

# Unilateral Creeping Destruction of Deformed Mandibular Ramus and Angle Associated with Extensive Facial Plexiform Neurofibroma in Neurofibromatosis Type 1: A Case Report with Analysis of the Literature for Diagnosing Osteolytic Events of the Mandible in Tumor-suppressor Gene Syndrome

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**Abstract.** *Neurofibromatosis type (NF1) is an autosomal dominant inherited tumor-suppressor gene syndrome of significant phenotypic variability with probable complete penetrance of the disease. Skeletal malformations of the skull belong to the phenotype of NF1. In the skull, defects of the calvaria and the sphenoid bone are diagnostically groundbreaking findings in NF1. Malformations of the facial skull are usually diagnosed in patients with NF1 in a topographical context with a plexiform neurofibroma (PNF). This report describes the rare occurrence of slowly advancing, unilateral destruction of proportions of the mandible in NF1, with the affected bone segment completely surrounded by a PNF. A malignant process was ruled out as a cause of partial organ loss. Various hypotheses on the pathogenesis of the rare finding are presented.*

Neurofibromatosis type 1 (NF1) is an autosomal dominant tumor disposition disorder with probable complete penetrance, the phenotype of which is extremely diverse (1). Neoplasms of nerve sheath cells are an essential characteristic of the disease (2), that are particularly noticeable by the cutaneous appearance of a specific tumor type that is called a neurofibroma (3).

NF1 is not only a disease of the bone that can affect the

entire skeletal system (e.g. evidenced by the comparatively short stature of these patients and their disposition to early development of osteoporosis), but also causes local disorders of bone structure (e.g. deformation and pseudarthrosis of long bones and skull defects) (4). Indeed, certain bone defects of the calvaria and of the sphenoid bone in particular are defining findings in establishing the clinical diagnosis of this hereditary disease (1, 4, 5). However, defects of the facial skull are relatively rarely reported findings in NF1 in contrast to those of the calvaria and the skull base (6, 7). Reports of skeletal findings in NF1 focus primarily on bone deformities associated with local hypoplasia or hyperplasia. The documentation of partial destruction of a bone of the facial skull presented here further contributes to the very variable phenotype. In addition, the question arises of the pathogenesis of organ destruction in this situation. Furthermore, the course of the disease indicates that the results of skeletal interventions on a bone encased in a plexiform neurofibroma (PNF) may not remain stable (8).

## Case Report

The 25-year-old female patient was noticeable from infancy through facial asymmetry, which was due to left-sided hypertrophy of the soft tissues (Figures 1 and 2). The patient was already clinically diagnosed as having NF1 by axillary and inguinal freckling, as well as the presence of more than six cafe-au-lait spots with a size of >15 mm (1). The lower jaw was already considerably deformed in the area of the tumor in childhood (Figure 3).

*Previous treatments.* From the age of 6 years, the patient has been treated in the Clinic for Oral and Craniomaxillofacial Surgery, specifically to reduce facial nerve sheath tumors that had already grown to very extensive sizes in early

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childhood. Initial surgical procedures aimed to restrict tumors from the infraorbital border of the affected left side of the face by local excision, thereby possibly preventing orbital infiltration (Figure 1). Further measures were used to reduce the very prominent tumor masses that infiltrated the cheek (Figure 1). Magnetic resonance imaging (MRI) revealed that the entire left anterior and middle skull region were affected by infiltrating tumor. Tumor had spread to the pharynx along the base of the skull (Figure 2).

Therefore, further surgical measures were aimed at maintaining the outer contour of the face as long as possible. However, over the years, there has been an increasingly marked weakness of the facial nerve and destruction of the tumor-infiltrated mimic and chewing muscles, such that repeated tumor debulking surgical procedures and face-lifting procedures on the left side have been used to alleviate facial disfigurement and down-hanging mouth angle (Figure 1). However, these measures were only of temporary success due to recurrent tumor growth and significant restriction of tissue elasticity.

