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Case Report

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Unilateral mandibular atrophy in neurofibromatosis-1: case report

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Abstract

Neurofibromatosis is an autosomal dominant neurocutaneous syndrome characterized by skin lesions and central or peripheral nervous system tumors. Although neurofibromatosis is a neurocutaneous disease, it also involves multiple systems. For example, bone lesions have been reported in 40% of patients. As in this case, pathologies associated with the mandible and temporomandibular joint in neurofibromatosis are rarely reported in the literature. In our case, we aimed to emphasize that skeletal malformations may also be present in the rich clinical picture of neurofibromatosis. Maxillofacial computed tomography of a 24-year-old female patient who was followed up at Selçuk University Hospital with a diagnosis of neurofibromatosis revealed an appearance compatible with atrophy in the right half of the mandible. The mandibular ramus was 41.27 mm on the right and 53.44 mm on the left; the diameter of the condyloid process was 10.31 mm on the right and 15.71 mm on the left. The joint distance was increased on the right. Radiologic examinations in neurofibromatosis syndrome should be performed considering the possibility of bone lesions. These examinations are especially important for the prevention of pathologic fractures in bones.

Keywords: bone lesion; mandible; neurofibromatosis

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Introduction

Neurofibromatosis (NF) is a genetically inherited heterogeneous disease. The clinical findings and pathological structures of neurofibromas were first described by von Renklinghausen in 1882. For this reason, NF-1 is also referred to as Von Renklinghausen disease.[1] Riccardi classified NF into 7 types.[2] However, two definitions are generally used: NF-1, known as the peripheral or generalized form, and NF-2, known as the central form. Among these types, NF type 1 is the most common (90%) and is an autosomal dominant neurocutaneous syndrome that occurs in 1 in 3000 live births. Despite autosomal inheritance, de novo cases have also been reported. Half of the cases develop due to spontaneous mutations. The NF-1 gene is located on chromosome 17q11.2 (long arm of chromosome 17).[3,4] This gene encodes the neurofibromin protein. Neurofibromin protein exerts a tumor suppressor effect by controlling cell proliferation through the Ras signaling pathway (negative regulation). Neurofibromin hydrolyzes GTP to GDP, generating Ras signaling and thus exerting a tumor suppressive effect. Therefore, the absence of neurofibromin function leads to uncontrolled cell growth.[5–7] During the disease process, ectodermal and mesodermal derivatives are affected due to defects in embryonic neural crest cells.[8] Since patients with NF-1 may have significant bone lesions, lesions in the mandible are especially important in dental procedures and oral and maxillofacial surgeries.[1] It can also cause aesthetic concerns as it can create facial asymmetry.

Case Report

A 24-year-old woman diagnosed with NF-1 presented to the clinic with a mass on the left upper eyelid. Preoperative maxillofacial computed tomography showed marked facial asymmetry (**Figure 1**) and an

appearance consistent with atrophy on the right side of the mandible. Considering the patient's past clinical history, facial asymmetry was not previously present. It is thought that the reduction in mandibular size occurred later. Therefore, the case was evaluated as atrophy. A neurofibroma with a diameter of approximately 1 cm was found in the subcutaneous soft tissue in the left orbital preseptal area (**Figure 2**). There was thinning of the bony cortex connecting the orbital borders on the left side due to neurofibroma compression. The maxilla and zygomatic bone had normal anatomical structure. The mandibular ramus measured 41.27 mm on the right and 53.44 mm on the left (**Figure 3a**); the diameter of the condyloid process measured 10.31 mm on the right and 15.71 mm on the left (**Figure 3b**). The joint distance was increased on the right. Therefore, the patient had facial asymmetry. Left mandibular cortex and medullary bone density were normal.

Discussion

NF-1 is an autosomal dominant neurocutaneous syndrome occurs in 1 in 3000 live births. Skin involvement is characteristic in NF-1. Café au lait spots are the most common skin findings and are among the diagnostic criteria (**Table 1**). They should be larger than 5mm for diagnosis and larger than 5 mm before puberty and larger than 15 mm after puberty.[9,10]

The presence of 2 or more findings in the table of diagnostic criteria is necessary for the diagnosis. Other cardinal findings: Neurofibromas, axillary-inguinal freckles and iris hamartomas called lish nodules. There is a wide variety of clinical presentations in NF-1. Although inherited as an autosomal dominant disease, symptoms and severity can vary even among affected family members. Skeletal involvement is among the diagnostic criteria in NF-1 and occurs in 40–50% of cases. Skeletal defects such as dysplasia, aplasia or local bone atrophy are thought to result from abnormalities of tissues originating from neuroectoderm and mesoderm.[11,12] Hunt and Pugh,[13] in a study of 192 cases in 1961, suggested that skeletal defects develop as a result of mesodermal dysplasia. According to some scientists, abnormal bone formations may develop as a result of a mesodermal defect in the periosteum.[14] Furthermore, decreased bone mineral density (reported in 90% of cases) and increased osteoclast activity also cause bone destruction. Local factors such as genetic etiology, physical activity and presence of tumors also influence bone malformations.[15] The most common skeletal anomalies are macrocephaly (20–50%)

