Intraosseous Neurothekeoma of the Mandible: A Rare Occurrence
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Abstract
Neurothekeoma, a benign dermal neoplasia, believed to be of the nerve sheath origin, is a rare condition that usually occurs in children with female predominance. It typically presents as a small, solitary, asymptomatic, subcutaneous, slow growing, and dome-shaped mass, covered by normal-looking skin. To our knowledge, this is the first reported case of an intraosseous mandibular neurothekeoma. Little is known or has been reported about the biologic behavior of this tumor when occurring in an intraosseous site. Consequently, the best treatment options and subsequent prognosis for the present case are not known. The adoption of a non-radical surgical approach in our case is supported on the premise that neurothekeoma is a benign neoplasm with a slow growth rate. The patient is presently on a monthly follow up schedule with no evidence of recurrence at one year mark. There is return of normal sensation to the patient's right lower lip and significant regeneration of bone seen on radiographic evaluation. Of relevance is the fact that the patient has been able to resume his normal activities since very early on, participating in sports, assisting to school, and eating a regular diet.

Keywords: Neurothekeoma; Myxoma; Nerve Sheath; Intraosseous; Neural Tumor; Benign; Dermal Neoplasia.

Introduction
Neurothekeoma, a benign dermal neoplasia, believed to be of the nerve sheath origin, is a rare condition that usually occurs in children with female predominance. It typically presents as a small, solitary, asymptomatic, subcutaneous, slow growing, and dome-shaped mass, covered by normal-looking skin. No hyper-pigmentation is present. These tumors show predilection for the head area although mucous membranes are rarely involved. Until recently, the medical profession believed that nerve sheath myxoma and the neurothekeoma were variants of the same tumor. Fetsh et al1 after a study of 178 neurothekeomas concluded that this lesion is not neural in origin, but rather fibroblastic. Immunohistochemistry and ultra-structural studies have demonstrated findings that are not characteristic of neural or peri-neural tissue.2,3 Laskin et al4 studied 22 neurothekeomas and concluded that cellular variants of these tumors fail to show evidence of neural differentiation, therefore, they warrant a different classification. Controversy still exists. The vast majority of neurothekeomas involve dermis; a few of them affect the sub-dermis and skeletal muscle. Grossly it appears as a whitish-tan, firm, nodular tumor with semi-glossy surface. The size varies from 0.5 to 3.0 cm and typically they do not show gross association with nerve.

Histologically, neurothekeomas are described as cellular, mixed and myxoid type, depending of the amount of myxoid tissue and cells. These tumors are not encapsulated and they are composed of multiple cellular nodules separated by thin collagen bands. Some of them show loose textured, myxoid areas, in some cases, associated with foci of dense, hyalinized collagen. The cells are commonly spindle and/or epithelioid with eosinophilic granular cytoplasm and often are forming whorls, however, fascicular growth is sometimes present. Cellular atypia and scattered mitotic figures, some of them non-typical are seen, but necrosis is absent. Occasionally multinucleated giant cells are present. Nonetheless, lymphocytes, plasma cells and eosinophils are rarely noted. Neurothekeoma is a hyaluronic acid rich tumor.5,6 Differential histologic diagnosis of skin neurothekeomas includes focal mucinosis, schwannoma, neurofibroma, myxoid malignant fibrous histiocytoma and myxofibrosarcoma.
Ultra-structural studies of neurothekeoma reveal tumoral cells showing dilated endoplasmic reticulum and no basement membrane which is consistent with fibroblastic origin.\(^5\) It is positive for CD 10, Vimentin and NK1C3 which is said to be characteristic of neurothekeoma. However, NK1C3 reflects the presence of lysosomes in the cytoplasm of the cells, and it is not specific for neurothekeoma but at the present, it is the most used immunostaining for its diagnosis. It may be weakly positive for CD99, collagen IV, NSE, CD68, actin, desmin and smooth muscle actin. None of these markers is neural or melanocytic specific. Neurothekeoma is negative for S100 protein, laminin, EMA, Melan A and HMB-45.\(^5\)\(^3\)\(^5\)\(^6\)

Neurothekeoma is not a highly recurrent tumor and there are no reports of metastasis. Complete excision, in a conservative way is believed to be curative, as reported for the dermal counterpart. An exhaustive literature review was performed and one report of an intraosseous neurothekeoma of the maxilla in a 15 month old male was found.\(^7\) In this article, we present the first reported case of a large, expansive, destructive intraosseous neurothekeoma of the mandible.

**Case report**

An otherwise healthy nine-year-old African American male presented to Nova Southeastern University, Oral and Maxillofacial Surgery Clinic for evaluation of an asymptomatic anterior mandibular swelling. The patient's father noticed a clinical change four months earlier. Two years previously, a large radiolucent lesion was discovered but the parents never pursued the referral. There is no significant medical, surgical or trauma history, no known allergies and no traveling outside of the United States. Physical exam revealed facial swelling of the right anterior mandible, hard, non-fluctuant, non-tender (Figure 1a). No paresthesia of the mandibular division of the trigeminal nerve was present. Intra-orally a large swelling covered by normal mucosa with considerable buccal expansion was present, extending from the distal of the left mandibular lateral incisor, across the midline, mesial to the first molar on the right side (Figure 1b). No lingual expansion or elevation of the floor of the mouth was appreciated. The anterior dentition exhibited displacement and mobility as did the deciduous right mandibular molars.