Orthodontic procedures were used to shape the dental arch and to allow contact of the occlusal surface despite considerable deformation of the jaw and rows of teeth (Figure 3).

Neither during the surgical procedure nor during the orthodontic treatment was the mandible denuded in the region of the mandibular angle or ramus.

Carious teeth were repeatedly present in the tumor area and could not be preserved. Their extraction proceeded without complications, and the wounds healed without irritation (Figure 3).

**Histology.** The tissue samples taken during the various surgical procedures repeatedly showed a nodular structure of enormously enlarged peripheral nerves with prominent and abrupt changes in diameter. The lesions were diagnosed as a nodular PNF. There were no instances of increased proliferative rate of the tumor cells or changes in the cell configuration of the resected tissue that would have given rise to the diagnosis of malignant degeneration of the extensive tumor.

**Course.** Some years after the last surgical intervention for reduction of soft tumor in order to alleviate facial soft-tissue asymmetry, the patient was clinically and radiographically examined for toothache appearing in the right side of the mandible (not affected by PNF). The orthopantomogram (OPG) revealed a carious tooth that was thought to be the cause of the toothache. A bone defect on the left mandibular side after former tooth extraction had ossified. Surprisingly, the complete loss of the left side of the mandible in the area of the angle and ramus was noted on the radiograph (Figure 3). The rarefaction of the ramus had always been very pronounced on all radiographs. The comparison of the OPG with the patient's earlier X-rays reveals that the known

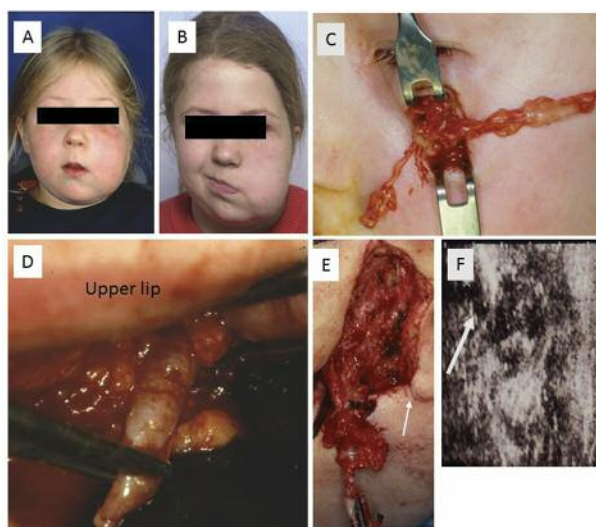


Figure 1. Clinical findings of patient. A: En face photo of the patient at the age of 6 years, showing left-sided cheek swelling and intact position of the left labial angle. B: At the age of 12 years, cheek swelling was more prominent and the labial angle points down. C: Detail of surgical exploration following infraorbital incision of the skin. The figure shows large tumorous nerves detached from the surrounding tissues close to the infraorbital foramen. D: Further detail of surgical exploration of the left cheek following incision of maxillary oral mucosa: Large tumorous nerves lie directly under the mucosa. In the histological examination, these tumors corresponded to nodular plexiform neurofibromas. E: View on surgical findings following preauricular skin incision of left side of the face. The tumor involved the complete parotid gland and other anatomical units is not possible, arrow points to pinna. F: Ultrasound of left cheek region taken prior to surgery revealed diffuse invasion of the soft tissues. Arrow points to mandibular surface.

mandibular deformity had remained almost stable during an observation period of about 16 years (Figure 3). Indeed, no significant progression of mandibular ramus rarefaction in the tumor area was evident on previously performed radiographs, indicating that the loss of the bone part must have occurred in a short time period (Figure 3). Further investigations showed a symptom-free patient with undisturbed speech function and unchanged chewing function.

