

Up-to date Review and Case Report

Neurofibromatosis type I and supernumerary teeth: up-to date review and case report

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Abstract – Introduction: Neurofibromatosis type I (NF1) is a genetic disease that may involve oral manifestations such as supernumerary teeth. **Case report:** A 17-year-old male patient with NF1 was referred by an orthodontist for avulsion of wisdom teeth and six supernumerary teeth. Ten teeth were removed under general anesthesia in December 2015. **Discussion:** Management of supernumerary teeth is very controversial and patient care of NF1 is complex. **Conclusion:** Even though the presence of supernumerary teeth in cases of NF1 is not well-known, patient care is extremely important and requires a team of specialists.

Mots clés :
neurofibromatose
de type i / maladie
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surnuméraires

Résumé – Les dents surnuméraires dans la neurofibromatose de type I : cas clinique et revue de la littérature. Introduction : La neurofibromatose de type I est une maladie génétique qui peut induire des manifestations orales comme la présence de dents surnuméraires. **Observation clinique :** Un homme de 17 ans présentant une NF1 a été adressé par son orthodontiste pour l'avulsion de ses dents de sagesse et 6 dents surnuméraires. Les 10 dents ont été extraites sous anesthésie générale en décembre 2015. **Discussion :** La prise en charge des dents surnuméraires est très controversée et la prise en charge des patients atteints de NF1 est complexe. **Conclusion :** Même si la présence de dents surnuméraires chez les patients atteints de NF1 est mal connue, la prise en charge de ces patients est très importante et une équipe pluridisciplinaire est nécessaire.

Introduction

Neurofibromatosis type I (NF1) is the most frequently autosomal dominant inherited disease. It occurs in 1 in 3,000 to 3,500 newborns worldwide. The *NF1* gene is located on chromosome 17 (17q11.2) and is composed of 59 exons. It is a tumor-suppressor gene, encoding the cytoplasmic protein neurofibromin.

In 1988, the National Institutes of Health (NIH) Consensus Development Meeting defined the criteria to diagnose NF1. The diagnostic criteria for NF1 are met in an individual if two or more of the following are found: six or more cutaneous café-au-lait macules over 5mm, two or more neurofibromas of any type or one plexiform neurofibroma, an optic glioma, two Lisch nodules, lentigos of the axilla or the inguinal region, and a first-degree relative with NF1 (Tab. I).

In the same family, phenotypic expression is highly variable. Many multisystemic complications such as cerebral tumors or vasculopathies could lead to death [1,2]. Oral and maxillofacial manifestations may also be found in patients with NF1, such as gingival enlargement and pigmentation, oral and perioral neurofibroma, osseous lesions of the maxilla or the mandible, and dental abnormalities [3-12].

However, literature is scarce on NF1 and the occurrence of supernumerary teeth, also called hyperdontia.

Case report

In July 2015, a 17-year-old male patient was initially referred by his orthodontist for avulsion of wisdom teeth and supernumerary teeth (Fig. 1 and Fig. 2). He presented an optic glioma with hyperprolactinemia. He had many cutaneous

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Table I. Diagnostic criteria for neurofibromatosis type I according to the National Institutes of Health (NIH) Consensus Development Meeting (1988).

Tableau I. Critères diagnostiques de la neurofibromatose de type I d'après le National Institutes of Health (NIH) Consensus Development Meeting (1998).

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- six or more cutaneous café-au-lait macules over 5?mm in greatest diameter in prepubertal individuals and over 15?mm in greatest diameter in postpubertal individuals
 - two or more neurofibromas of any type or one plexiform neurofibroma
 - lentigos of the axilla or the inguinal region
 - an optic glioma
 - two or more Lisch nodules
 - a distinctive osseous lesion such as sphenoid dysplasia, or thinning of the long bone cortex with or without pseudarthrosis
 - a first-degree relative with NF1
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Fig. 1. Panoramic X-ray before orthodontic treatment (10/03/2010):

- class II crowding
- superior endoalveoly
- anterior overbite
- supernumerary tooth between 36 and 37
- wisdom teeth.

Fig. 1. Radiographie panoramique avant traitement orthodontique (10/03/2010) :

- classe II dysharmonie dento-maxillaire
- endoalvéolie maxillaire
- béance antérieure
- dent surnuméraire entre 36 et 37
- dents de sagesse.

café-au-lait macules on the chest and back, as well as Lisch nodules. Moreover, he had visual deficiency. As a child, he presented early puberty and difficulties learning and writing. He was treated for epilepsy with levetiracetam (Keppra®).

His father also had NF1 with Lisch nodules and many neurofibromas, including deep and painful ones. He had surgical removal of a large malignant abdominal neurofibroma. His medical history also included one epileptic seizure when he was 15 years of age. He did not have supernumerary teeth.

