

Solitary Intraosseous Mandibular Neurofibroma: Clinical Case Study

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Abstract

A neurofibroma is a benign neurogenic tumor of the peripheral nerve sheath with variable cellular components. The treatment of this neurofibroma required surgical excision. The following report describes a case of a solitary intraosseous mandibular neurofibroma in a 70-year-old female located in the right posterior mandible. Clinical findings and radiographic evidence, along with histopathological evaluation and immunohistochemistry, confirmed the diagnosis of neurofibroma. Due to rare occurrence of neurofibromas presenting intraorally in the mandible, this case was deemed necessary for documentation. A literature review detailing prior cases of intraosseous neurofibromas is also presented in this report.

Keywords: Solitary neurofibroma; Benign tumor; Intraosseous; Nerve sheath; Mandible

Introduction

A neurofibroma, according to the World Health Organization, is “a benign tumor of the peripheral nerve sheath phenotype with mixed cellular components which includes Schwann cells, perineural hybrid cells, and intraneural fibroblasts.”

Neurofibromas can be caused due to the inactivation/mutation of NF1 gene which encodes for the protein, neurofibromin, known to play a role in cell signaling [1]. The presence of neurofibromas can be multiple or solitary. Neurofibromas are most commonly found in the skin and its multiple appearances is highly associated with von Recklinghausen's disease and poliglandular syndrome MEN III [2]. A solitary neurofibroma is a single lesion that occurs in an individual who does not have hereditary neurofibromatosis. This condition may be difficult to identify at first because a single neurofibroma may be the first sign of neurofibromatosis [3].

In 1954, Bruce gave the first description of solitary neurofibroma of the oral cavity. Since then, only a few cases have been documented in the literature. The various sites of occurrence intraorally in the soft tissue are the tongue, floor of mouth, buccal mucosa, edentulous alveolar ridge, gingiva and pharyngomaxillary spaces [4]. In this report, we discuss a case of a 70-year-old female patient who presented with a solitary neurofibroma of the mandible along with review of the clinical and histological examination.

Case Report

Evaluation

A 70-year-old female was referred for evaluation of lytic lesion of the right posterior mandible. She had been seen by her dentist who had seen a large periapical lesion associated with tooth number 31 on a panoramic radiograph (Figure 1). She was referred for endodontic evaluation and treatment. Upon endodontic evaluation, the tooth was found to be vital, and her endodontist referred the patient for evaluation of lytic lesion and surgical treatment. A pre-operative cone bone CT was taken for enhanced visualization of the lesion (Figure 2).



Figure 1. Pre-operative panoramic radiograph revealing periapical lesion associated with tooth #31.

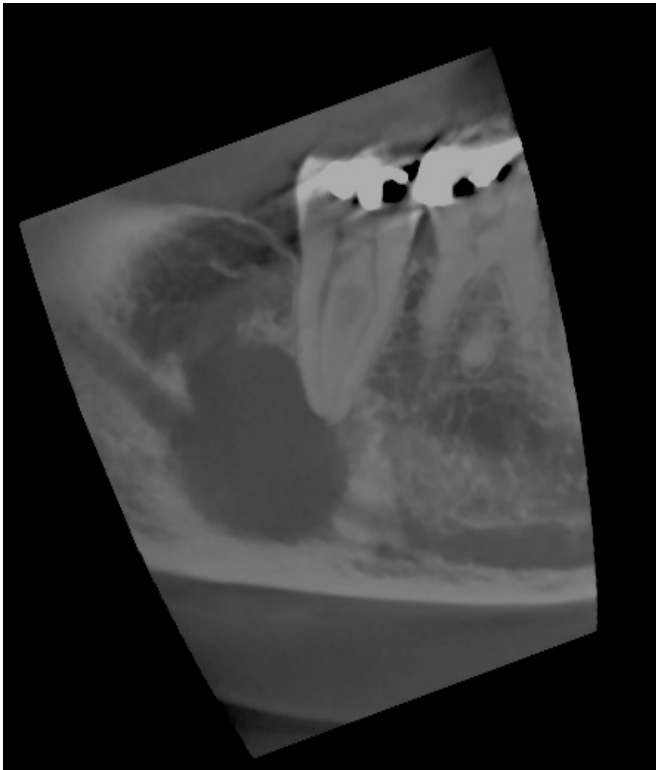


Figure 2. Pre-operative cone beam CT scan revealing enhanced visualization of the lesion in the longitudinal plane.