## Discussion

This report describes the gradual unilateral destruction of the dorsal mandibular body and ramus without a malignant tumor or osteomyelitis being the cause of this phenomenon. Rather, bone destruction had occurred within an extensive PNF surrounding the bone. PNF is considered a benign tumor but with the property of being a pre-cancerous stage from which a malignant peripheral nerve sheath tumor

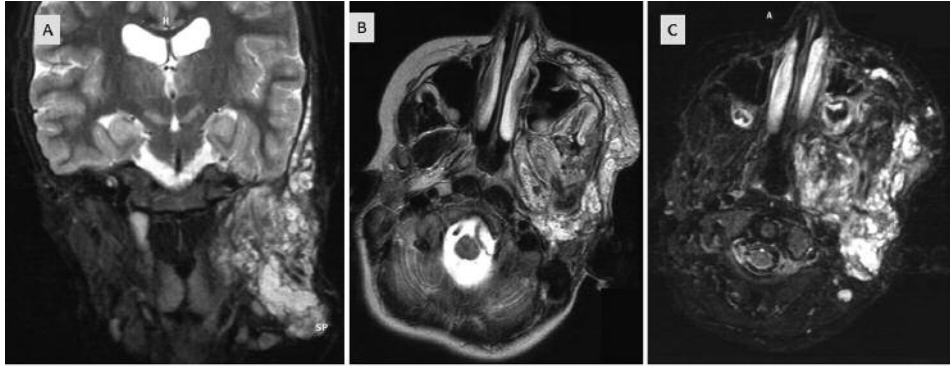


Figure 2. Magnetic resonance images of the patient in coronal (A) and axial (B, C) sections. All images illustrate the extensive tumor of the left side of face and skull base. The tumor invaded the pharyngeal region. Retromaxillary extension of the tumor masses was associated with differences in maxilla position in sagittal plane.

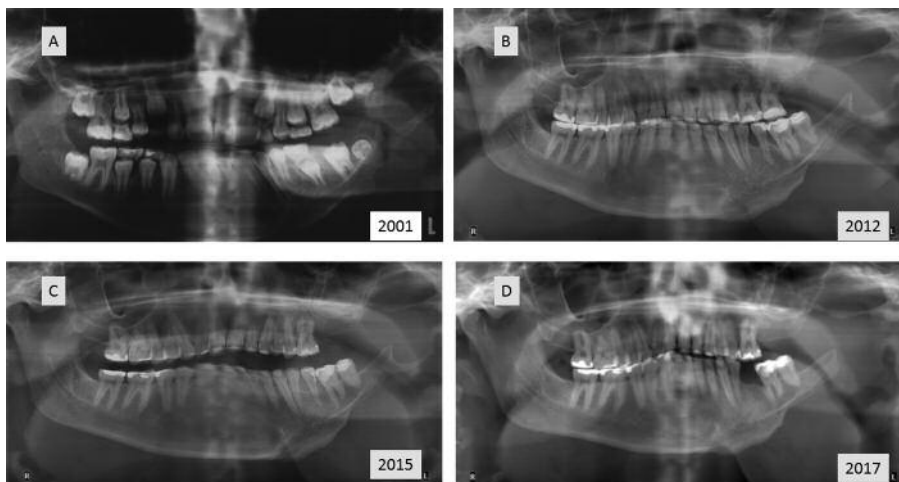


Figure 3. A series of orthopantomograms (OPG) of the patient covering a period of almost 17 years. A: At 9 years old, the patient showed an extensive deformity of the left side of the mandible, in particular the ramus and angle region. The coronoid process and also the articular process were both extremely thinned. The articular process did not make contact with the glenoid fossa. B: Eleven years later, the outline of the left side of the mandible showed discrete alterations in the mandibular angle: The angle was absorbed up to the mylohyoid line. The remaining outline appeared to be unaffected compared to the OPG taken at 9 years of age. The row of teeth was formed by orthodontic measures. The proximal contacts of the crowns of the teeth in the tumor area were established by orthodontic tooth movement. Some molars had been extracted. Bone regeneration in these sites was complete and there were no differences between the affected and unaffected sides. C: Three years later, an OPG was taken prior to extraction of the left lower second premolar. D: Two years later, the alveolar process in the region of the extracted left lower second premolar appeared to be completely ossified. However, the residual ramus had been resorbed.

