Case Report

Intramandibular plexiform schwannoma presenting as a nonspecific benign lesion: How specific can we be? A case report with a review of the literature

ABSTRACT

Schwannoma, a benign nerve sheath tumor, is quite rare and more so in jawbones. We report a rare case of a plexiform variant of mandibular schwannoma in a 12-year-old female with a swelling in the left mandible. Clinical features were suggestive of dentigerous cyst as a result of missing premolars and canine. Occlusal and panoramic radiography revealed an osteolytic lesion with scalloping margins, bicortical plate expansion, and agenesis of several teeth. Odontogenic keratocyst, central giant cell granuloma, odontogenic myxoma, and ameloblastic fibroma were given as radiological differential diagnoses. Histopathological examination revealed features of plexiform schwannoma which was given as the final diagnosis. The lesion was treated with surgical excision. Although odontogenic cysts/tumors are often thought of in differential diagnosis whenever well-defined radiolucencies in the jaw are encountered, it is prudent to include schwannoma. This exceptional case adds light to the fact that schwannoma should not be overlooked though it is a rare possibility and must be included in differential diagnosis of odontogenic cysts/tumors.

KEY WORDS: Differential diagnoses, intraosseous, mandible, neurofibromas, nonspecific lesion, plexiform schwannoma

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INTRODUCTION

Schwannoma (neurinoma, neurilemmoma, neurolemmoma, perineural fibroblastoma, peripheral nerve sheath tumor, and peripheral glioma), a rare, neurogenic tumor is derived from Schwann cells covering myelinated nerve fibers including cranial nerves, the spinal nerves, and autonomic nervous system with the exception of optic and olfactory nerves as they lack Schwann cells and is a slow-growing benign neoplasm.[1-4] The most common site for this benign nerve sheath tumor is the head and neck occurring as a soft-tissue tumor (25%–48%) and the flexor surfaces of the extremities.[5-7] The extensive migration of Schwann cells during embryogenesis might be the reason for this special preference in the head region.[8] Intraoral involvement is quite rare about 1%.[9]

Intraosseous schwannomas constitute <1% of benign tumors of the jaws and thus are even rarer.[9] The mandible is the most common involved site.[5] Schwannomas can occur in peripheral nerves and have a strong preference for sensory nerves (as they have a thick layer of the myelin sheath).[7]

As the clinical and radiographic features of schwannoma are nonspecific encompassing a well-defined unilocular radiolucency suggesting an odontogenic cyst or tumor causing an array of frequent misdiagnosis, it would be worthwhile to gather germane data on how specific we dentists can be in arriving at a conclusive diagnosis. The aim of this rare case report is to create awareness among dentists with regard to this rare benign neoplasm which mimics other common ones.

A rare case of intramandibular plexiform schwannoma is presented with a review of the

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literature and special emphasis on differentiating between schwannoma and its closest contender, neurofibroma.

CASE REPORT

A 12-year-old female patient reported to the department of oral medicine and radiology with a chief complaint of pain and swelling in the left region of the lower jaw for 6 months. The swelling increased in size gradually to attain the present size. There was no history of trauma, bleeding, or pus discharge in the area.

Extraoral examination revealed asymmetry as a result of well-defined swelling in the left lower two-third region of the face [Figure 1] measuring about 13 cm × 11 cm in size and extending from about 2 cm in front of the tragus of the ear obliterating the nasolabial fold crossing the symphysis to involve the right parasymphyseal region.

Superoinferiorly, it extends from about 2 cm below the inferior orbital rim till the inferior border of the mandible extending about 3 cm below it with overlying skin appearing stretched [Figure 2] resulting in incompetent lips and slightly inferiorly placed left corner of the mouth. The vertical height of the left anterior body of the mandible seems to have increased owing to the downward bowing of the mandible. Local temperature was not raised. Neurosensory examination revealed paresthesia in relation to the left buccal mucosa and the lower lip.

Intraoral examination revealed a diffuse swelling in the left canine–premolar region of the mandible obliterating the labial and buccal vestibule with smooth overlying mucosa. The swelling was extending from the mesial of the left first molar to the right canine region. The swelling was tender and bony hard in consistency. The central incisors and the left first molar were of Grade 2 mobility. Hard-tissue examination revealed missing left permanent lateral incisor, canine, premolars, and right lateral incisor [Figure 3].

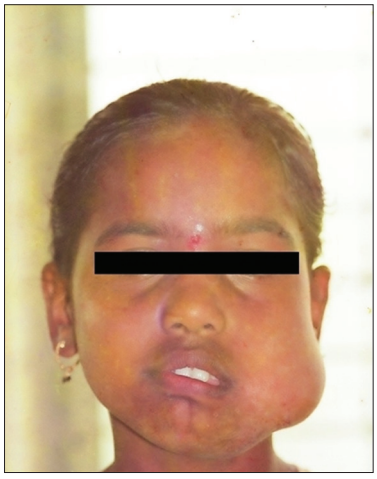

Figure 1: Well-defined swelling in the left lower two-third region of the face

Based on these findings, the dentigerous cyst was given as a provisional diagnosis. Odontogenic keratocyst and tumors such as mural ameloblastoma, central giant cell granuloma, odontogenic myxoma, and ameloblastic fibroma were listed as possible differential diagnoses. A mandibular occlusal radiograph was made [Figure 4].