Evaluation of the patient demonstrated a healthy 70-year-old female with no contributory medical issues. Clinically, there was no expansion of the lower right mandible either on the buccal or lingual aspects. The tooth was found to be vital. Surgical decision was made for a biopsy of the area.

Surgical Technique

The patient was anesthetized under general anesthesia. The vestibular incision was made on the lower right mandible with a distal vertical release. A full-thickness mucoperiosteal flap was elevated. A bony window was made. The lesion was identified immediately after removal of the window. The lesion was firm and curettage able to enucleate vast majority of the lesion. There was adherence to inferior alveolar nerve. Both blunt and sharp dissections were completed to remove the lesion off the inferior alveolar nerve. The specimen was sent to pathology for histopathological evaluation. Surgical follow-up showed no postoperative complications.

Post-Operative

To address concerns surrounding post-operative healing of the patient, several follow-up appointments were scheduled with the patient with the longest duration follow-up at 1 year. A cone beam computed tomography (CBCT) scan was performed at the 1 year follow up (Figure 3). Not only does this scan show good bone fill in the region of the neurofibroma, but also vitality testing of the adjacent teeth performed by both the patient's oral surgeon and endodontist demonstrated that the teeth in question remained vital at 1 year post-op. It should be noted that the patient demonstrated an initial patch of paresthesia on the lower right lip; however, this resolved over the course of six months. An extended follow-up period (past 1 year) for this particular patient was not carried out due to patient cooperativity.



Figure 3. Post-operative cone beam CT scan after 1 year.

Histopathological Features

The histopathological evaluation was conducted through the Department of Pathology at North Shore Long Island Jewish Medical Center. The specimen was preserved in formalin and consisted of two pieces of tan soft tissue. The appearance of the specimen measured 1.5 x 0.7 x 0.6 cm. Histopathological evaluation indicated a benign neural neoplasm consistent with neurofibroma. Features included spindle shaped bundles of cells with wavy nuclei and admixture of predominantly inferior alveolar nerve fibers and fibrous tissue. Immunohistochemistry revealed positive staining for S100 protein. Figures 4 and 5 show histological staining of the sample at 20x and 60x magnification, respectively.

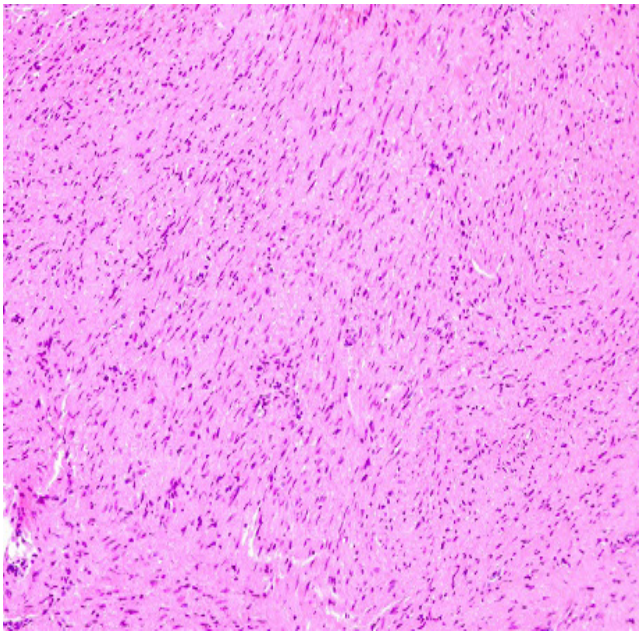


Figure 4. Histological staining at 20x magnification.

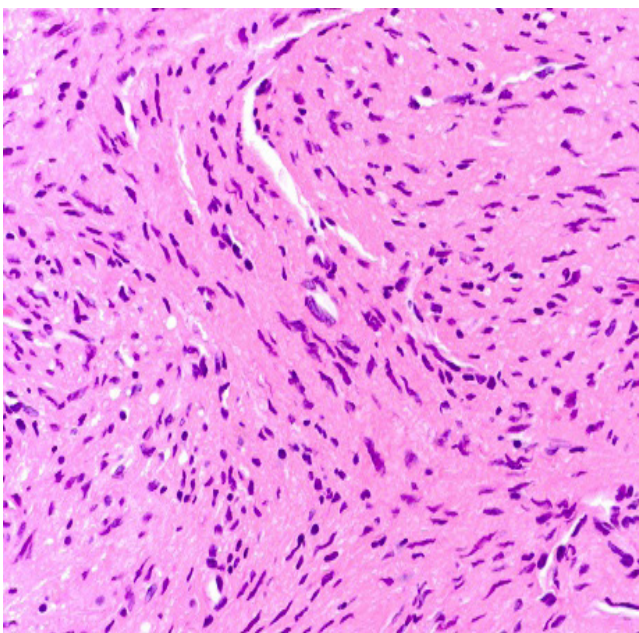


Figure 5. Histological staining at 60x magnification.