Both of the patients were monitored by the reference center for rare diseases in ophthalmic genetics (CARGO) at Strasbourg University Hospital. Gene sequencing in the father showed total suppression of exon 15 due to a c.2410G>A mutation, leading to NF1. The extra-oral examination of the young man showed no facial asymmetry, and no neurofibroma on his face (Fig. 3). Intra-oral examination showed bilateral class 1, with centered inter-incisive points. No supernumerary teeth were visible in the mouth. Any sign of neurofibromatosis type I was



Fig. 2. Panoramic X-ray after orthodontic treatment (29/05/2014).
Fig. 2. Radiographie panoramique après traitement orthodontique (29/05/2014).



Fig. 3. Extra-oral view.
Fig. 3. Vue extra-orale.

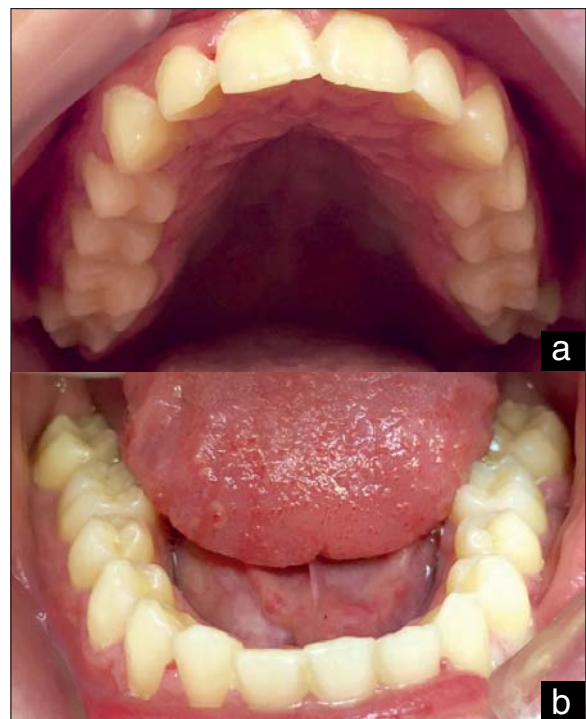


Fig. 4. Intra-oral view. a. Maxilla. b. Mandible.
Fig. 4. Vue intra-orale. a. Maxillaire. b. Mandibule.

observed intra-orally (Fig. 4). On the panoramic X-ray (Fig. 5), four wisdom teeth and six supernumerary teeth (14bis, 34bis, 35bis, 35ter, 44bis and 48bis) were present and impacted. Moreover, some specific features of NF1 were found, such as enlargement of mental foramina. On cone beam computed tomography (CBCT) (Fig. 6), the supernumerary teeth were all

found to be in palatine or lingual position. They were eumorphic, i.e. they had the same morphology as permanent teeth.

Following the consultation, the team decided to avulse ten teeth under general anesthesia in December 2015, with the use of prophylactic antibiotics (amoxicillin 2?g) and steroidal anti-inflammatory drug (methylprednisolone 2?mg per kg)



Fig. 5. Panoramic X-ray before surgery (12/11/2014).

Fig. 5. Panoramique dentaire avant chirurgie (12/11/2014).

during induction. On the day of the intervention, a palatine and lingual total-thickness flap was raised, followed by alveolectomy, luxation and avulsion of all the teeth. The surgeon performed curettage of dental follicles, rinsed the alveolar cavity with saline solution, and closed gingival flaps using Rapid Vicryl 3.0. The patient stayed in hospital overnight because of the risk of post-operative mouth floor edema due to the bilateral lingual surgical approach.

Antibiotics, analgesic therapy, and mouth rinses were prescribed in the first week. A control X-ray was performed after surgery (Fig. 7).

The authors declare that the patient provided consent for this publication, including medical history, x-rays and pictures.

Discussion

In the literature, the incidence of hyperdontia is between 0.15% and 3.9%. However, less than 1% of cases present more than five supernumerary teeth [13]. Non-syndromic cases with many supernumerary teeth are extremely rare [14]. The etiology of hyperdontia is poorly known. Some genetic and environmental factors are thought to be responsible for this anomaly, even though the subject is still controversial [15]. Syndromic hyperdontia shows that genetic factors are responsible for supernumerary teeth. However, not all patients with the same syndrome, even in the same family, have supernumerary teeth, showing that gene expression is variable and phenotype penetrance is incomplete.

In this case, the father and the son presented the same disease (NF1) but with different phenotypic expressions. Neurofibromatosis type I is considered to have an autosomal dominant pattern of inheritance with variable phenotypic

expression [2]. In this case, the deletion of the NF1 gene was not large, leading to a mild phenotype.

Although it is a genetic disease, some environmental factors are also involved and could influence the phenotype in a family. The genes influenced by environmental factors are not located at the NF1 locus. For example, they may be responsible for epilepsy, optic glioma, and learning difficulties [5].

