Nigeria which could be due to lack of awareness of diverse manifestation of the disease and lack of resource of the patients to under-go intensive neuro-radiological investigations.

The trunk is the commonest site of presentation than the head, face and neck which is in conformity with the hypothesis that NF1 occurs in skin areas with higher temperature [20]. NDHC grade 1 was the commonest stage of presentation; however most cases were not followed up for a long period to monitor their progress or long term complications of the conditions.

One patient come in with complication of osseous and severe hypertension and subsequently developed stroke and died. Further screening of her family members show that two of her daughters have derma fibromas that are currently being followed up in our clinics. Other complications were not recorded such as auditory disorders, learning disabilities, macrocephaly and short stature due probably to lack of awareness by the attending physicians to these complications.

CONCLUSION

This study has documented that NF1 is not an uncommon disorder in this region and has no sex predilection and present commonly within the second and third decade of life when dermal neurofibroma start to occur in the skin; the trunk , head and face being the commonest area of affliction. Only few studies, paid attention to neurological, ophthalmological and auditory system in the evaluation of the patients and are followed up for a long term to evaluate the long term complications[18,19,22].

RECOMMENDATION

All cases of neurofibromatosis type 1 should be management by a multi disciplinary medical team and be evaluated by neurologist, ophthalmologist, psychiatrist, plastics and ENT surgeons geneticians. Long terms follow up of these is also recommended because of possible danger of neoplasm and malignant transformation.

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