Discussion

Neurofibromas (NF) are neurogenic neoplasms that originate from the cells that constitute the nerve sheath. It is for this reason that solitary neurofibromas should be carefully evaluated to eliminate the possibility of Von Recklinghausens disease [7]. In the oral cavity, NFs often involve the trigeminal and upper cervical nerves. A literature review was performed using keywords “solitary neurofibroma of mandible” and the results have been summarized in Table I. When solitary neurofibroma occurred in the mandible, there was definite female predilection.

The head and neck are commonly involved because of rich innervations in this area. In terms of occurrence, roughly 25% of neurofibromas are observed in the head and neck region; only 5.6% of neurofibromas occur in the oral cavity [33]. Superficial involvement of soft tissue with NFs is more frequent than deeper locations. In the oral cavity, NF is reported to occur on the tongue, lip, palate, gingiva, major salivary glands, and the jaw bones [3,5].

It has been discovered that NF is caused by a mutation in the NF1 gene located at 17q11.2 chromosome. This gene is tumor suppressing and encodes for the protein neurofibromin, which is involved in neural cell signaling [34].

Most intraosseous NFs present asymptomatic in the early stages, with possible pain and numbness on affected side presenting in the later stages [5]. Radiologically, the tumor appears as a nonspecific, unilocular or multilocular, poorly defined or well demarcated, radiolucency [10]. Histopathologically, NFs exhibit an irregular pattern with interlacing bundles of spindle shaped cells with round or fusiform nuclei, and eosinophilic cytoplasm within a loose myxomatous matrix of fine fibrillar collagen.

NFs are unencapsulated and composed of a mixture of Schwann, perineural-like and fibroblastic cells. Mast cells, lymphocytes, and small nerve fascicles can also be seen in the tumor [5,12,15]. NFs are immunopositive for S-100 protein, indicating its neural origin. Histopathological analysis supported by immunohistochemistry is essential for the correct diagnosis of these oral soft tissue growths [5].

It is important to differentiate NFs from other spindle cell lesions such as schwannomas. Although NFs and schwannomas are both benign tumors of the peripheral nerve sheath, the absence of verocay bodies and the presence of mast cells and fine fibrillary collagen matrix should distinguish NFs from schwannomas [35]. Furthermore, there are slight anatomical considerations associated with these tumors as well. Schwannomas will typically displace the root of the nerve they are associated with, while NFs will attempt to encase the nerve fiber. This anatomical difference was observed with this case report due to adherence to the inferior alveolar nerve. Due to this consideration, complete surgical removal of a solitary neurofibroma is difficult and may attribute to cases of recurrence.

Table 1: Clinical, radiographic, histological and immunohistochemistry features of reported intraosseous neurofibroma of the mandible.