Panoramic x-ray revealed a large 6 x 4 cm radiolucent lesion with no deformation of the inferior border of the mandible. (Figure 1c) The tumor has shifted the root of the right lateral incisor mesially and superiorly.

The patient was then sent for computed tomography (CT) of the mandible and a stereolithographic model was fabricated to further aid in treatment planning. The CT demonstrated a well-defined, expansive, destructive mass of the anterior mandible with the inferior border intact. Two small perforations were present on the lingual surface of the mandible. No extension was seen into the surrounding soft tissues. (Figure 1d & e)

With a differential diagnosis of odontogenic keratocyst, ameloblastoma and central giant cell tumor an incisional biopsy was performed under local anesthesia. The incised gross specimen was lobulated, white, glossy and firm. The histopathological examination of the tumor mass showed a plexiform nodular architecture composed of nests and bundles of epithelioid to spindle cells with eosinophilic cytoplasm and moderate hyperchromasia, in a prominent myxoid stroma, separated by collagenized and hyalinized fibrous septa. Mild cytological atypia and 1 - 2 mitosis per high power field were noted. There was no evidence of necrosis (Figure 2a & b). Immunohistochemistry revealed positive staining for Vimentin, NSE, NKIC3 (Figure 2c) and CD10. Stains for smooth muscle actin, desmin, S100 protein (Figure 2d), calponin, CD31, CD34, pancytokeratin (AE1/AE3), EMA, P63 were negative. A diagnosis of cellular neurothekeoma was rendered.

A rationale for the management of this lesion was developed based on the histopathology, clinical and radiographic presentation, in concert with the review of the literature. A non-radical surgical approach consistent of enucleation and curettage of the lesion with preservation of the nerve and mandibular contour to allow for spontaneous osseous regeneration was determined. Due to the rarity of the presentation, the treatment was discussed, not only in a tumor board, but also with the parents. The possibility of the necessity of a radical surgery in case of recurrence and / or failure to heal was contemplated. In the operating room vestibular approaches with a combined sub periosteal and supra tumoral dissection was
performed to gain access to the tumor. The right mental nerve was identified, and dissected free from the neoplasm and in this fashion preserved during the procedure. The mass was removed from its bony cavity by enucleation and where firmly adhered to the soft tissues, these were sharply excised. No specific attempts were made to verify tumor free surgical margins. The six mandibular teeth involved in the lesion were removed along with the lesion. The large defect was curetted and a Resorb-X® resorbable plate (KLS-Martin, LP, Jacksonville, FL) was placed to return appropriate mandibular contour and prevent collapse of the soft tissue into the defect. SyringeAvitine™ (Davol Inc., Warwick, Rhode Island) was used to fill the defect to reduce dead space and help with hemostasis (Figure 1f & g).

Figure 1: Initial facial swelling on the right anterior mandible (a). Intraoral swelling covered by normal mucosa (b). Panoramic radiograph showing a large radiolucent lesion (c) and CT scan (d) and stereolithographic model (e) show destructive mass with perforations of the cortical surface. The surgical procedure (f) where nerve was carefully preserved (g). Seven months post-operative clinical appearance (h) and panoramic radiography showing bone formation (i).
The lower lip was undermined and advanced to the remaining lingual tissue for primary closure. Histopathology of the complete lesion confirmed the diagnosis of neurothekeoma. The patient's post-operative hospital course was uneventful and early healing occurred without complications. Seven months later, the patient is in good condition with no recurrence (Figure 1h) and the panoramic radiography shows new bone formation (Figure 1i).

Future multidisciplinary treatment plan includes: Orthodontic and occlusion evaluation and treatment. Removable prosthesis was prepared in cooperation with prosthodontics and pediatric dentistry Departments. The final step of treatment is expected to be implants placement. Follow up at least for five years by pathology, surgery and radiology departments is scheduled.

Figure 2: Histopathological examination of the tumor mass composed of eosinophilic cells with hyperchromatic nuclei and occasional mitoses (Hematoxylin and eosin staining under X100[a] and X400[b]). Immunohistochemical staining for NKIC3 was positive (c) and for S100 was negative (d).

Discussion
To our knowledge, this is the first reported case of an intraosseous mandibular neurothekeoma. Complete surgical excision has been recommended in the treatment of soft tissue neurothekeomas and it should be noted that even when the tumor is incompletely excised, the recurrence rate is low. Little is known or have been reported over the biologic behavior of this tumor when occurring in an intraosseous site. Consequently, the best treatment options and subsequent prognosis for the present case are not known. The adoption of a non-radical surgical approach in our case is supported on the premise that neurothekeoma is a benign neoplasm with a slow growth rate. This known tumor biology in turn permits planning for an initial approach as the one we described that
allows for surgical re-intervention on recurrence, adjusted to the behavior/aggressiveness of the lesion. The patient is presently on a monthly follow up schedule with no evidence of recurrence at one year mark. There is return of normal sensation to the patient’s right lower lip and significant regeneration of bone seen on radiographic evaluation. Of relevance is the fact that the patient has been able to resume his normal activities since very early on, participating in sports, assisting to school, and eating a regular diet.

We felt compelled to report our case early in the hope this will increase the familiarity of surgeons/pathologists with this rare entity, assist with its diagnoses and encourage reporting of their experiences and outcomes, as to provide further understanding of this disease, its management and prognosis. A future long term follow up report of our case is planned to contribute with the above as well.

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**References**


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