Original Article

Oral Neurofibroma: 10-Year Experience in Enugu

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Abstract

Background: Neurofibroma (NF) is a neural tumour derived from the proliferation of Schwann cells. Oral NF is rare, and no known study exists in the Nigerian literature. **Aims:** The aim was to study the clinicopathologic features of oral NF in a tertiary hospital in Enugu and review of the literature. **Materials and Methods:** This was a retrospective study conducted in a tertiary health institution in Enugu from April 2012 to March 2022. The clinical records, radiographs, and histopathology reports of patients seen at the department of oral pathology and oral medicine were examined for cases of NF. The data were analyzed using descriptive statistics, and Chi-square statistics for association between the variables. **Results:** There were only 11 oral peripheral neural sheath tumours, and all were diagnosed as NF. These constitute 1.1% of 897 orofacial biopsies received. Solitary oral NF constituted 90.9% of cases, while 9.1% was associated with neurofibromatosis type I. One of the solitary cases occurred with ameloblastoma. The mean age at the onset of the tumour was 38 ± 24.4 years (range: 8–85 years). A male-to-female ratio of 1.8:1 was obtained, and a majority of lesions, 7 (63.6%) of 11, were located in soft tissue sites only. The tongue (27.3%) and the mandible (27.3%) were the most common intraosseous and soft tissue sites. Pain (18.2%) and recurrence (54.5%) were observed. **Conclusion:** Oral NF was the most common peripheral nerve sheath tumour, with a low prevalence, male predilection, and frequently extraosseous.

Keywords: Neural tumours, oral neurofibroma, peripheral nerve sheath, Schwann cells

Introduction

An intraoral case of solitary neurofibroma (NF) was first reported in 1954.[1] This neural tumour is derived primarily from Schwann cells and other nonproliferating cells from the peripheral nerve sheath such as perineurial cells, fibroblasts, and mast cells.[2] Germline mutation in the NF1 suppressor gene has been implicated in the etiology of NF.[3] Some authors, however, consider it a hamartomatous malformation caused by factors like trauma.[4] NF is classified as a peripheral nerve sheath tumour (PNST), a spectrum of benign and malignant tumours of neural origin, and includes schwannoma, perineurioma, hybrid nerve sheath tumour, and malignant PNST (MPNST).[5]

A study of oral PNSTs in Brazil for 40 years identified only 10 (28.6%) cases of solitary NF and two other NF cases (5.6%) associated with neurofibromatosis type I.[6] Another study in India found only 14 cases of oral NF over a 20-year period, with a recurrence rate of 14.3% and malignant transformation in 7.1%.[7]

Oral solitary NF is therefore rare, and there is no publication on the subject known to the author in the Nigerian literature. This study would help highlight the prevalence, improve awareness of the lesion, and provide baseline data on oral NF in a tertiary health institution in Enugu, South East Nigeria.

Materials and Methods

This was a retrospective cross-sectional study of 11 patients diagnosed with oral NF by histopathology studies, at the oral pathology unit of a tertiary health centre in Enugu, from April 2012 to March 2022. All clinical and pathological records pertaining to each patient were obtained from the departmental archives. Archival documents, tissue blocks, case files, histopathology reports, and records were used to identify and extract information of the cases. Histopathologic diagnosis of oral NF cases were based on H and E staining method only.

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Access this article online

Quick Response Code:

Website: www.njmonline.org

DOI: 10.4103/NJM.NJM_133_22

How to cite this article: Nwoga MC. Oral neurofibroma: 10-year experience in Enugu. Niger J Med 2023;32:35-8.

Submitted: 29-Dec-2022 **Revised:** 04-Feb-2023
Accepted: 17-Feb-2023 **Published:** 25-Apr-2023

Statistics

The statistical product, IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA), was used in the statistical analysis. The data were analyzed using descriptive statistics and frequency, while Chi-square statistic was used to test the statistical association between the variables at a 95% confidence interval.

There was no interface with patients in this study due to its retrospective character, and the Helsinki Declaration on medical protocol was followed for this investigation.