References	Age (yrs)	Gender	Radiographic features	Histological features	Immunohistochemistry features
Reebye 2017	70	F	Well-defined radiolucent region	Spindle shaped bundles of cells with wavy nuclei and admixture of predominantly inferior alveolar nerve fibers and fibrous tissue	S-100 positive
Gujjar 2015[5]	28	F	Homogenous radioopacity surrounded by a thin uniform radiolucent border	spindle shaped cells with wavy nuclei and collagen fibres within a myxoid stroma	S-100 positive
Jagnam 2014[6]	62	F	Well-defined radiolucency	admixture of nerve fibers (mostly inferior alveolar nerve) and fibrous tissue; no malignancy	S-100 positive
Diechler 2011[7]	14	M	Unilateral radiolucency	regular spindle cells with wavy, hyperchromatic nuclei and scanty cytoplasm, in a richly vascularized myxoid stroma, with presence of collagen fibers and connective tissue cells	Tumor cells: vimentin positive, neurospecific enolase (NSE) positive and anti S-100 negative Residual nerve fibers: S-100 positive; NSE positive
Tao 2010[8]	16	F	Multilocular and irregular edges	spindle-shaped, aligned in a plexiform manner	S-100 positive
Depprich 2009[9]	64	M	Little to moderate interdental loss of bone between teeth 37 and 38	proliferative spindle cells with a stroma composed of irregular collagen fibers	S-100 positive
Vivek 2006[4]	39	F	Well-circumscribed radiolucency	spindle shaped cells with wavy and tapered nuclei	Lack of encapsulation; S-100 positive
Apostolidis 2001[10]	67	F	Well circumscribed and elliptical radiolucency	spindle shaped cells with wavy nuclei and collagen fibres within a myxoid matrix along with mast cells; No malignancy	Not reported
Alatli 1996[11]	37	F	No abnormality	spindle cells arranged to form roundish foci and wavy, thin bands within fibrous connective tissue	Not reported
Ueda 1993[12]	37	M	Oval radiolucent area	Spindle shaped cells intermingled with a delicate fibrillar stroma along with numerous mast cells	S 100 positive
Papageorge 1992[13]	4.5	M	Unilocular, well-defined radiolucency	spindle cells with slight to moderate nuclear pleomorphism	S-100 protein and vimentin positive
Weaver 1991[14]	22	F	Radiolucent, well-circumscribed lesion	Spindle shaped cells and flowing bundles of cellular connective tissue	S-100 positive
Polak 1989[15]	60	M	Unilocular radiolucent area	spindle-shaped cells intermingled with a delicate fibrillar stroma along with mast cells	S-100 and anti-Leu positive
Papadopoulos 1981[16]	15	M	Radiolucency	Neoplastic cells with ovoidal, elongated nucleus; No pleomorphism; No encapsulation	Not reported

Gnepp 1981[17]	24	F	Non expansile, moderately well-defined unilocular radiolucent	Bundles of mildly pleomorphic spindle shaped cells in fibrous stroma	Not reported
Gnepp 1981[17]	39	F	Well demarcated, slightly expansile, unilocular radiolucent	Interlacing bundles of elongated spindle shaped cells in fibrous stroma	Not reported
Larsson 1978[18]	25	F	Extense bone resorption	Irregular nerve fiber strands intermingled with collagen fibers and abundant cells	Not reported
Larsson 1978[18]	46	M	Bone destruction with slightly radiopaque areas	Spindle cell with elongated or oval nuclei forming cords	Not reported
Ellis 1977[19]	41	F	Poorly defined multiloculated radiolucency	Slight morphologic variability in cells with no mitotic activity	Not reported
Ellis 1977[19]	4	F	Well demarcated radiolucency	Abundance of small nerves with several enlarged nerve fascicles	Not reported
Ellis 1977[19]	8	M	Well demarcated radiolucency with sclerotic borders	Dense, wavy tissue of collagenous type with fibers in random orientation and cells with spindle shaped nuclei with no mitotic figure	Not reported
Ellis 1977[19]	23	F	Indistinct radiolucent-radiopaque lesion	Loose, myxomatous and fibrillary nature with more abundant mucoid matrix	Not reported
Ellis 1977[19]	4	M	Multilocular radiolucency	Dense, wavy tissue of collagenous type with fibers in random orientation and cells with spindle shaped nuclei with no mitotic figure	Not reported
Singer 1973[20]	30	F	Radiolucent fusiform enlargement	Interlacing cords of fusiform cells with thin tapering nuclei associated with fibrillar stroma	Not reported
Cundy 1972[21]	55	F	Large radiolucency	spindle cells with ovoid nuclei arranged in parallel rows with intertwining fascicles	Not reported
Prescott 1970[22]	5	M	Circumscribed radiolucent	Irregular bundles of nerve tissue and whorls with ovoid elongated and comma shaped basophilic nuclei and pale acidophilic cytoplasm	Not reported
Cassalia 1971[2]	16	F	Multilocular radiolucency	delicate intertwining network of collagen fibres together with numerous small nerve fibrils	Not reported
Sharawy 1968[23]	22	F	Multilocular radiolucent	Delicate connective tissue fibrils, fibroblasts and nerve tissue with few woven bone trabeculae	Not reported
Gutman 1964[24]	5	F	Unilocular, translucent area	Spindle cells arranged in ranks or small whorls embedded in a non-cellular, collagenous, connective tissue; No signs of malignancy	Not reported
Villa 1962[25]	2.5	M	Radiolucent lesion	Infiltrating small bands of skeletal muscle; Inferior alveolar nerve showed increase in fibrous tissue	Not reported

