Facial Plexiform Neurofibroma in a 13-year-old Girl with Neurofibromatosis-1

Satya Ranjan Misra, G Maragathavalli, Pavitra Baskaran, Varun Rastogi

ABSTRACT

Neurofibromatosis (NF) is an autosomal dominant disorder that affects the bone, the nervous system, soft tissue and the skin. NF is a nevocutaneous condition that can involve almost any organ system existing in two subtypes. NF1 is the most common subtype and is referred to as peripheral NF. Plexiform neurofibromas are diffuse, elongated fibromas coursing along the nerves. These lesions frequently involve the trigeminal or upper cervical nerves. Though plexiform neurofibroma occurs in only 5% of patients with NF1, it is considered pathognomonic feature of NF1. We present a case of plexiform neurofibroma in the left side of the face in a 13-year-old girl with NF1.

Keywords: Type I neurofibromatosis, Plexiform neurofibroma, von Recklinghausen’s disease, Café au lait macules.


INTRODUCTION

Neurofibromatosis type 1 (NF1) was described in 1882 by Friedrich Daniel von Recklinghausen, who suggested the name neurofibroma for neural tissue tumors present in this disease and NF for the condition with multiple neurofibromas. Plexiform neurofibroma (PN), also called plexiform neuroma, pachydermatocele or neurofibromatous elephantiasis (elephantiasis neurofibromatosa), is classified as a benign peripheral nerve sheath tumor that surrounds multiple nervous fascicles. It is a nonmetastatic, highly vascularized, locally invasive tumor that has slow growth. PNs are one of the significant complications of NF1, which may occur during childhood and rarely develop after adolescence. PN can originate malignant peripheral nerve sheath tumor, which occurs in 2 to 5% of patients with PN.

CASE REPORT

A 13-year-old female patient came to the hospital with the chief complaint of deformity on the left side of the face which was present since birth (Figs 1 and 2).

History reveals that the patient was born with facial deformity on the left side of the face. There was swelling of the left eye and at the age of 1 year she underwent surgery following which the left eye was removed. Three months after the surgery, she underwent radiation therapy for the deformity, but she did not complete the treatment. The facial skin in the deformed region turned brownish black in color after the radiation treatment. The deformity has not grown in size. She had again undergone surgery for the correction of the same facial deformity twice about a year back at government hospital. She gives history of a swelling present in the left side of the palate since birth. She also gives history of the presence of multiple brownish black pigmented spots all over her body.

On examination, three swellings are seen on the left side of the face:
1. A single, localized swelling is seen in the left supraorbital region, ovoid in shape, brownish black in...
color, with well-defined margins; the skin over the swelling has hypertrichosis. It is soft in consistency, nontender on palpation. Skin over the swelling is pinchable, there are no secondary changes and no pulsations are felt. A nodular freely movable firm mass is felt on palpation.

2. A single diffuse swelling is present on the left side of the face. The left eyeball is missing and there is ptosis of the upper eyelid. Due to the swelling the left nostril appears raised deviating the nose to the right. The upper lip is swollen and the swelling is diffuse crossing the midline and there is deviation of the mouth toward the right side. There is ptosis of the left side of the upper lip. The color of the swelling is brownish black and it is irregular in shape. The margins of the swelling are ill defined; the surface is irregular with areas of hypertrichosis. A linear surgical scar is present over the malar region extending up to the angle of the mouth on the left side, measuring about 4 cm in length. The nasolabial sulcus is obliterated on the left side. It is soft in consistency and there is no tenderness on palpation. The surface is irregular, margins are ill defined and there is no discharge from the swelling or pulsations felt on palpation.

3. A single localized sessile growth present in the midline of the upper lip, circular in shape, 4 mm in diameter, smooth surfaced, with well-defined margins. It is nontender and firm in consistency. The skin over the swelling is not pinchable and the surface is smooth with well-defined margins. Presence of multiple café au lait macules of varying sizes and smooth margins on the neck, back, trunk, belly, upper and lower extremities (Figs 3 to 8).

The shape of the mouth is irregular and there is diffuse swelling of the upper lip, drooping of the angle of the mouth on the left side. The mouth opening is normal. A freely movable firm mass can be felt on palpation of the labial sulcus in the anterior maxillary region. A single diffuse swelling is present on the left buccal mucosa. The swelling measures about 5 × 4 cm in size causing obliteration of the maxillary and mandibular buccal vestibule on the left side. The margins are ill defined, it is of the mucosal color, smooth surfaced and there are no secondary changes. On palpation the swelling is soft, nontender and there is no fluctuation or discharge from it. A single diffuse swelling is present on the hard palate on the left side measuring about 9 cm anterioposteriorly and 5 cm mediolaterally. The shape is irregular with ill defined margins. The surface is lobulated and there are folding present on the swelling. Focal areas of hyperpigmentation are also seen. The cusps of unerupted 21, 23 are seen. There are no secondary changes. The swelling is firm on palpation, nontender, surface lobulations are felt, and there is no fluctuation, compressibility or reducibility and no discharge (Fig. 9).
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As history reveals the facial deformity is present right from the birth with accompanying brownish pigmentation in different parts of the body, it is a congenital swelling and can be provisionally diagnosed as PN with NF.

