

NEUROFIBROMATOSIS OF THE MAXILLOFACIAL REGION

Khalid A. Al-Ruhaimi, BDS, MSc, Dr Med Dent;* Hermann F. Sailer, Dr Med, Dr Med Dent**

عرض في هذه الدراسة سبعة عشر مريضاً بمرض الأورام العصبية الليفية في منطقة الوجه والفكين، لم يكن هناك اختلاف كبير في حدوث المرض بين الذكور والإناث بنطاق عمر ما بين ١ - ٧٥ سنة (متوسطة ٢١.٥ سنة). وقد وجد في هذه الدراسة أن ٨٢٪ من المرضى لديهم بقع بنية في مختلف أجزاء الجسم، ٢٩.٥٪ لديهم تواريخ طبية إيجابية بوجود المرض لدى عوائلهم و ٢٣.٥٪ لديهم عقد جلدية متعددة. جميع حالات هذه الدراسة كانت وحيدة الجانب، وقد كانت حالات المرضى في الفك السفلي أكثر (٦٥٪).

In this study seventeen patients with neurofibromatosis in the maxillofacial region were presented. There was no great difference in the incidence of the disease between males and females. The patient age range was 1 to 75 years with a mean age of 21.5 years. Family history was positive in 5 cases. The spectrum of the clinical manifestations of this disease, known for its protean characteristics, were evident in all of our 17 patients. 14 (82.4%) patients had cafe'au-lait spots; 3 (17.6%) had multiple cutaneous nodules; malignant transformation was documented in only one case (5.9%). Psychologic depression was recorded in 2 (11.8%) cases, and one (5.9%) case had grand-mal epilepsy. A rare location of neurofibromatous nodules, i.e. in eye (iris nodules), was reported in only one (5.9%) case. The most frequently performed procedure in our cases was excision of the tumor mass which was, in most instances, incomplete. However, massive bleeding during surgical intervention was prominent in four cases and was overcome with extensive packing removed after approximately two weeks. An interesting finding in this study was the incidence of radiologic findings which was higher (76.4%) than previously reported. All cases of this study were unilateral and involvement of the mandible (65%) was more than that of the maxillae.

Neurofibromatosis was first described by Aken-side.¹ However, Friedrich von Recklinghausen² was the one who concluded that multiple tumors of nerves and skin (neuromas and fibromas) existed simultaneously and were structurally related, and thus justified the name neurofibromatosis, which later became known as Recklinghausen's disease.

Recklinghausen's disease is an inherited disease transmitted as an autosomal dominant trait with a positive family history in most cases. It is considered to be one of the most devastating and destructive diseases in mankind.

In addition to the associated skeletal lesions, neurocutaneous syndrome is characterized by cutaneous and subcutaneous fibrous tumors of the

skin, cafe'au-lait pigmentations, vascular and lymphatic anomalies, neurofibromas of the peripheral and central nerves. These are in addition to the associated skeletal lesions.

Materials and Methods

The data for this study was gathered from seventeen patients with neurofibromas in the maxillofacial region. The patients were seen between 1970 and 1987 at the Department of Oral and Maxillofacial Surgery of the Zurich University Hospital. Cases with inadequate information, or patients whose records could not be traced, were not included in the study.

When diagnosis was made, the patients were analyzed for age, sex, family history of the disease, associated complications and other diseases. Evidence of malignant transformation, clinical site of neurofibromas, associated radiologic findings, and, finally, surgical procedures that were carried out for treating deformities caused by the disease were also noted.

*Oral and Maxillofacial Surgery
Department of Biomedical Dental Sciences
College of Dentistry, King Saud University

**Oral and Maxillofacial Surgery
Zurich University Hospital & Dental School, Zurich

Address reprint requests to: Dr. K.A. Al-Ruhaimi, Dept. of Biomedical Dental Sciences, College of Dentistry, King Saud University, P.O. Box 60169, Riyadh 11545, Kingdom of Saudi Arabia

Results

Age, Sex and Family History:

Table 1 shows the ages of the seventeen patients when diagnosis was made. There was a wide age distribution from 1 to 75 years (mean : 21.5 years). However, the incidence of neurofibromas was slightly higher in females than males. Ten (58.8%) were females and seven (41.2%) were males.