Caldwell 1961[1]	2.5	M	Radiolucent lesion	Infiltrating small bands of skeletal muscle; Inferior alveolar nerve showed increase in fibrous tissue	Not reported
Johnson 1959[26]	34	F	Radiolucent	Interlacing bundles of elongated spindle shaped cells with wavy nuclei	Not reported
Cornell 1955[27]	65	F	Cystic character with not well defined borders	Encapsulated tumor with thick myelinic nerve filaments towards the centre	Not reported
Bruce 1954[28]	36	M	Osteolysis in mandibular alveolus	Rows of palisaded nuclei separated by a band of fibers without nuclei	Not reported
Blackwood 1951[29]	41	M	Large radiolucent area	Type A: parallel arrangement of cells and intercellular fibres giving a regimented appearance; Type B: loose meshwork of cells and shows the presence of numerous intercellular vacuoles or microcysts	Not reported
Goldman 1944[30]	33	M	Large cystic lesion	Reticulated mesenchymal tissue with occasional nerve filaments. Spindle shaped cells with small nuclei arranged in bundles	Not reported

Lastly, the choice of treatment for this clinical case should be discussed. Marx states in *Oral and Maxillofacial Pathology – 2nd Ed*: “In contrast to the schwannoma, a neurofibroma arises from the internal portion of a nerve clinically. In most cases the parent nerve is not identifiable. In some cases the nerve can be seen to enter the proximal end of the tumor (Figures 10-32a and 10-32b). Because the nerve is incorporated into and is actually part of the neurofibroma, it cannot be preserved (Figure 10-33).” p.421 (*Oral and Maxillofacial Pathology, 2nd Edition*) [36].”

Although the surgical treatment of a neurofibroma as outlined by Marx may not involve the preservation of the incorporated nerve, we believe our choice of treatment was appropriate in this particular case. Several factors were taken into consideration when determining the appropriate course of treatment with this particular patient; such factors include occurrence and recurrence rates of neurofibromas in the oral cavity, absence of Von Recklinghausen’s Disease (VRD), likelihood of malignant transformation, patient age, patient informed consent, and size/localization of the lesion. Due to the fact that this patient did not present with VRD, it was extremely rare that this individual would develop a neurofibroma in her lifetime, especially in the head and neck region. As previously stated, it is believed that approximately 5% of neurofibromas arise in the oral cavity [33]. Furthermore, at 70 years of age it was deemed highly unlikely for this individual to experience recurrence of the neurofibroma once excised. There is a significant lack of literature surrounding neurofibroma recurrence rates in the oral cavity due to their rarity. Some sources simply state the likelihood of recurrence as “rare” in the case of Alatlí et al [11] while other sources attempt to quantitatively measure the rate of recurrence as less than 20% [37].

Additionally, the possibility of malignant transformation of the tumor was discussed. It is estimated that the risk of developing a malignant transformation in neurofibromas is approximately 2-5% [38]. With that being said, the prospect of this patient presenting with recurring neurofibroma of the oral cavity with a malignant transformation at 70+ years of age is highly unlikely.

Moreover, the patient’s intentions were taken into account. The risks outlined above were discussed with the patient in detail providing full informed consent. With these risks in mind, the patient elected a surgical approach that would attempt to fully excise the lesion while preserving the inferior alveolar nerve and therefore preserve sensory perception in the regions innervated by this nerve. Lastly, due to the relatively small size of the lesion in question, as well as the apparent localization, the surgical decision to perform blunt and sharp dissections of the lesion was carried out.

We believe that the treatment decision should involve a multi-factorial approach. Although this approach may not coincide with that of Marx, we were able to achieve success with exemplary results.

Conclusion

It is important for dental practitioners to be aware of the radiographic and clinical presentation of neurofibromas and their manifestation in the oral cavity. The recognition of neurofibromas is critical as they could be the initial manifestation of neurofibromatosis. Although neurofibromas are benign, there have been reports of neurofibroma recurrence and transformation into malignant tumors. As such, it is essential to conduct clinical and radiographical examination, as well as long term follow up to ensure there is no recurrence.

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