NEUROFIBROMA OF THE MANDIBLE IN A CHILD WITH NEUROFIBROMATOSIS TYPE 1

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ABSTRACT

This case report describes intraosseous neurofibroma located in the alveolar ridge on the posterior region of the mandible, causing bony expansion and impaction and displacement of the permanent molars in a child with Neurofibromatosis 1 (NF-1).

The clinical, radiographic, and histopathologic features and surgical treatment of the tumor is described.


KEY WORDS: Neurofibroma; neurofibromatosis; von recklinghausen’s disease.

INTRODUCTION:

Neurofibromatosis type 1 (NF-1), also known as Von Recklinghausen’s disease, is a multisystem genetic disorder, characterized by increased cell proliferation and tumor development. It affects 1 out of 3000 to 4000 live births.1 An abnormality of the NF-1 gene located on chromosome 17 is found with this disease. NF-1 is inherited in an autosomal-dominant fashion but also appears as a result of a new mutation. In the disease process, ectodermal and mesodermal derivatives are affected due to the defect in the embryonic neural crest cells.

According to the National Institute of Health (USA) Consensus Development Conference,2 the diagnosis of NF1 is based on the presence of two or more of the following criteria:

- Six or more cafe-au-lait spots (melanin pigmentation of the skin)
- Two or more neurofibromas of any type, or one or more plexiform neurofibroma
- Freckling in the axillary or inguinal region
- Optic glioma (tumor of the optic pathway)
- Two or more Lisch nodules (iris hamartomas)
- A distinctive osseous lesion such as dysplasia of the sphenoid bone or dysplasia or thinning of long bone cortex
- A first degree relative with NF-1

Neurofibroma is a benign peripheral nerve sheath tumor. It is derived from the cells that constitute the nerve sheath and is composed of perineural cells, Schwann cells, and fibroblasts within a collagenous or myxoid matrix. Although neurofibroma may be seen as an isolated solitary form, it is a predominant feature of NF-1.3 In NF-1 patients, neurofibromas occurring in the skin, mucous membranes and viscera may be seen anywhere in the body. Despite their common occurrence in the head and neck region, neurofibromas are comparatively rarely encountered in the oral cavity. Reported cases usually affect the soft tissues, the most frequent site being the tongue. Other common sites include gingiva, palate, cheeks and the floor of the mouth.4-6 Intraosseous involvement of neurofibroma in NF-1 patients is reported very rarely.4-5 Here, we report a case of intraosseous neurofibroma located in the alveolar ridge on the posterior region of the mandible, causing bony expansion and impaction and displacement of the permanent molars in a child with NF-1. The clinical, radiographic, and histopathologic features and surgical treatment of the tumor is described.

CASE REPORT:

A 5-year old girl was referred to the clinics of Pediatric Dentistry, Dental Faculty of Süleyman Demirel University for the evaluation of gingival enlargement on the posterior region of the left mandible. The enlargement had become noticeable for the last four months. Previously she was prescribed antibiotic by her dentist for the assumption that the swelling was due to odontogenic infection. However no favorable outcome was attained.
On intraoral examination, a submucosal diffuse enlargement of the alveolar ridge extending from the left incisors to the retromolar area was noted. The overlying mucosa was intact. The enlargement had a rubbery texture on the retromolar area but was rigid on teeth bearing area. The patient was symptom-free and no signs of inflammation were observed. The lower left primary first and second molars, right primary first molar and upper left primary molar were decayed. In addition, the crowns of maxillary incisors and first molars showed both clinical and radiological hypomineralisation. The panoramic graphy showed a poorly defined, diffuse rarefaction located on the superior aspect of the posterior mandible above the germs of permanent molars (Figure 1). Enlargement of the inferior alveolar canal (Figure 2), especially towards the mental foramen, narrow condylar process and notching of the angulus were also observed on the affected side (Figure 1).

**Figure 1.** Panoramic graphy at presentation showing poorly circumcised refaction above the unerupted permanent molars.