Results

There were 11 cases of oral NF diagnosed, and these constitute 1.1% of the 897 orofacial lesions and biopsy cases managed. They were the only peripheral neural sheath tumours identified. One case (9.1%) was associated with neurofibromatosis type I, while another case was associated with an odontogenic tumour, ameloblastoma. There were 7 (63.6%) male and 4 (36.4%) female patients. The mean age of the patients at the onset of the tumour was 38 ± 24.4 (range: 8–85) years, while at clinic presentation, the mean age was 42.9 ± 23.9 (range: 17–85) years. Patients in the 21–30 years decade at the onset of the lesion had the most lesions, 4 (36.4%). Most lesions, 6 (54.6%), were observed when patients were below the age of 40 years. Recurrence was reported in association with 6 (54.5%) cases of oral NF.

The mean duration before diagnosis was 5.11 ± 7.0 (range: 0.08–20) years. The mean diameter of the lesion was 3.9 ± 4.3 cm (range: 1.5–14 cm). Ten (90.9%) of the 11 cases were solitary NFs in the oral cavity, and only 1 (9.1%) case was part of a generalized syndrome of neurofibromatosis type I. One of the solitary NF cases was observed to coexist with ameloblastoma.

A majority of the lesions, 7 (63.6%), were found in the soft tissue, while the intraosseous occurrence was 3 (27.3%), and one case involved both soft and hard tissues [Table 1]. The mandible [Figure 1] was the most common intraoral intraosseous site, 3 (27.3%), while the tongue was the most common orofacial soft tissue site with a frequency of 3 (27.3%) [Table 2]. The tongue and the mandible were the most common sites of occurrence, 6 (54.6%). Soft tissue NF was the most common type with 7 (63.6) cases.

The nerves involved in the lesions based on the nerve supply to the oral tissues (tongue, cheek, mandible, lateral to the nostril, the floor of the mouth, and oropharynx) involved more than one cranial nerve, and the specific nerves were not delineated. There was a single case of lip paraesthesia, while swelling was the most common symptom observed in all cases. Other clinical features reported included pain in 18.2% (2) and tooth mobility and displacement, tooth loss, and restriction of tongue movement which affected speech. Radiographic examinations showed a range of features from well-circumscribed to irregular radiolucencies and bone resorption for intraosseous cases.

The microscopic examination showed hypercellular stroma consisting of neoplastic spindle cells with wavy nuclei, arranged in occasional fascicules and infrequently in storiform patterns [Figure 2].

The intraosseous cases were treated by radical surgery, and radical excision of soft tissue tumours was carried out. Patients' follow-up ranged from one year for the most recently managed cases to 9 years for the older cases. There has not been any report of recurrence after surgical treatment of the 11 cases.

Table 1: Clinical summary of 11 neurofibroma cases

Sex/age at presentation (years)	Duration (years)	Age at onset (years)	Site	Depth	Size (diameter) (cm)	Imaging features	Recurrence	Diagnosis
Male/19	11	8	Cheek (buccal)	Soft tissue	2	Nil	Nil	NF
Male/49	0.7	49	Mandible	Intraosseous	4	Well-circumscribed radiolucency, marked bone resorption	Yes	NF
Female/73	0.1	73	Tongue	Soft tissue	3	Nil	Nil	NF
Female/85	0.5	85	Tongue	Soft tissue	-	Nil	Nil	NF
Male/28	0.2	28	Lateral to nostril	Soft tissue	1.5	Nil	Yes	NF
Male/17	5	12	Tongue	Soft tissue	3	Nil	Nil	NF
Male/25	1.5	24	Cheek (buccal)	Intraosseous and soft tissue	3	Multilocular radiolucency with bone destruction	Yes	NF
Female/43	15	28	The floor of the mouth	Soft tissue	3	Nil	Yes	NF
Male/71	20	51	Oropharynx and submandible	Soft tissue	10	Nil	Nil	NF
Female/23	0.3	23	Mandible	Intraosseous	-	N/A	Yes	NF and ameloblastoma
Male/39	2	37	Mandible	Intraosseous	14	N/A	Nil	NF