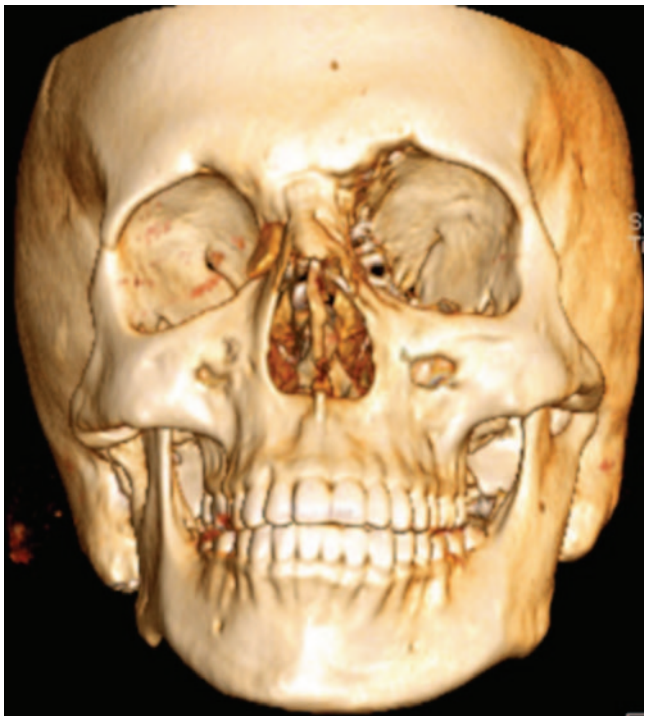

Figure 1. Three dimensional image of facial asymmetry on computed tomography.

and scoliosis (5–10%).[16] Deformities such as dysplasia of the sphenoid bone, spina bifida, pseudoarthrosis, thinning of the long bone cortex, local bone growth and absence of patella may also be seen. Pseudoarthrosis is

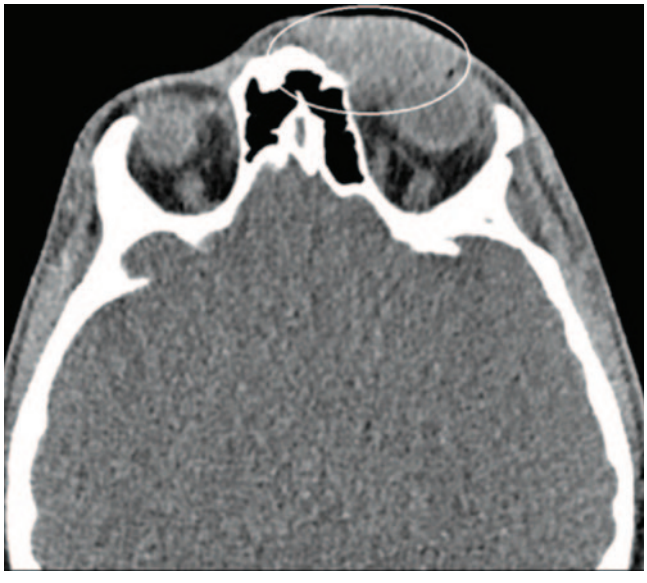

Figure 2. Computed tomography image of neurofibroma in the left orbital preseptal area in the axial plane.