The patient was subjected to radiographic investigations. Maxillary cross-sectional occlusal radiograph shows bone destruction in the left side with expansion of the buccal cortex on the left side, the nasal septum is deviated to the right, there is alveolar bone loss seen anteriorly and there is spacing between the anterior teeth (Fig. 10). Posteroanterior view of the skull show opacification and obliteration of the left orbit and maxillary antrum, deviation of the nasal septum to the right side, the skull is enlarged on left parietal region and there is thinning of the mandible on the left side (Fig. 11).

Computed tomographic (CT) scan shows destruction of the left zygomatic bone with a hypodense space occupying lesion, the left orbit is not visualized. The maxillary antrum is obliterated on the left side with deviation of the nasal septum to the right side (Figs 12 and 13).

An incisional biopsy was done under local anesthesia. Two bits of tissue measuring 3 mm in diameter were taken from the swelling in the anterior palate and subjected to histopathological investigation.

Section shows cells with elongated, bent nuclei separated by abundant, fine and sinuous collagen fibers. There is presence of nerve bundles, mild vascularity and areas of hemorrhage. Overlying epithelium in orthokeratinized stratified squamous epithelium of normal thickness (Figs 14 and 15), van Gieson stain positive for collagen fibers (Fig. 16) and immunohistochemistry S-100 positivity is seen in few spindle cells and nerve bundles (Fig. 17) Histopathology is suggestive of neurofibroma.

Correlating the history, clinical finding, radiological findings and histopathological findings the diagnosis of NF1 with facial PN was made. The patient was referred to a pediatric surgeon for further management.

DISCUSSION

The characteristic feature of NF1 is the occurrence of peripheral nerve sheath tumors, neurofibromas, which are the most common cause of symptoms and disfigurement in NF1. The term ‘plexiform neurofibroma’ is used to describe a network-like growth of tumor involving multiple fascicles of a nerve, leading to a diffuse mass of thickened nerve fibers surrounded by proteinaceous matrix. PNs can be deep or superficial in location or a combination of the two.

These tumors appear in utero or during early childhood in some patients and, therefore, they are present to interact with the skull, orbital structures and globe while they are still developing. The tumors affect nearby bone and invade almost all of the orbital structures, including the globe, extraocular muscles, optic nerve sheath and branches of the sensory nerves.
NF1 is due to an alteration of the NF1 gene and the prevalence is about 1:4,000. This gene is a tumor suppressor gene located in the long arm of chromosome 17 (17q11.2). The loss of this gene’s function due to a mutation determines an increase in cell proliferation and the development of tumors. National Institutes of Health (NIH), 1990 has given the following criteria for the diagnosis of NF1.

Diagnostic criteria of NF1 (National Institutes of Health, 1990) are as follows:
1. Six or more café au lait spots >5 mm in prepubertal patients or >15 mm in postpubertal patients.
2. Two or more neurofibromas of any type or a PN.
3. Ephelides in axillary and inguinal regions.
4. Two or more Lisch nodules.
5. A characteristic bone lesion, such as sphenoid bone dysplasia or thinning of cortex of long bones, with or without pseudoarthrosis.
6. Incomplete status, but having a first-degree relative (parent, brother or son) who meets NIH criteria.
7. Two or more criteria are needed for diagnostic confirmation of NF1.

Pigmented lesions are a common manifestation in NF1. These lesions usually appear during the first years of life or are present at birth, either as café au lait spots or as freckles. Café au lait spots are hyperpigmented maculae that may vary in color from light brown to dark brown, their borders may be smooth or irregular. They may appear anywhere on the skin, but they are less common on the face. Inguinal and axillary freckles (Crowe’s sign) are frequently present. Multiple skin neurofibromas as well as angiomas are also characteristic in NF1. There exist two main clinical forms of neurofibroma: Localized and PNs. Localized neurofibroma is the most frequent one in NF1. It develops along a peripheral nerve as a focal mass with well-defined margins. It is rarely present at birth but appears in late childhood or early adolescence. The number of localized neurofibromas generally increases with age, and there is an increase in size and number of the lesions during pregnancy and puberty.
Facial Plexiform Neurofibroma in a 13-year-old Girl with Neurofibromatosis-1

PN spreads along the peripheral nerve and may affect some nervous rami. This is a poorly circumscribed and locally invasive tumor. About 21% of patients with NF1 are affected with PNs. Morbidity of PNs in NF1 is high since they tend to grow until reaching a great size and producing disfigurement. Besides, the risk of malignization is between 2 and 5%. Due to its diffuse involvement/ appearance and soft consistency, palpation of neurofibroma is similar to that of lipoma, vascular malformation, lymphangioma or rhabdomyoma.