(MPNST) can emerge (9). However, according to our experience, the development of MPNST from a facial PNF in NF1-affected individuals is rare. In fact, the presented tumor consistently exhibited benign characteristics over the long course of observation. It can be surmised that PNF properties are of considerable pathogenetic importance in osteolysis. The clinicoradiological phenomenon shown here requires diagnostic differentiation from other findings on the

bones of patients with NF1, which, at least in part, can produce similar skeletal changes.

*Impact of mutation of the NF1 gene on bone regeneration.* Double inactivation of the *NF1* gene was identified in tibial pseudarthroses of patients with NF1 (10). Recent study indicated that second-hit mutations in the *NF1* gene of osteoprogenitor cells, in general, may be crucial in bone

regeneration and bone repair of patients with NF1 (11). This condition may be involved in bone malformations of these patients. The molecular genetic findings can help to explain why some local skeletal changes in patients with NF1 can be found without a topographically related PNF. However, for the majority of skeletal malformations of the mandible, a trigeminal nerve PNF, especially of the nerve's third branch, can be clearly demonstrated in NF1-affected individuals on the side of mandibular malformation (7).

*Impact of neurofibroma on bone deformation and degradation.* The dissolution of bone adjacent to a PNF has been described for various body regions, such as the long bones (12), calvaria (5), and skull base (6, 13). However, there are also reports of growth disorders or major defects in the bones of these regions, without evidence of a PNF (14). It is currently unclear whether in these cases, without evidence of PNF, bone deformation actually occurs without adjacent tumor or the PNF has developed only small volume and affects only a few nerve branches, so that the detection of the tumor can be missed in a tissue sample. It has been demonstrated in follow-up that these bone defects do not remain static in every case. Enlargement of the bone defects may occur (15). However, the pathogenesis of the enlargement of NF1-associated bone defects has not been fully elucidated. Intracranial pressure was pointed to as a factor that leads not only to enlargement of sphenoid bone dysplasia (15) but also to possible osteolytic properties that originate from PNF adjacent to the defective bone (2). The osteolytic properties of a benign soft-tissue tumor such as PNF are poorly understood. Explanatory verifications, which emphasize the pressure of the swelling volume of solid tumors, convince little because the transmission of increased physical forces does not necessarily lead to a complete loss of organic matter. In fact, isolated local hypertrophies of the facial skull have occasionally been described in areas where a PNF had developed (4, 16). Neurogenic effects on bone formation and maintenance are an emerging field of research (26-28). Impact of the mandibular nerve on the shape of the mandible is likely to occur during bone formation and nerve development (26-28). Both developments are spatially and temporally linked (26-28). The pattern of bone changes suggests that the tumorous mandibular nerve triggers temporo-spatial development of the organ. Indeed, the deformity can be demonstrated in children with NF1 (Figure 4). The very conspicuous and routinely expected combination of mandibular malformations in the supply area of the third branch of the trigeminal nerve affected by a diffuse PNF highlights the influence of the tumor on the phenotype. However, the assumption that the malformation is already manifested early in childhood, remains stable and changes only insignificantly in the further course is refuted for some patients (15).