Most articles considering NF1 describe missing teeth [4,6]. Hyperdontia is poorly described, especially as an isolated facial manifestation, as in this case report. Freeman and Standish [9] and Shapiro *et al.* [5] first mentioned hyperdontia with NF1. The presence of supernumerary teeth is more likely associated with other facial abnormalities, such as a tumor-like plexiform neurofibroma [6,16-18]. Most articles hypothesize that the missing or supernumerary tooth are related to local tumor expression of NF1. This could be understandable in cases associated with other facial abnormalities, but in a case with a high number of isolated supernumerary teeth, the mechanism is far from being understood. Hyperdontia when described in NF1 [6,10,16-18] only appears as retained or impacted teeth, as in the case of our patient.

NF1 can also induce jaw malformations, such as enlarged mandibular foramina, wide inferior alveolar canals, and intra-bony lesions [5,14,19].

Patient care is also controversial. In fact, some authors advocate conservative management when teeth are impacted and do not cause any complications. They follow a “wait and see” approach. This therapeutic abstention consists in regular controls (radiological and clinical examination) [20,21]. On the contrary, some authors recommend removal of supernumerary teeth [22-24]. They suggest that this avoids root resorption of adjacent teeth due to pericoronal follicles. When supernumerary teeth are on the arch they have to be removed. This is

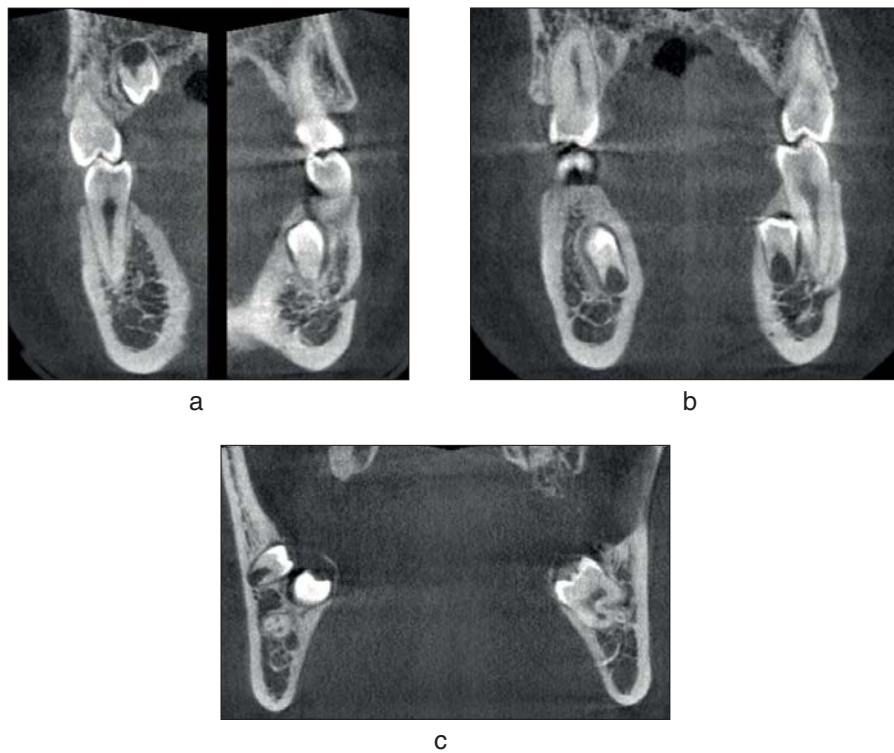


Fig. 6. CBCT: Supernumerary teeth were impacted. a. 14bis and 34bis. b. 34bis and 44bis. c. 38, 48 and 48bis
Fig. 6. CBCT: Les dents surnuméraires sont incluses. a. 14bis and 34bis. b. 34bis and 44bis. c. 38, 48 and 48bis.



Fig. 7. Panoramic X-ray after surgery (15/01/2016).
Fig. 7. Radiographie panoramique après chirurgie (15/01/2016).

when all teeth are present, but are not in the right position, i.e. in vestibular or in palatal/lingual position [21].

The approach depends on the age of the patient, the position of supernumerary teeth, and the risk of complications. In this case report, the decision on teeth removal was taken by different members of the team (oral surgeon, maxillofacial surgeon, and orthodontist). Supernumerary teeth were close to

adjacent roots and their removal was simple. This avoided complications such as root resorption, eruption, and permanent teeth movement, after orthodontic treatment was performed.

The time of diagnosis is also important to take a decision. Some authors prefer to avulse teeth immediately after diagnosis [22] and others later [23]. In this case report, some

teeth only appeared at the end of the orthodontic treatment so the decision was uncomplicated. Above all, at the age of 17, the benefit/risk balance of the “wait and see” approach was too demanding (high intensity care, risk of radiation, time and costs for the patient).

Conclusion

The oral and maxillofacial manifestations of NF1 are rather poorly known. The treatment of this disease is mainly symptomatic. Multidisciplinary management is necessary because treatment planning depends on many factors.

Conflicts of interests: none declared.

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