NF: Neurofibroma

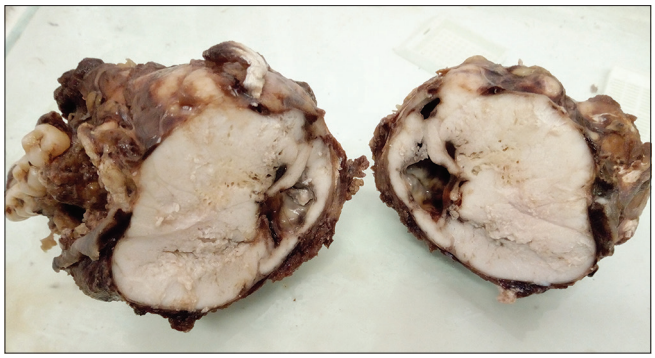

Figure 1: A hemimandibulectomy specimen of a large intraosseous NF: neurofibroma

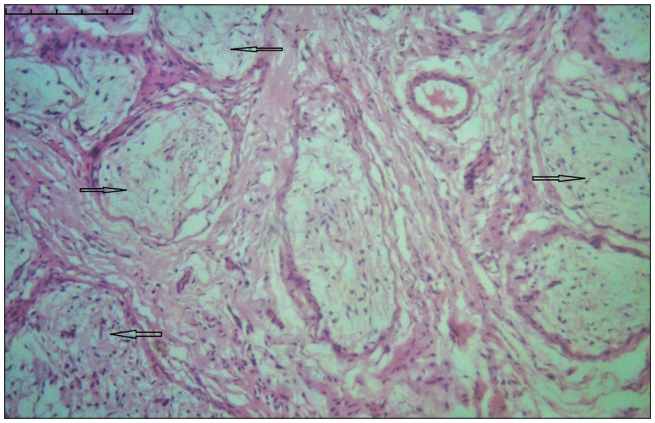

Figure 2: Photomicrograph of oral neurofibroma showing several nerve fascicles (arrows) separated by the collagen bundles. Each fascicle consists of a hypocellular matrix containing fibroblasts, Schwann cells, and mucin, (H and E, ×160)

Discussion

The rarity of oral NF could explain the paucity of literature in Nigeria and the prevalence of 1.1% of orofacial lesions in this study. Other centres in Nigeria have no known report of the prevalence value NF in orofacial tumours. Oral NF was the only PNST identified during this period. The rarity of other PNSTs in this study, such as neurilemmoma (schwannoma), traumatic neuroma, palisaded encapsulated neuroma, and MPNST, could also be due to such cases not getting to the oral pathology centre.

The paucity of reported cases of oral NF is not peculiar to Nigeria since few cases were reported in other studies.[6,7] Oral involvement in neurofibromatosis NF-1 has been reported,[8,9] and this affected only 4%–7% of such patients.[10] The association of NF with neurofibromatosis type I was observed in only 1 (9.1%) of 11 cases in this study. Oral NF has been reported in association with other lesions, including systemic lupus erythematosus,[11] fibrous dysplasia,[12] and cherubism.[13] Similarly, one of the cases in this study was associated with ameloblastoma. Although oral NF has rarely been documented in Nigeria, the observation of cases in Enugu was not unexpected since 25% of all NFs are located in the head and neck region, and 5.6%–6% of these are known to occur in the oral cavity.[14]

Table 2: Frequency of sites and depth of neurofibroma cases (n=11)

Site	Frequency (%)
Oropharynx	1 (9.1)
Cheek (buccal soft tissue)	2 (18.2)
Mandible	3 (27.3)
Tongue	3 (27.3)
Lateral to nostril	1 (9.1)
The floor of the mouth	1 (9.1)
Depth	
Soft tissue	7 (63.6)
Intraosseous	3 (27.3)
Intraosseous and soft tissue	1 (9.1)