There was positive family history in five patients (29.4%) as shown in Table 1. Types of complications and other associated lesions seen in these patients are presented in Table 2 and they were as follows:

- i) Cafe au lait spots, an important diagnostic sign in neurofibromatosis were found in 14 (82.4%) patients.
- ii) Multiple cutaneous nodules were seen in three (17.6%) patients.
- iii) Evidence of malignancy was found in only one (5.9%) patient and this malignancy was reported histopathologically as leiomyosarcoma.
- iv) Four (23.5%) patients had mental retardation.
- v) One case had grand-mal epilepsy.
- vi) Psychologic depression, a social problem in patients with this disease, was noticed in two (11.8%) patients.
- vii) Hemorrhage, a difficult operative problem, was encountered in four (23.5%) cases.
- viii) Iris nodules were reported in one (5.9%) case.

Clinical Sites:

The distribution of the lesions in various anatomical sites is shown in Table 3. All cases of this study were involved unilaterally. The tumor masses affected one or several anatomical locations. However, the lower jaw was involved in 11 (64.7%) out of the seventeen cases.

Upper jaw lesions were recorded in nine (52.9%) cases. Lips were deformed in six (35.3%) patients. Tumor mass in the nose was evident in two (11.8%) patients. Cheek was disfigured with hyperplastic masses of the tumor in six (35.3%) patients. Orbit and eyelids were involved in three (17.6%) patients. Unilateral macroglossia was evident in two (11.8%) cases while deformity of the ear was present in one (5.9%) patient.

TABLE 1. Age, sex and family history of each patient.

Patient numbers	Age at diagnosis	Sex	Family history
1	19	M	—
2	8	M	—
3	16	M	+
4	26	F	+
5	4	M	+
6	17	F	—
7	23	F	—
8	1	F	+
9	31	F	—
10	8	M	—
11	22	M	—
12	12	F	—
13	17	F	—
14	75	F	—
15	8	F	+
16	39	F	-
17	40	M	-

TABLE 2. Associated lesions and other complications seen in seventeen patients.

Type	Frequency	% Total
Cafe au-lait spots	14	82.4
Multiple cutaneous nodules	3	17.6
Malignancy	1	5.9
Mental retardation	4	23.5
Grand-mal epilepsy	1	5.9
Psychologic depression	2	11.8
Massive operative bleeding	4	23.5

Site	Frequency	% Total
Upper jaw	9	52.9
Lower jaw	11	64.7
Lips	6	35.3
Nose	2	11.8
Cheek	6	35.3
Facial/occlusal asymmetry	8	47.2
Orbit/eyelid	3	17.6
Tongue	2	11.8
Ear	1	5.9

TABLE 3. Clinical sites of neurofibromas.

Radiologic Findings:

Radiologic findings of this series are listed in Table 4, and skeletal manifestations, in some cases, are illustrated in Figs. 1 to 4. Skeletal involvements associated with the tumor masses were encountered in 13 (76.4%) cases. These cases were reported as bony changes in the maxilla, clinically presenting as hypoplasia of the maxilla and maxillary sinus 6 (35.3 %), dental impaction, spacing and displacement of the teeth 5 (29.4%), and outwardly curvature of the zygomatic arch 2(11.8%)