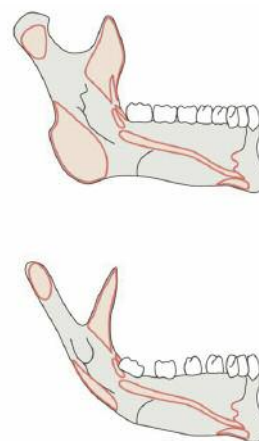


Figure 4. Schematic and simplified drawing of the left side of the mandible in lateral projection, lingual aspect. The upper drawing illustrates the outline of a healthy hemimandible with insertion areas of masticatory muscles. The lower figure shows the lower jaw, which has the typical characteristics of the deformation predominantly in the area of the ramus and angle, which can be registered in patients with neurofibromatosis type 1 with an adjacent extensive plexiform neurofibroma of the mandibular nerve. The lower figure shows the fictitious residual muscular attachments to the deformed bone. The illustration shows the significantly reduced attachment areas of some masticatory muscles to the dysplastic bone. The bony changes mainly affect the attachments of the lateral and medial pterygoid muscles as well as the temporalis muscle. The schematic drawing implies that the remaining parts of muscles are preserved. The mandibular foramen is shown here as enlarged and should thereby indicate that the plexiform neurofibroma of the mandibular nerve extends up to the entrance of the mandibular canal. Bone deformation affects both areas, which adhere to muscles as well as to those without direct contact to masticatory muscles. The drawing does not consider the potential neurovascular effects of the tumor on bone shape.

The extent of PNF can vary considerably, both with respect to the affected segment of the nerve and with respect to the individual tumor volume and invasion direction of the tumor (17). In other words, the extent of PNF around the mandible is not linearly related to the deformation of the bone. Microscopic examination regularly uncovers a diffuse invasive PNF, often combined with nodular tumors that can form grotesque deformities of single or multiple nerve branches (2). This structure of the tumor was also evident in the presented case.

In many cases, growth disturbances and deformations of the mandible occur in patients with NF1 in association with a PNF, which originates from the fibers of the third trigeminal nerve branch (16, 17). These bone malformations are typically detected in early childhood (18). This finding underlines the hypothesis that PNFs in patients with NF1 are of congenital origin (1) and that bone deformities can be explained as a coincidence of the simultaneous and interdependent development of an already tumorous nerve with the developing mandible (26, 27). However, in clinical

practice, tumor-associated malformations of the mandible usually do not present with interruption of bone continuity, such as reduction of bone at its processes or pseudoarthrosis.

Evidence of this type of partial destruction of the mandible was recorded in a former case of our own series of patients with NF1 (13). Our review of the literature (13, 16) revealed similar findings in the case presented by Heine (6) and by Winiker-Blanck and Biedermann (19) but not in more recent reports on the subject of mandibular deformities. This finding is also not reported in publications later than a review based on larger groups of patients with NF1 (20-25). Clearly, we cannot guarantee that we surveyed the entire literature on mandibular deformities in NF1, but the findings presented here have obviously been reported very rarely (16). Both reports demonstrate evidence of extensive facial PNF on the side of bone loss (6, 19).

The few cases presented up to now concerned adults of advanced age with facial PNF who were affected by partial mandibular bone loss. This report describes probably the youngest patient with loss of the mandibular ramus in NF1.

*Impact of muscles on bone shape.* The activity of muscles has a decisive influence on bone shape (29-32). The masticatory muscles are innervated by the trigeminal nerve. Slow destruction of the facial muscles surrounded by the tumor is observed in the course of the disease in many cases with facial PNF. Deficiency in chewing muscles may also affect the shape of the mandible when individual muscles attach to this bone. The patient presented here undoubtedly developed a very extensive PNF, which subsequently led to unilateral loss of function of the chewing and mimic muscles in the perioral and cheek area. Therefore, it cannot be ruled out that involution or destruction of the muscles contributed to the change in the shape of the mandible. However, such involution may lead to the transformation of the jaw shape (*e.g.* in the absence of masticatory muscles, but not to dissolution of the bone) (Figure 4). In fact, the masticatory muscles do not adhere to the entire surface of the ramus, so that the direct transmission of force to the muscles occurs only on part of the bone. Therefore, the destruction of the muscles is unlikely to be capable of causing complete bone loss. However, with respect to the impaired function of the chewing and mimic muscles that can occur in early childhood, the lack of activity of the masticatory muscles can be involved early in organogenesis and may also lead to characteristic bone deformation.