Bone involvement in NF1 may be due to both external resorption and internal osteolytic defects. External resorption may be due to the pressure applied on the bone by the neurofibroma, as it happens in the case here reported. It is well known that in NF1 bone malformations such as kyphoscoliosis or pseudoarthrosis may appear, and the temporomandibular joint (TMJ) may be involved. Skeletal involvement is present in almost 40% of patients with NF1, being scoliosis the most common skeletal pathology. Iris hamartoma, acoustic neuroma, central nervous system tumors (glioma, glioblastoma), macrocephaly and mental retardation (up to 40% of cases) can also be found. Oral cavity involvement appears in 66 to 72% of the cases of NF1. Lengthening of fungiform papillae happens in 50% of cases and is the most frequent finding. In 25% of NF patients oral neurofibromas can be seen. There is no racial, gender or age predilection for the development of oral neurofibromas in NF1. Neurofibromas may appear in every tissue, soft or hard, in the oral cavity. The most commonly affected site is the tongue. In the case here reported the neurofibroma was located in the gum, which is not a common location. Shapiro et al state that gum involvement by neurofibroma in NF1 patients is 5%.

Localized oral neurofibromas usually appear as...
asymptomatic nodules covered by normally colored mucosa. However, when adjacent to cranial nerves, they can impair motor function of facial or hypoglossal nerves or the sensitivity of trigeminal nerve.

Gingival neurofibromas may cause dental malposition or impaction. NF1 patients may also show facial disfigurement due to hypoplasia or hyperplasia of maxilla, mandible, malar bone and TMJ. Facial PNs may also cause a facial asymmetry as seen in the present case. Exophthalmos may also be present due to a dysplasia of the sphenoid major wing. Radiological findings in oral neurofibromas include mandibular channel, mandibular foramen and mental foramen widening. Neurofibromas may seldom be primarily intraosseous; in that case they usually appear as a unilocular, well-defined radiolucency. In the case here reported radiological manifestations, such as destruction of bone and sphenoid dysplasia were found. Most neurofibromas show low attenuation in CT scans, although some of them may show soft tissue density. Low density lesions contain a variable amount of Schwann cells, which are rich in lipids, cystic degeneration and xanthomatous alterations.

High density areas are thought to represent collagen rich or cellular areas. In magnetic resonance imaging (MRI), lesions show a low signal in T1 and a high signal in T2, with a variable highlighting with the contrast. A high peripheral signal with a low central signal in T2 weighted images (bull’s eye sign) is a typical sign of neurofibromas. A similar sign can be seen in CT; in this case there is a central high signal. Histologically, neurofibromas are composed of a mixture of Schwann cells, perineural cells and endoneural fibroblasts, and they are not encapsulated. Schwann cells account for about 36 to 80% of lesional cells. These constitute the predominant cellular type and they usually have widened nuclei with an undulated shape and sharp corners. On electron microscopy Schwann cells can be seen embracing axons. These can be highlighted with silver or acetylcholinesterase staining or with immunohistochemical techniques when using the fluorescent microscope. It is estimated that between 0.7 and 31% of cells are perineural cells. In seldom cases this type of cells can predominate.

Neurofibromatous lesions usually evolve slowly, without pain, but during growth, puberty or pregnancy their evolution may be accelerated. PN can be symptomatic at birth or become symptomatic through time. Early occurrence supports the idea that PN are congenital lesions, although there may be patients that develop PNs after 20 years of age. Total or partial resection of neurofibromatous lesions is the treatment of choice to solve esthetic or functional problems; it is advisable to wait for treatment until growth has been completed thus diminishing the risk of recurrence. Total resection with 1 cm margins whenever feasible is the treatment of choice for accessible and small tumors. Friedrich et al suggest that early surgical interventions in small-sized PN in children can be advantageous, especially in the strategy to prevent their progression. Radiotherapy or chemotherapy are not recommended for treatment. Thalidomide has been used to treat pain in PNs. Malignant transformation rate of neurofibromas in NF1 is 3 to 5 %. NF1 patients must receive genetic counseling since this is an autosomal dominantly inherited disease and the likelihood of transmission to the children is 50% in both sexes. Malignant transformation to neurofibrosarcoma bears a very bad prognosis and distant metastases are frequent, being the mean survival of 15% at 5 years. Some authors state that recurrence may appear after surgical resection and that multiple recurrences increase the risk for malignant transformation.

CONCLUSION

Emphasis must be made on the fact that while examining the oral cavity, dental surgeons should keep this disease under consideration when oral lesions characteristic of NF1 are present. These patients must be reviewed long-term because of eventual complications, especially that of malignant transformation.

REFERENCES

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ABOUT THE AUTHORS

Satya Ranjan Misra (Corresponding Author)
Reader, Department of Oral Medicine and Radiology, Institute of Dental Sciences, Bhubaneswar, Odisha, India, e-mail: drsatyaranjanmds@gmail.com

G Maragathavalli
Professor and Head, Department of Oral Medicine and Radiology Saveetha Dental College, Chennai, Tamil Nadu, India

Pavitra Baskaran
Lecturer, Department of Oral Medicine and Radiology, SRM Kattankulathur Dental College, Chennai, Tamil Nadu, India

Varun Rastogi
Lecturer, Department of Oral Pathology, DJ Dental College, Modinagar Uttar Pradesh, India