

# Cranio-Orbital-Temporal Neurofibromatosis With Cerebral Hemiatrophy Presenting as an Intraoral Mass: A Case Report

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**ABSTRACT** Neurofibromatosis, NF, is a group of genetic disorders that primarily affect the cell growth of neural tissues. Cranio-orbital-temporal neurofibromatosis is an uncommon subtype of neurofibromatosis characterized by neurofibromas, cranial defects, and specific bone lesions. This case report presents the signs of cranial defects in a 24-year-old Caucasian woman with type 1 NF. Mandibular malformations due to NF and dental defects caused by intraoral masses and radiographic images are presented.

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The term “neurofibromatosis,” NF, is used to define a group of genetic disorders that primarily affect the cell growth of neural tissues. There are two forms of NF: neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2).<sup>1,2</sup> These two forms have few common features and are caused by mutations of different genes.<sup>2</sup> Cranio-orbital-temporal neurofibromatosis (NF-1), also known as von Recklinghausen’s disease, is an autosomal dominant inherited disorder that presents with abnormalities of the skin, nervous system, bones and soft tissues.<sup>3,4</sup> It is one of the most frequent human genetic diseases, with a prevalence of one case in 3,000 births, and with no prevalence for gender or

race.<sup>5</sup> The neurofibromas are neither circumscribed nor encapsulated, and diffusely infiltrate tissues.<sup>6</sup> The incidence of head and neck involvement ranges from 1 percent to 22 percent.<sup>7</sup>

This case report presents the signs of type 1 NF in a Caucasian woman.

## Case Report

A 24-year-old Caucasian woman was referred to the oral diagnosis and radiology clinic with the chief complaint of dental caries and difficulty chewing. She had been diagnosed with cranio-orbital-temporal neurofibromatosis since 1987 and was a regular patient of the ophthalmology and neurology departments. Right ophthalmic enucleation was performed due to orbital neurofi-

broma-related pulsatile exophthalmos in 1994. Reportedly, several reconstructive operations had been performed thereafter to repair the cranial defects. Her family history was positive for neurofibromatosis in both her cousin and grandfather.

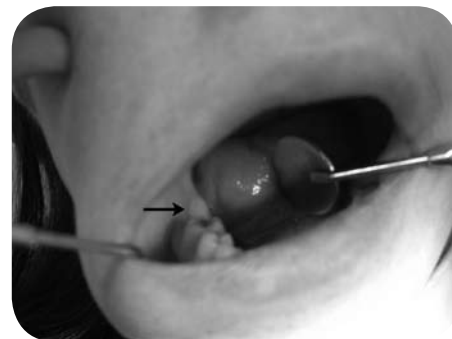
Clinical examination revealed facial asymmetry and deviation of the mandible rightward during opening. There were café au lait spots on the chest, and right palatal and retromolar intraoral masses (**FIGURES 1 AND 2**). The lesions were rubber-hard to palpation and painless. Previous biopsies of the ophthalmic enucleation reported NF. The patient did not approve additional biopsies of the intraoral masses.

Panoramic radiographic examination presented a poorly developed right posterior body and condyle of the mandible, enlarged right mandibular foramen, and a hypoplastic right zygomatic arch. The mandibular right second and third molars and maxillary molars were unerupted. The maxillary right second premolar was rotated (**FIGURE 3**). Because of the unerupted teeth, the patient had difficulty in chewing, which confirmed her chief complaint.

In order to evaluate the craniofacial abnormalities, a 3-D craniofacial CT was obtained. The 3-D CT presented hypoplasia in body and condyle of the right mandible and zygomatic arch, and aplasia of the right sphenoid wing (**FIGURES 4 A-B**). A previous MRI of the patient demonstrated right hemiatrophy, enlargement of the right third ventricle. Additionally, there was enhancing and extension of the right temporal lobe into the right infratemporal fossa, maxillary, and enucleated ocular area. Although surgery of the affected sites, including removal of impacted teeth, was offered as a treatment plan, the patient refused to undergo treatment except for caries control that required conservative treatment. Therefore, the patient was scheduled for regular recall examinations.



**FIGURE 1.** Intraoral mass in the right palatal region.



**FIGURE 2.** Intraoral mass in the right retromolar region.



**FIGURE 3.** Panoramic radiograph revealing several impacted teeth, enlarged right mandibular foramen, hypoplastic right zygomatic process, and hypoplastic condyle of the right mandible.