**Figure 2.** Coronal section of MR image showing the enlargement of the inferior alveolar canal on the left side.

Medical history revealed that she was diagnosed with neurofibromatosis type 1 (NF1) at the age of 4 and was under the care of her pediatrician. On physical examination, several cafe au lait spots with varying diameters on the front and back trunk together with freckling on the neck and axillary region was noted (Figure 3 a and b). She also had short stature for her age and had a mild scoliosis. The parents reported that she had mild learning disability. Family history revealed that she had no immediate or distant relatives who were diagnosed with NF 1 or had any similar complaints, the case representing a sporadic case.

**Figure 3a.** The clinical photograph showing the café au lait spots with varying diameters on the front trunk and freckles on the arm pits.

**Figure 3b.** The clinical photograph showing the café au lait spots on the back.

Based on the medical history and the clinical presentation, a provisional diagnosis of neurofibroma was made and a treatment plan to closely follow the tumor growth was agreed.

By the age 8, on clinical examination, although the tumor seemed to grow very slowly (Figure 4) it was noted that the first molar on the affected side failed to erupt. Panoramic graphy revealed a radiolucent lesion with a well-demarcated and scalloped border, extending from the distal aspect of the second primary molar to the retromolar area. The lesion included and displaced the unerupted permanent first and second molars (Figure 5). The MR images showed that the lesion was extended to both lingual and buccal aspects of the mandible with bony destruction (Figure 6). She had no paresthesia on the tongue or lips. Extraorally she had mild swelling on the left side of the mandible.

**Figure 4.** Panoramic graphic showing the radiolucent lesion.
Neurofibroma of the mandible

Unilateral enlargement of the alveolar ridge extending from incisor region to the retromolar area. The lesion was bony hard on the teeth bearing area and was rubbery on the retromolar area.

She was then seen by the Oral and Maxillofacial Department for the evaluation and possible surgical excision of the lesion. Aspiration biopsy was carried out but was not productive. An incisional biopsy was performed and the specimen was sent for histopathological examination. Microscopically, interlacing bundles of spindle-shaped nerve cells that exhibit wavy nuclei, associated with delicate collagen bundles and variable amounts of myxoid matrix (Figure 7). Immunohistochemical detection of S-100 protein which is specific for cells of neural crest origin (Schwann cells) was performed to confirm the neural origin of the lesion. Focal cytoplasmic and/or nuclear S100 protein positivity was evident. Based on the histological findings a definitive diagnosis of simple neurofibroma was established.

A decision was made to surgically excise the tumor under local anesthesia. The lesion was removed together with primary second molar, unerupted permanent first and second molars. During surgery, while the intraosseous part of the mass was easily enucleated, the parts of the lesion attached to the lingual and buccal mucosa was difficult to remove by blunt dissection as the lesion was firmly attached to the soft tissues. No surgical intervention was performed on the alveolar bony enlargement around primary canine and primary first molar.

On a one year follow up, although the bony enlargement of the alveolar ridge around the canine and first deciduous molar was still present, there was no sign of recurrence of the tumor.

DISCUSSION:

Pigmented skin lesions (due to the focal melanosis in the epidermis), cafe au lait spots and freckling, are the hallmark features of NF1. These lesions may be present at birth or become obvious during the early years of life. The patient presented in this report had numerous café au lait macules especially in the front and back of the trunk and freckling under the arm and neck. She also had short stature for her age, had mild scoliosis and had mild learning disability, which are also among common features of NF-1. Our patient had not developed cutaneous neurofibromas and Leish nodules of the iris which are pathognomonic of NF-1. However these lesions do not usually appear until adolescence and young adult years. NF-1 is a progressive disease but has a wide range of severity. Future disease severity and prognosis in a child with this disease is not possible to predict. Therefore, patients with NF-1 should be reviewed regularly for the early detection and appropriate management of any disease complications such as optic gliomas which may cause visual loss or field defects.