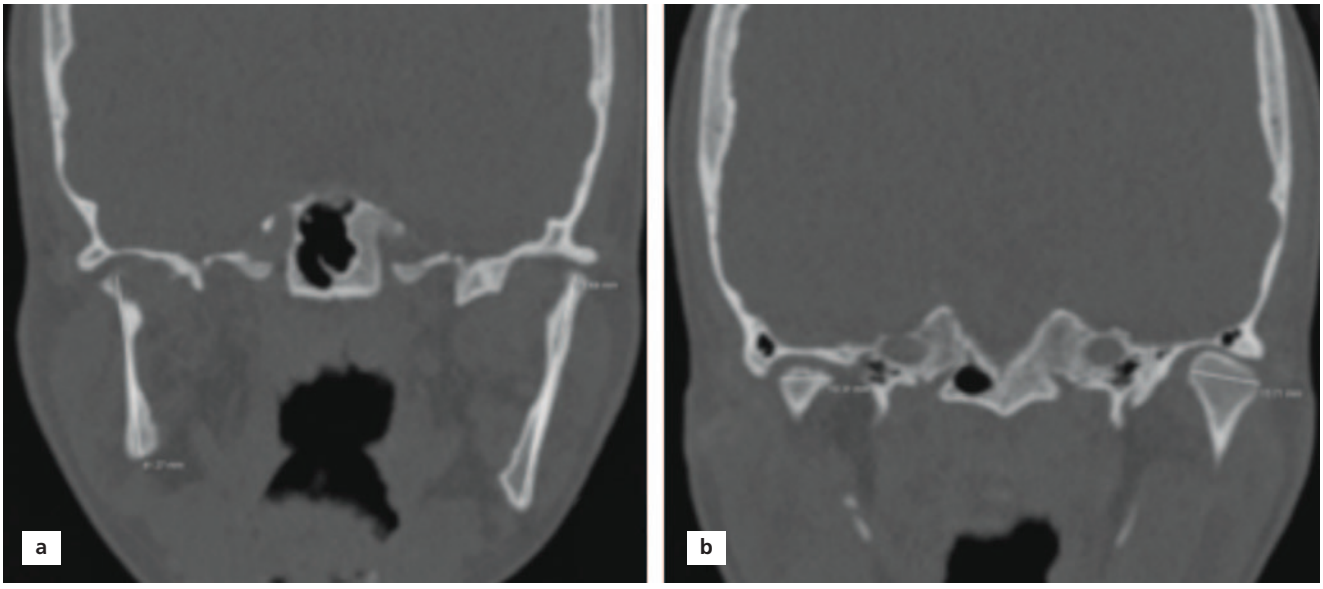

Figure 3. (**a**) mandibular ramus measurements; (**b**) condyloid process measurements in the coronal plane on computed tomography.

highly diagnostic, but it is very rare and starts with bending, especially in the tibia.[3,17,18]

Cutaneous, subcutaneous and plexiform variants of neurofibromas can be seen in NF-1. Plexiform neurofibromas are seen in 25% of patients. These can cause hypertrophy of soft tissue and bone, leading to bending of the head, neck and extremities. Neurologic problems may also occur as a result of pressure on the nerves. Especially when the trigeminal nerve is compressed, pain accompanies clinical findings.[19]

Previous studies have revealed that approximately 70% of NF-1 patients have oral pathologies. The tongue, buccal mucosa, labial mucosa and palate are usually affected and neurofibromas are frequently located in these areas. As neurofibromas grow in the mouth over time, the patient may develop gingival and dental problems, especially facial asymmetry, and bone lesions such as hypoplasia, aplasia or atrophy. Although oral pathologies are common, the rate of NF-1 patients with jaw malformations has been reported to be 28%.[19,20]

Cases involving the temporomandibular joint are rarer and occur in 4–7% of cases. Koblin and Reil[20] reported that temporomandibular joint hypoplasia and related joint dysfunction may develop in neurofibromatosis. Van Damme et al.[21] reported that mandibular atrophy in neurofibromatosis may result in early molar tooth loss and facial asymmetry due to transposition of the temporalis muscle. This may cause dysfunction and pain in the temporomandibular joint. Medial depression of the mandibular ramus was reported in another case of neurofibro-

Table 1
Clinical criteria for the diagnosis of neurofibromatosis-1.

Six or more cafe au lait spots, >0.5 cm diameter at prepubertal age and >15 mm diameter at postpubertal age
Two or more neurofibromas of any kind or a plexiform neurofibroma
Axillary or inguinal freckles - Crowes sign
Optic glioma
Two or more Lisch nodules: pigmented bilateral hamartomas, that appear as copular elevations on iris surface
Distinctive bone lesion, sphenoidal dysplasia, dysplasia or thinning of long bones cortical
Relatives in first degree with NF-1

matosis.[22] In a study evaluating the images of 10 patients with neurofibromatosis, it was found that the mandibular angle was reduced in 6 cases. Deformity of the condyles was also observed.[23] Neurofibromas in the cheek, ear or similar areas may grow directly into the joint. In 1988, Sailer et al.[24] reported 12 pathognomonic changes related to mandibular involvement. These changes include deviation of the mandible on the affected side, minimal swelling of the cheeks or intraoral soft tissue, coronoid notch deformity, pseudo-elongation of the condyles, ramus hypoplasia, increased mandibular angle, mandibular body deformity or hypoplasia, impacted tooth on the affected mandibular side, atrophy of the ipsilateral maxilla and zygomatic bone, impacted tooth in the ipsilateral maxilla, external ear deformity. According to the literature, the most common jaw malformations are bony lesions, thickened mandibular canal and enlarged foramen mandible. When bone lesions are present in oral pathologies, it becomes difficult to maintain oral hygiene.[24–26]

Conclusion

Bone lesions can be seen in neurofibromatosis. These lesions may cause pathologic fractures. In addition, bone dysplasia in the facial region may cause dysfunction in the temporomandibular joint and facial asymmetry.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

BS: data collection, manuscript writing; NÜD: project development, manuscript editing; AB: data collection, data analysis, editing; BP: data analysis, manuscript writing; ZF: project development, manuscript editing.

Ethics Approval

This case report was written in accordance with ethical principles and informed consent was obtained from the patient prior to the CT examination.

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