TABLE 4. *Radiologic findings.*

Findings	Frequency	% Total
<i>Maxilla:</i>		
- Hypoplasia of the maxilla/ maxillary sinus	6	35.3
- Spacing/Impaction deviation of teeth	5	29.4
- Hypoplastic zygomatic convexity	2	11.8
<i>Mandible:</i>		
- Hypoplasia/flatening of contour	10	58.8
- Small condyle and flat glenoid fossa	7	41.1
- Obtuse gonial angle	8	47.1
- Large funnel-shaped ID canal opening	6	35.3
- Large mental foramen	1	5.9
- Increased depth of sigmoid notch	7	41.1
- Deviation of the mandible	5	29.4
- Intra-osseous cystic formation	6	35.3
- Spacing/Impaction/ deviation of teeth	10	58.8
<i>Orbit:</i>		
- Enlargement of the orbit	1	5.9
- Hypoplastic deformities of the lateral orbital wall, floor and inferior rim	1	5.9

In the mandible the bony changes were found in 12 (70.6%) cases. They were recorded as: hypoplasia and flattening of the contour 10 (58.8%), small condyle and flat glenoid fossa 7 (41.1%), obtuse gonial angle 8 (47.1 %), large funnel-shaped inferior dental canal opening 6 (35.3%), large mental foramen 1 (5.9%), increased depth of the sigmoid notch 7 (41.1 %), deviation of the mandible 5 (29.4%), intra-osseous cystic formation 6(35.3%), spacing, impaction and displacement of the teeth 10(58.8%).

Orbital involvements were noticed in two (11.8%) cases. The characteristic changes seen were enlargement of the orbit in one (5.9%) case and hypoplastic deformity of the lateral wall, floor, and inferior rim in another case (5.9%)



FIGURE 1. Panoramic view of the jaws showing unilateral hypoplasia of the mandible (1), small condyle and flat glenoid fossa (2), obtuse gonial angle (3), large funnel-shaped inferior dental canal opening (4), increased depth of sigmoid notch (5), intra-osseous cystic formation (.6), and drifting of the teeth (7).



FIGURE 2. Panoramic radiograph showing enlargement of the left mental foramen (arrowed).



FIGURE 3. Water's radiographic view showing outwardly curved left zygomatic arch (arrowed).



FIGURE 4. Water's radiographic showing enlargement of the left orbital outline (arrowed).

Surgical Management:

Methods used in the surgical management of these patients are listed in Table 5.

The most frequent operative procedure was excision of the tumor mass. Incomplete excision of the tumor lesions was carried out in 11 (84.6%) patients. Complete removal of the mass was done in five (31.3%) patients. One patient failed to present for surgical treatment after being scheduled.

TABLE 5. *Surgical procedures carried out on the patients.*

Procedure	Frequency	% Total
Incomplete excision of the tumor mass	11	34.6
Complete excision of the tumor mass	5	31.3
Sagittal splitting	3	17.6
Genioplasty	2	12.5
LeFort I osteotomy	1	6.3
Nose correction	1	6.3
Parotidectomy	1	6.3
Extraction/releasing fibrous tissue from crowns	7	43.8
Radical neckdissection/upper jaw resection	1	6.3
Partial glossectomy/face lifting/eyebrow lifting	2	12.5
Extensive tamponment packing of the operative site	4	23.5

Dental extraction of impacted teeth or surgical release of fibrous hyperplastic tissue from crowns of teeth was carried out on seven (43.8%) cases.

Surgical correction of the facial or occlusal asymmetry included sagittal splitting, genioplasty, and LeFort I osteotomy, in three (17.6%), two (12.5%), and one (6.3%) patient(s), respectively.

Correction of the nose was performed in one (6.3%) case. Two (12.5%) patients had undergone partial glossectomy for removal of unilateral hyperplastic tissue. One (6.3%) case had radical neck dissection because of evidence of malignant transformation. Parotidectomy was done in one (6.3%) case. Face lifting and eyebrow lifting for improved cosmetic outcome were performed in two (12.5%) cases.

Overcoming spontaneous massive hemorrhage during surgical intervention was achieved in four (23.5%) cases by application of massive packing at the operative site. The tamponade was removed or renewed after approximately two weeks.

Discussion

Neurofibromatosis is, by no means, a rare disease although it is not a very common one.