The clinical diagnosis of neurofibroma was fairly straightforward in our case because in addition to clinical presentation i.e. unilateral, diffuse enlargement of the alveolar ridge together with radiolucent lesion on the
radiography, she showed the other clinical features of NF-1 and the medical history revealed that she was previously diagnosed with the disease. However, schwannoma, traumatic neuroma, fibroma, granular cell tumor and other benign mesenchymal tumors should also be considered in the differential diagnosis of unilateral, diffuse, fibrous enlargement on the alveolar mucosa and gingiva. Radiographic differential diagnosis for the case presented includes odontogenic cysts, odontogenic tumors, and other benign and malignant tumors owing to features of unilocular radiolucency associated with impacted teeth with well-defined, sclerotic border.

There are two types of neurofibroma seen in NF-1, simple (disseminated, cutaneous) neurofibroma and plexiform neurofibroma both of which can occur in the oral mucosa. While simple neurofibroma is usually small in size plexiform neurofibroma is often widespread and can grow extensively. Friedrich et al reported 22 patients with disseminated neurofibroma and 26 patients with plexiform neurofibroma affecting oral and maxillofacial region in NF-1 patients. They showed that while patients who had simple neurofibroma had very few jaw malformations, majority of patients with plexiform neurofibroma had jaw malformations such as impacted, displaced teeth or tooth aplasia on the affected area. They also showed that 21 of 24 patients with plexiform neurofibromatosis had the tumor invading the alveolar ridges of the affected side. The histological diagnosis of our case was simple neurofibroma but the tumor caused fairly large bony destruction as well as displacement of tooth buds and delay in eruption.

Apart from neurofibromas, NF-1 may have various other manifestations in the oral cavity. The common findings include enlarged fungiform papillae, bony deformities, wide inferior alveolar canal and enlarged mandibular foramen. The radiographic examination of our patient also showed malformations of the condylar process and angulus as well as enlargement of the inferior alveolar canal. It was stated that enlargement of the mandibular canal of the affected side indicates tumor invasion of the inferior alveolar nerve. In addition, the jaw deformities observed on the same side were reported to imply the embryogenic origin of the tumor.

The dental status of NF1 patients has not yet been fully investigated. A recent study which recruited 110 NF-1 patients showed that NF1 per se does not predispose to caries. Although they found a lower incidence of caries in NF1 patients under 35 years of age, as compared to age group controls, the differences between NF1 patients and the reference population diminished with age. Another study compared the dental caries prevalence of 18 NF1 affected individuals with their unaffected siblings and found a similar prevalence of caries in the affected subjects and their unaffected sibs. The caries rate of our patient was considered in normal range for her age group.

It is generally agreed that the management of neurofibroma formation in NF-1 patients is close observation of the patient. Excision is considered in large, painful or strategically placed tumors if the risks to the patient are low. Tumor may also be reduced for aesthetic and/or functional purposes. Neurofibromas are slow growing tumors but may show an accelerating growth especially during preadolescent/adolescent period. In our case, during the follow up period from the age of 5 to 8, the tumor showed intrabony growth causing expansion of the bone and displacement of tooth buds and failure of eruption. Therefore excision of the tumor was decided upon.

Bekisz et al reported neurofibroma affecting gingiva around all teeth on the right side of both the maxilla and mandible which hindered eruption of the teeth. Instead of total resection of the tumor, they removed only the thick gingival sections that seemed to impair tooth eruption. They reported that this procedure allowed the eruption of the teeth in the involved area. However, in their case, no bony invasion of the tumor was evident during the period of tooth eruption. On contrary, our patient had significant bone destruction by the growing tumor and the first and second permanent molars were displaced considerably inside the tumor with resultant failure of eruption. The involved teeth had to be sacrificed for the total removal of the tumor.

As NF-1 is a progressive disease, lifelong evaluation of the patients for newly forming or pre-existing lesions is important. The annual evaluations include dermatological examination, ophthalmologic examination, evaluation of the physical development in children and further examinations on the basis of signs and symptoms. Regular intraoral examination should also be performed. Although extremely rare, one serious complication of neurofibroma is malign transformation, hence rapid growth or pain associated with the lesions should be biopsied immediately to rule out the possible malign transformation. Pediatric dentists may be the first clinicians to identify neurofibroma occurrence in the oral cavity, therefore the medical history of the pediatric patients should be taken into account for the differential diagnosis of any swellings in the oral cavity.

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