## Discussion

NF-1, is an autosomal dominant inherited disorder that presents abnormalities of various systems and tissues.<sup>3,4</sup> Despite the advances in molecular diagnostic techniques, the diagnosis of NF is still based on clinical criteria. The National Institute of Health Consensus Development Conference originally established the diagnostic criteria for NF1 and NF2 in 1987.<sup>8</sup> Two or more neurofibromas constitute an important feature of NF1. Additionally, café au lait spots, axillary and inguinal freckling, optic glioma, Lisch nodules, and specific bone lesions are also common clinical features of NF1.<sup>2</sup> At least two of these clinical criteria are required to diagnose NF1.<sup>9</sup> In the present case, both café au lait spots and bone lesions were detected in the patient.

Cranio-orbital-temporal NF is an uncommon subtype of NF-1 characterized by orbital neurofibromas, pulsatile exophthalmos, sphenoid wing dysplasia, expansion of the temporal fossa, and herniation of the temporal lobe into the orbit.<sup>10</sup> Right pulsatile exophthalmos,

right sphenoid wing aplasia, expansion of the right temporal fossa and herniation of the temporal lobe into the orbit were also observed. In a majority of NF-1 patients with sphenoid dysplasia (as with the authors' patient), the lateral wall of the orbit is deficient and leads to the decompression of neurofibromatous tissue or retrobulbar fat into the temporal fossa.<sup>11</sup> An increase in overall cerebral volume has been stated to be the reason for changes in the structure of the sphenoid. Abnormal vascularity may be the reason for bone resorption adjacent to orbital fissure.<sup>12</sup>

Skeletal defects such as aplasia, dysplasia, or local bone atrophies may occur as a result of expansive growth of neurofibromas within the medullary cavity.<sup>13</sup> The main features in the craniofacial region include bony craniofacial anomalies such as ethmoid and maxillary hypoplasia, sphenoid bone dysplasia, hypertrophy and atrophy of facial bones, radiolucent bone defects, and widened mandibular canal and mental foramen.<sup>14</sup> In addition, certain malformations of the mandible attributable to NF include deviation of the man-



FIGURES 4A AND B. Three-dimensional craniofacial CT demonstrating multiple cranial deformities.

dible, minimal swelling of the intraoral soft tissue, coronoid notch deformity, pseudoelongation of the coronoid process, deformity of the ramus, flattened or missing gonial angle, deformity or hypoplasia of the body of the mandible, impacted teeth, and hypoplasia of the mandible and zygoma were also determined.<sup>15</sup>

The authors' case is a typical presentation of NF associated with certain malformations of the mandible, including a poorly developed right posterior body and condyle of the mandible, enlarged right mandibular foramen, and a hypoplastic right zygomatic arch was detected. The presence of displaced, impacted, or missing teeth, particularly in the mandible, was recognized as oral manifestations of NF-1.<sup>15</sup>

In the present case, the mandibular right second and third molars and maxillary molars were impacted. In NF1, gingival neurofibroma is uncommon.<sup>1</sup> However, in the authors' case, the gingival masses in the right palatal and retromolar regions were considered as gingival neurofibromatosis, although the patient did not permit confirmation of this finding by biopsy. Presumably, the mandibular right second and third molars and right maxillary molars were unerupted as a result of these lesions. All the soft and hard tissue lesions were on the right side of the patient.

Due to the patient's preference, neither the biopsies nor the surgical resection of the neurofibromas and removal

of impacted teeth could be performed. However, since the diagnosis of NF is based on mostly clinical criteria, the clinical findings of the patient were deemed valid for the definitive diagnosis.<sup>9</sup>

Cranio-orbital-temporal NF, together with cerebral atrophy, has not been described previously and these pathologies were not limited to cranium. Progressive prolapse of cranio-orbital-temporal NF may cause facial deformities. Therefore, malformations of the facial skeleton in NF have to be carefully investigated for the existence of tumors adjacent to the bone in order to determine or exclude their dependence on neoplastic soft tissue. The tumor mass may probably not be directly associated with the severity of facial skeletal malformations, jaw malformations, or tooth aberrations.<sup>13</sup> Thus, even a slight facial asymmetry or intraoral mass caused by a NF could be associated with several mandibular malformations and dental aberrations. These concepts may have significant implications for the necessity for treatment.

Because the diagnosis of NF is based on clinical criteria, such as intraoral mass or missing teeth, and radiographic signs should be interpreted with caution, it is important that clinicians consider this disease when oral lesions characteristic of NF1 are present. These patients must be followed in the long term because of eventual complications, including malignant transformation.<sup>9</sup> ■■■■

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