It is probably the most common genetic disease in mankind.³ The incidence is recorded in most of the reports as 1 in 3000 live births.^{4, 5, 6}

The age distribution of patients in this study is in the same range reported by others.^{7, 8} There appears to be no significant difference in the incidence of disease between males and females in this series. In most of the previous reports, the sex ratio was approximately equal.^{5, 9}

Family history may be detected in some instances, and, in our study, it was positive in 5 (29.5%) cases. Other reports have shown inherited transmission in 10 to 50 percent of cases.^{8, 10}

The presence of cafe'au-lait spots ordinarily may be normal, but association of clinical and skeletal lesions is considered to be a characteristic diagnostic feature of neurofibromatosis.¹¹

These cutaneous brown spots were found in 14 (82.4%) of our cases in agreement with previous reports.^{11, 12}

Multiple cutaneous nodules are mainly found after puberty and are usually manifestations of long standing or adult disease.^{13, 14} They were recorded in only 4 of our patients. Maceri and Saxon⁹

reported that 66.6% of their 63 patients had these nodules, whereas Crawford¹² found only 18% of his 116 children with neurofibromatosis nodules.

Incidence of malignancy is rare with neurofibromatosis, although it is, beyond question, part of the disease considerations. It is recorded in only one case of our group. Others^{8, 15, 16, 17} found malignant frequency of between two and five percent. Mental retardation in patients with neurofibromatosis¹⁸ was associated with four of our patients. Psychologic depression¹⁰ is a problem of patients with neurofibromatosis due to isolation from the surrounding society. Two of our patients suffered from this problem. Other clinical findings reported by others,^{10, 19} which we also found in our series, were grand-mal epilepsy and iris nodules (one case each).

Hemangiomatous and lymphangiomatous malformations in neurofibromatous lesions are anomalies of vascular and lymphatic systems contributory to massive bleeding.²⁰⁻²⁶ However, in our study, four patients did show this problem and were managed without difficulty. Preliminary ligation of feeding vessels was not considered by us, as advocated by some authors,²⁶ since the procedure increases vascularity by opening up the collateral vessels.

Adekeye et al¹⁷ used boiling water as a sclerosing agent. This caused operative difficulty and post-operative hematoma in 7 of their 28 patients. Intra-arterial embolisation by introducing strips of lyophilized dura into the main feeding vessels was recommended by Littlewood and Stillwell.²⁷ Frame et al²⁸ suggested the use of Gelfoam and Polyvinyl sponges as embolising agents. However, extensive tamponment packing was used to overcome spontaneous massive hemorrhage in our cases. It was left in the operative site and removed after approximately two weeks without significant post-operative bleeding. Pressure dressing was applied to reduce post-operative hematoma. The neurofibromatous changes of this series were exclusively unilateral, whereas Vincent and Williams²⁹ reported a rare case of bilateral involvement.

In contrast to the report of Koblin and Reil,²⁵ the lower jaw was the most involved site in our patients (11 out of 17 cases). Occlusal plane distortion and facial asymmetry are common findings with this disease^{14, 16, 30} and were noticed in 8 of our patients. Tongue is a common site for neurofib-

romatous lesions,^{6, 22, 31-32} and two of our patients presented with unilateral macroglossia. Hyperplastic deformities of other common sites, as reported by other authors,^{21, 32} were also encountered in this series in the palate and alveolar process, lips, nose, cheek, orbit, and ear. Rather surprisingly, skeletal lesions were associated with 76.4% of our cases whereas other comparable studies^{4, 6, 7, 9} reported bone lesions in the range of 18-70% of the cases.