*Gorham–Stout syndrome.* The course of bone loss in our case is reminiscent of the characteristics that apply to diagnose a case for Gorham–Stout syndrome. Gorham–Stout syndrome is the eponymous term for describing the ‘spontaneous’ idiopathic dissolution of a bone, this means neoplastic, inflammatory, or other causes can be safely excluded after having applied adequate diagnostic procedures (33, 34). Gorham–Stout

syndrome has also been described in a few patients who had lost all or part of the lower jaw or temporomandibular joint region (35-39). The bone dissolution of the facial skull in Gorham–Stout syndrome is usually one-sided. Bilateral loss in this region is reported very rarely (39, 40).

Applying the definition criteria for Gorham–Stout syndrome, both external and internal causes of bone destruction cannot be excluded with certainty in the present case. Firstly, the surrounding tumorous infiltrated soft tissue should be recognized as an essential factor of bone loss (31). Secondly, vascularization of the PNF may be insufficient for the nutrition of the bone (39). Although PNFs are highly vascularized neoplasms, the functional quality of the vascular supply to the bone surrounded by a PNF is unknown. Thirdly, it is unknown whether bone in the region of a facial PNF is capable of physiological regeneration due to the constitutional mutation of osteoblasts in contact with the nerve sheath tumor. Finally, it has been suggested that the constitutional mutation of osteoclasts is not solely responsible for general or local bone resorption and that further modifying factors must be included in the explanation of these phenomena (42). For these reasons, the present case does not meet the criteria for diagnosis of Gorham–Stout syndrome.

Interestingly, the mandibular bone loss was confined to the supply area of the mandibular nerve in the present case. The infraorbital nerve has also been affected by the PNF and a substantial midfacial deformity was registered on radiographic images, such as deformation of the zygomatic arch and maxillary sinus. In both nerve branches, the tumor appeared to arise in the nerve’s branches after the passage through the foramina. The expansion of the tumor with reference to the innervation of the facial skin corresponded to the sensitive innervation region of the second and third branches of the left trigeminal nerve. Further peripheral regions, such as the orbit or frontal skin, were not (yet) affected. It remains speculative whether nerve and vascular supply from the opposite side of the facial region contributed to the preservation of the further anterior parts of the left side of the mandible.

In addition to the unknown interaction between tumor and haplo-insufficient bone (42), there are also formal reasons that do not allow the diagnosis of Gorham–Stout syndrome. Typically, the diagnosis of Gorham–Stout syndrome is made after the radiological findings and as a result of lack of evidence of neoplastic events in the affected region. Diagnosis requires synopsis of radiological, clinical, and histological findings (37). In the present case, only histological findings of the PNF were available. An exploration of the facial region formerly completed by bone did not take place because of the lack of symptoms and, therefore, was unreasonable for ethical reasons. Therefore, an intrinsic reaction within the bone which led to its dissolution cannot be completely excluded, and there was no evidence of which tissue was present at this site instead of the bone. However, the extensive tumor volume in

this area and the restriction of bone loss to the part of bone adjacent to the major tumor mass suggest the high probability that the tumor triggered bone loss. A syndromic background of bone loss is considered an exclusion criterion for the diagnosis of Gorham–Stout syndrome (34).