The mean age at clinic presentation of 42.9 years from this study is higher than those reported in other studies of 27.5 years, 30 years, and 31.2 years, respectively, by Gujjar *et al*.[14] Gosavi *et al*.,[7] and Salla *et al*.[6] The higher mean age of the patients in Enugu could be due to the wider occurrence age and long delays before the presentation. In this study, NF affected mostly those in the third decade, similar to the report by Gosavi *et al*.,[7] but lower than the fifth decade of life reported by Thompson *et al*.[15]

The male gender predilection of 63.6% obtained in this series contrasts with the reports of the absence of gender predilection.[9,10,16,17] Other authors reported a slight female predilection.[7,14] Salla *et al*.[6] observed a strong female predilection in their Brazilian study, with a male-to-female ratio of 1:9. The variations in the gender predilection could be a result of the small study samples.

NF is known to affect the tongue, lip, palate, gingiva, major salivary glands, and jaw bones.[14,18,19] In this study, soft-tissue NFs (63.6%) were prevalent, and those were mostly submucosal, discrete swellings. This study also observed the tongue as the most common orofacial soft tissue site and the mandible as the most common intraosseous site, while the buccal mucosa (cheek) was the third-most common site of occurrence. These observations were equally reported by other authors who identified the tongue, followed by the buccal mucosa as the most frequent intraoral soft tissue location for oral NF; while the posterior mandible was the most common intraosseous location.[3,6,7,17] Gujjar *et al*.[14] also reported that intraosseous NF is mostly found on the posterior mandible.

Broly *et al*.[8] noted that solitary NF is rarely painful. This may explain why the majority of the NF patients in this study did not make any complaint of pain. Pain was reported only in 18.2%, and there was a single case of lip paraesthesia. Pain and paraesthesia are documented as symptoms due to compression of involved nerves.[20]

The nerves involved in the lesions in these cases were the 5th cranial nerve branches (the trigeminal nerve). Nerves from the 5th cranial nerve supply the tongue, lip, palate, gingiva, major salivary glands, and jaw bones, and have been mostly involved in NF of the craniofacial region.[14] The upper cervical nerves and rarely the 7th cranial nerve (facial N) involvement are also documented.[8] Some authors have reported a solitary NF from the lingual nerve trunk of the hypoglossal nerves.[8,21]

In this study, solitary NF was observed to be slow-growing and with late presentation. Based on the patient's report of the duration of lesions, some NF cases presented at the clinic after 11, 15, and 20 years. The delayed presentation could be due to the absence of pain in the majority of our orofacial cases. The slow growth has also been documented by other authors.[6,8,22]

Differential diagnosis of solitary oral NF includes spindle peripheral neural sheath tumours and tumours with spindle components. These include schwannoma, nerve sheath myxoma, ganglioneuroma and traumatic neuroma, dermatofibrosarcoma protuberans, and desmoplastic malignant melanoma.[23] Similarly, other spindle cell lesions could be differentials and include benign fibrous histiocytoma, spindle carcinoma, and amelanotic melanoma.[14] Schwannoma is the closest differential of NF, but while verocay bodies are specific to Schwannoma, the presence of mast cells and fine fibrillar collagen matrix are features of NF.[24] A traumatic neuroma is associated with a history of trauma.

The limitations of this study include the small number of cases due to the rarity of orofacial NF lesions and the paucity of literature of cases from Nigeria for comparison of findings. The multiplicity of clinical and histological differentials could pose challenges in some cases and require detailed clinical history, examination, and histological diagnostic experience. Limiting diagnosis to only H and E staining methods without immunohistological studies reduced the scope of differential diagnosis.

Conclusion

Oral NF was the most common PNST seen in Enugu. Most of the lesions are solitary, with male predilection, and frequently extraosseous. Oral and maxillofacial soft tissue masses should include NF in the clinical differential diagnosis. Advanced confirmatory studies using immunohistochemistry may help resolve challenging differentials while increasing awareness of the availability of oral pathology diagnostic services could improve oral specimen pooling and discovery of other rarer oral peripheral neural sheath tumours.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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