All skeletal deformities of our cases were of hypoplastic features. Several authors^{9, 25, 33-35} drew attention to deformities of the facial bones in patients with neurofibromatosis as hypertrophy, hypoplasia, asymmetry, and radioluscent defects. However, the bony defects in this study which had been reported in various previous studies were recorded as hypoplasia of the maxilla and maxillary sinus, maxillary teeth impaction and spacing,¹⁶ hypoplasia of the zygoma with prominent convexity of the zygomatic arch,³⁶ mandibular hypoplasia with flat contour,¹⁴ small size of the mandibular condyle and flatness of the glenoid fossa,³⁷ obtuse gonial angle, large funnel-shaped opening of the inferior dental canal, enlargement of the mental foramen,³⁸ increased depth of the sigmoid notch,³⁵ intra-osseous cystic radiolucencies,^{4, 39, 40, 41} deviation of the mandible,³⁴ mandibular teeth impaction and spacing,²⁵ enlargement of the orbit, and hypoplastic deformities of the lateral wall, floor, and inferior rim.^{33, 38, 42, 43}

As yet there are no means of curing or even arresting neurofibromatosis, it is generally recommended that deforming, or symptomatic lesional tissue masses, be surgically removed electively. In doing this, the benefit of surgical resection must be weighed against the final aesthetic result and the function preserved.

Shack and associates⁴⁴ recommended total excision when feasible, and judicious subtotal extirpation when vital structures are involved, or when total excision would produce considerable deformity. However, the most frequently performed procedure in our cases was excision which was, in most instances, incomplete.

References

1. Akenside M. Observation on cancers. *Med Trans Coll Phys Lond* 1768;1:64.
2. Von Recklinghausen FD, *Über die multiplen fibrome der haut und ihre beziehung zu den multiplen neuromen.*