Reference to the delineation of NF1-associated osteolysis to Gorham–Stout syndrome is not only of theoretical interest. Recently there was a case reported of unilateral deformation of the facial skull, which, according to the authors, fulfilled the criteria of Gorham–Stout syndrome (43). The discussion of this recently published case is of interest for the analysis of the current case because it allows various aspects of the diagnosis to be discussed: i) The importance of clinical findings in confirming the diagnosis of NF1; ii) the certain exclusion of syndromic disorders for the establishment of the diagnosis of Gorham–Stout syndrome; and iii) the variability of skeletal malformations of the mandible, in particular in NF1. The radiographic illustrations of that report (43) show several important findings on the affected mandibular side: rarefaction of *processus muscularis* and *processus articularis*, deep sigmoid notch, shortening of the mandibular *corpus* and retained molars with significant spacing from the anterior teeth, associated deformities of the glenoid fossa, and a cup-like osseous defect at the lower edge of the mandible near the angle. Severe hypoplasia of the mandibular *corpus* in the region of the retained molars in all dimensions was also shown (43). The radiological aspect of that case (43) demonstrates a combination of dysplastic mandibular changes already described by Sailer *et al.* (44). Sailer *et al.* reported this set of skeletal findings in the mandible to be pathognomonic for neurofibromatosis (44). The lack of articulation of the far-protruding, pencil-like *processus articularis* (43) is also a typical NF1-associated dysplastic feature (7, 16) and not a sign of osteolysis. All these findings are one-sided in NF1 (16, 44). In fact, the authors describe their radiological finding without considering whether the deformation (and not osteolysis) of the mandible may have always existed (43). In the referred case, several small, slightly elevated skin tumors are visible on the perioral region of the patient's face (43). Looking closely at the *en face* photo, the pinna of the affected side is in a lower position than the pinna on the opposite side. This phenomenon is also reported for patients with NF1 who have developed this characteristic mandibular deformity (44). Furthermore, the clinical picture of a tumor arising from the mucosa of the alveolar process of the left side of the lower jaw is photo-documented. Histological analysis of this tumor is presented and interpreted as a granuloma-like characteristic. This finding is assessed as being nonspecific and was suggested to be an angiomatous neoplasm, according to the authors. This finding is discussed in connection with the possible angiogenic pathogenesis of Gorham–Stout syndrome (43). The reported case history (43) shows that he had undergone surgery on an astrocytoma years earlier. Both the

skin findings of the forehead in the photo and the radiographic findings of frontal bone surgical access to the brain bear witness to the patient's osteoplastic reconstruction following brain surgery. MRI of the head and neck region was apparently not made. The further history of jaw radiography shows a focal increase in osteolysis of the affected side of the mandible in the vicinity of the retained molars during an observation period of 14 months. The authors assessed these findings as proof for the case of mandibular Gorham–Stout syndrome in their patient. In contrast, the abovementioned findings (typical unilateral mandibular deformities, retained permanent molar teeth, brain tumor, and skin tumors) speak in favor of a patient with previously undiagnosed NF1 (1, 16, 44). The oral tissue finding does not contradict this assumption, because the examination was carried out on the opposite side of the conspicuous skeletal deformation. Here the proof of a neurofibroma is not necessarily expected. Clinical findings and histological description suggest a so-called epulis developing in association with numerous destroyed teeth as shown on OPG. The diagnosis in this case resulted in treatment with bisphosphonates, without the effect of this measure being reported. The efficacy of these drugs in the treatment of NF1-associated osteoporosis has yet to be clarified (45).

The documentation of progressive osteolysis within a relatively short time interval is interesting in that specific case (43). However, the bone loss was quite small in size and did not lead to a pseudarthrosis of the mandible, and the remaining outline of the ramus appeared to be stable in comparison to the previous X-ray. Nevertheless, this course of focal radiological bone changes confirms our own observation that the absorption of parts of the lower jaw in a patient with NF1 can take place during a short time, thereby simulating neoplastic disease. In addition, this examination of our own findings with the literature confirms the value of the diagnostic criterion that the diagnosis of Gorham–Stout syndrome should only be made if other syndromes certainly has been excluded. In the case of osteolysis in a patient with NF1 without adjacent PNF, Gorham–Stout syndrome would, in principle, be discussed if the exclusion criterion 'known syndrome' was abolished. However, this change in the diagnostic criteria would then deprive the term 'Gorham–Stout syndrome' of any diagnostic relevance.