- Festschrift fur Rudolph Virchow, Berlin, Hirschwald, 1882.
3. Stewart RE, Prescott GH (editors). Oral facial genetics. St. Louis, The Mosby Company 1976;615-618.
 4. Hunt JC, Pugh DG. Skeletal lesions in neurofibromatosis. *Radiology* 1961;76:1-20.
 5. Hope DG, Mulvihill JJ. Malignancy in neurofibromatosis. *Adv Neurol* 1981;29:33-56.
 6. Shapiro SD et al. Neurofibromatosis: Oral and radiographic manifestations. *Oral Surg* 1984;58(4):493-498.
 7. Adekeye EO, Abiose A, Ord RA. Neurofibromatosis of the head and neck: Clinical presentation and treatment. *Maxillofac Surg* 1984;12:78-85.
 8. Griffith BH, Lewis VL, McKinney P. Neurofibromatosis of the head and neck. *Surg Gyn Obst* 1985;160:534-538.
 9. Maceri DR, Saxon KG. Neurofibromatosis of the head and neck. *Head and Neck Surg* 1984;12(2):78-85.
 10. Crowe FW, Schull WJ, Neil JW. A clinical, pathological and genetic study of multiple neurofibromatosis. Springfield, Ill.: Charles C. Thomson, 1956.
 11. Crowe FW, Schull WJ. Diagnostic importance of cafe-au-lait spots in neurofibromatosis. *Arch Intern Med* 1953;91:758-766.
 12. Crawford AH. Neurofibromatosis in children. *Acta Orthopaed Scand Sup* 1986;218(51):1-60.
 13. O'Driscoll P. The oral manifestations of multiple neurofibromatosis. *Br J Oral Surg* 1965;3:22-31.
 14. James PL, Treggiden R. Multiple neurofibromatosis associated with facial asymmetry. *J Oral Surg* 1975;33:439-442.
 15. Yaghmai I, Tafazoli M. Massive subperiosteal hemorrhage in neurofibromatosis. *Radiology* 1977;122:439-441.
 16. Badger GR. Solitary neurofibromatosis in the maxilla: Report of oral findings. *J Am Dent Assoc* 1980;100:213-4.
 17. Eldridge R. Central neurofibromatosis with bilateral acoustic neuroma. *Adv Neurol* 1981;29:57-65.
 18. Chao DHC. Congenital neurocutaneous syndromes in childhood: I, Neurofibromatosis. *J Pediat* 1959;55:189-199.
 19. Inster MS, Helm C, Napoli, S. Congenital hamartoma in neurofibromatosis. *AM J Oph* 1985;99(6):731-33.
 20. Goetsch E. Schadelveranderungen bei Neurofibromatose Recklinghausen. *Fortsche. Rontgenstra* 1955;83:225-9.
 21. Kragh LV, Soule EH, Masson JK. Neurofibromatosis (Von Recklinghausen's disease) of the head and neck: Cosmetic and reconstructive aspects. *Plast Reconstr Surg* 1960;25(6):565-573.
 22. Wannemacher MF, Becker. Orale Manifestation der Neurofibromatose Recklinghausen. *Dtsch Zahnarztl Z* 1969;24:976-982.
 23. Sailer HF. Mandibular asymmetry associated with perimandibular hemangiomas. *J Maxillofac Surg* 1973;104:109.
 24. Mukherji MM. Giant neurofibroma of the head and neck. *Plast and Recon Surg* 1974;53:184.
 25. Koblin I, Reil B. Changes in facial skeleton in cases of neurofibromatosis. *J Maxillofac Surg* 1975;3:23-7.
 26. Berggren RB, Mohier LR, Ferraro JW. Excision of massive hemangio-neurofibroma of the face. *Plast and Recon Surg* 1976;58(4):444-9.
 27. Littlewood AHM, Stilwell JH. The vascular features of plexiform neurofibroma with some observations on the importance of pre-operative angiography and the value of preoperative intra-arterial embolisation. *Br J Plast Surg* 1983;36:501-506.
 28. Frame JW et al. Therapeutic arterial embolisation of vascular lesions in the maxillofacial region. *Br J Oral Maxillofac Surg* 1987;25:181-194.
 29. Vincent SD, Williams TP. Mandibular abnormalities in neurofibromatosis. *Oral Surg* 1983;55(3):253-8.
 30. Freedus MS, Doyle PK. Multiple neurofibromatosis with oral manifestations. *J Oral Surg* 1975;33:360-363.
 31. Epstein JB, Schubert MM, Hatcher DC. Multiple neurofibromatosis. *Oral Surg* 1983;56(5):560-562.
 32. Baden E et al. Neurofibromatosis of the tongue: A light and electron microscopic study with review of the literature from 1849-1981. *J Oral Med* 1984;39(3): 157-164.
 33. Meulen J. Orbital neurofibromatosis. *Clin Plast Surg* 1987;14(1):123-35.
 34. Moore BH. Some orthopaedic relationships of neurofibromatosis. *J Bone Joint Surg* 1941;23:109.
 35. Muller H, Slootweg P. Maxillofacial deformities in neurofibromatosis. *J Maxillofac Surg* 1981 ;9:89-95.
 36. Gupta SK, Kaur S, Sharma OP. Craniofacial neurofibromatosis: A Roentgen Profile. *Australas Radiol* 1984;28:97-105.
 37. Lorson EL et al. Neurofibromatosis with central neurofibromas of the mandible: Review of the literature and report of a case. *J Oral Surg* 1977;35:733-738.
 38. Gupta SK et al. The radiological features of craniofacial neurofibromatosis. *Clin Radiol* 1979;30:553-557.
 39. Holt JF, Wright EM. The radiologic features of neurofibromatosis. *Radiology* 1948;51:647-664.
 40. Henstey CD. Rapid development of subperiosteal bone cyst in multiple neurofibromatosis: Case report. *J Bone and Joint Surg* 1953;35-A:197-203.
 41. Burrows EH. Orbitocranial asymmetry. *Br J Radiol* 1978;51:771-781.
 42. Jackson IT, Laws ER, Martin RD. The surgical management of orbital neurofibromatosis. *Plas Reconstr Surg* 1983;71(6):751-758.
 43. Zimmermann RA et al. Computed tomography of orbital facial neurofibromatosis. *Radiology* 1983; 146:113-116.
 44. Shack RB, Reilley AF, Lynch JB. Neurofibroma of the head and neck. *South-Med J* 1985;78(7):801-4.