*Giant cell granuloma (GCG) of mandible in NF1.* GCG can cause extensive osteolysis of the facial skull. GCG can occur in the jaws of patient with NF1 (46-49). Loss of heterozygosity of the *NF1* gene was detected in the GCG of one patient with NF1 (50). A second mutation of the *NF1* gene was identified in patients with NF1 with the Noonan phenotype (51). This association has also been demonstrated in another patient with NF1 with GCG without these specific phenotypic constellations (52).

Typically, GCGs in patients with NF1 are intraosseous lesions (53). So-called peripheral GCGs can lead to external erosion of the jaw (54). The pattern of bone dissolution in the current case, however, does not resemble the pattern which can be observed as a result of a peripheral GCG. Therefore, the association of bone degradation with a GCG is very unlikely in the current case.

*Osteoporosis in NF1, medication-related osteonecrosis, oral squamous cell carcinoma invasion of the mandible, and malignant peripheral nerve sheath tumor of mandible.* Patients with NF1 are at risk for early osteoporosis due to insufficient vitamin D metabolism (55, 56). Serum vitamin D<sub>3</sub> levels are often too low, even in children with NF1 (57). Early supplementation of vitamin D in patients has a positive effect on bone formation and, according to recent findings, clearly delays the onset of osteoporosis (58). Supplementation of vitamin D for the patient with NF1 presented here did not appear to affect local bone resorption or bone loss.

Recently, *in vitro* and *in vivo* attempts to influence osteoblasts of patients with NF1 using bisphosphonates have yielded contradictory results for the suitability of this group of compounds for the treatment of NF1-associated osteoporosis (59-62). The patient presented here had not been medicated with bisphosphonates, therefore the effect of this group of substances has only theoretical significance with respect to the pathogenesis of bone disintegration in NF1 in the presented case. The pattern of bone resorption of bisphosphonate-associated *osteonecrosis* is not mimicked in our case neither by the radiological course nor the clinical findings; the bone was never open intraorally (63, 64). The therapeutic effect of *bisphosphonates* on bone resorption in NF1 has not yet been described in the case of progressive osteolysis of the mandible.

The most common cause of mandibular erosion by a malignant tumor is oral squamous cell carcinoma. The much rarer adenocarcinomas in this location can also lead to destructive infiltration of the mandible. The case presented here had developed a tumor with radiographic characteristics of an invasive, partly nodular, partly diffuse PNF (65) throughout the entire observation period. The oral mucosa was intact and unremarkable at each examination. Tissue examinations during several procedures for contouring the face and in oral surgery always confirmed the diagnosis of a PNF.

Primary intraosseous MPNST is very rare (66). When intraosseous MPNST occurs, the mandible is unusually frequently affected (66). However, mandibular MPNSTs predominantly arise in patients not affected by NF1 (66, 67). MPNST of the mandible in patients with NF1 have become known only from a few single reports [review in (67)]. In the present case, at no time was tumor degeneration into an MPNST or development of a malignant tumor of other histogenesis considered.

## Conclusion

In patients with NF1, characteristic changes may occur in the jaw associated with facial PNF of the same body side. Deformations of bone predominate the phenotype in patients with NF1 affected with facial PNF. Partial mandibular osteolysis can be observed as a rare association of a PNF affecting the mandibular branch of the trigeminal nerve. The reported observations should be considered when assessing facial skeletal findings in patients with NF1 in order to differentiate dysplastic, dystrophic, and neoplastic features of the disease. Assessment of the dysplastic component of the mandible in cases of extensive facial PNFs may help to avoid unnecessary resections (68). In addition, the finding justifies withholding major facial reconstructive skeletal measures in the region of an extensive facial PNF in NF1 patients, because the osseous reconstruction may not remain stable.

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