Panoramic radiography revealed mixed dentition with erupting maxillary canines. A large osteolytic lesion about 9 cm × 8 cm in size involving the body of the left mandible extending from 43 to the mesial of 36 was observed. There was a destruction of the alveolar bone with agenesis of 42, 32, 33, and 34, as there was no history of extraction of these teeth. Soft-tissue shadow of the lesion was seen. 31 and 72 appeared to be displaced and mesial tipping of 36 seemed to be obstructing the eruption path of 35. No root resorption was evident. The scalloping outline seemed to be giving a false sense of multilocularity to the lesion. There was downward bowing and thinning out of the inferior border of the mandible in the left parasymphyseal and body region, leading to increased vertical height of the left side of the mandible. The course of the inferior mandibular canal could not be outlined in the lesion [Figure 5].

Odontogenic keratocyst, central giant cell granuloma, odontogenic myxoma, and ameloblastic fibroma were given as radiological differential diagnoses. Since schwannoma is quite rare, it was not considered in differential diagnosis.

A biopsy was performed from the intraoral site revealing histopathological findings of hematoxylin and eosin-stained sections of the lesion showing the structure of a benign tumor with plexiform architecture and nuclear palisading. It is characterized by multiple interlacing and interconnecting fascicles and nodules composed predominantly of Antoni Type A cells. A typical biphasic pattern is not prominent. Hypocellularity of Type B Antoni cells was seen with macrophages, collagen fibers, and hyalinized vessels. The cellular matrix was well confined within the capsule without

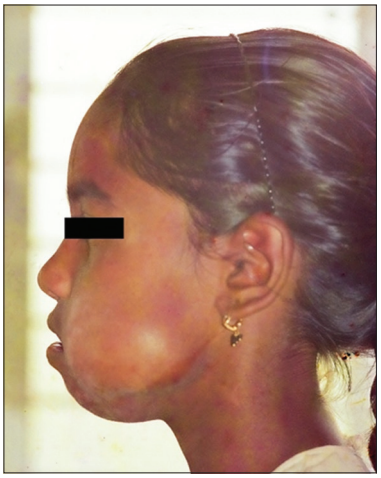

Figure 2: Extension of the swelling

any region of necrosis and myxoid change. Histologically, no evidence of malignant change was observed [Figure 6].

The above features were suggestive of plexiform schwannoma which was given as a final diagnosis.

The patient underwent surgical excision of the lesion which was reconstructed with a bone plate. Some inferior alveolar nerve fibers connected to the tumor were removed and the remaining nerve fiber bundle was preserved. The resected specimen on histopathological analysisconfirmed the diagnosis of a plexiform schwannoma arising from the inferior alveolar nerve. The patient was followed up for 1 year with no recurrence.

DISCUSSION

Schwannoma was named after Theodor Schwann (1810–1882). In 1908, Jose Verocay designated them as neurinoma. Later, the term neurilemmoma was coined in the year 1935 by Arthur Purdy Stout.[5] In 1932, Masson proposed the term schwannoma.[7]

Schwannoma is quite rare in the oral cavity; they affect the tongue in 50% of cases (peripheral variant).[9] Central variant schwannomas are even rare, <1%. When it occurs, the mandible is the mostly affected site. The most favored site being the posterior location (body and ascending ramus) conforming to the lengthy intraosseous route of the inferior alveolar nerve but can also involve the anterior body, symphysis being the rarest site.[9,5] The present case is also one of those rare types, wherein the tumor was located in the left anterior body and symphysis of the mandible.

The likely mechanisms of schwannomas involving the bone are:

a. A tumor could possibly develop centrally within the bone (common)
b. Or within the nutrient canal (common)
c. Soft tissue or a periosteal tumor could possibly erode the bone (rare).[5]

The present case is an example of schwannoma arising within the nutrient canal.

According to the English language literature, 34 proven cases of intrabony schwannoma of the mandible have been reported.[5]

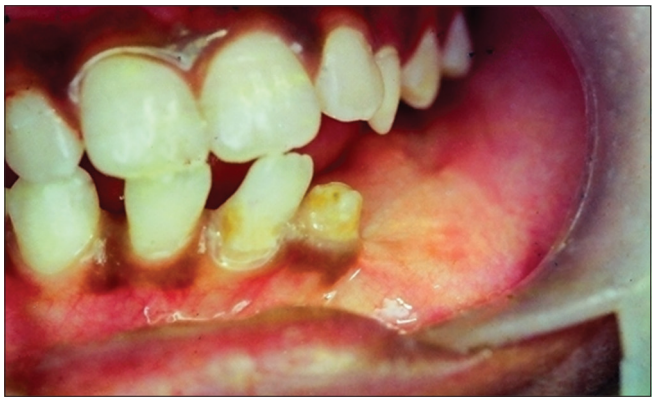

Figure 3: Intraorally, a diffuse swelling in the left mandible obliterating the labial and the buccal vestibule with smooth overlying mucosa and crossing the midline is seen (Below)

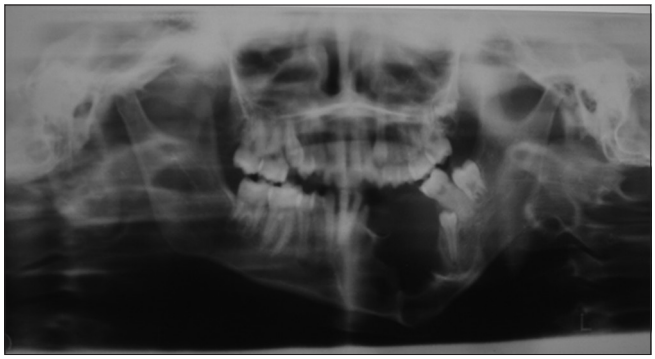

Figure 5: Panoramic radiography revealing destruction of the alveolar bone with agenesis of 42, 32, 33, and 34 and a scalloped outline

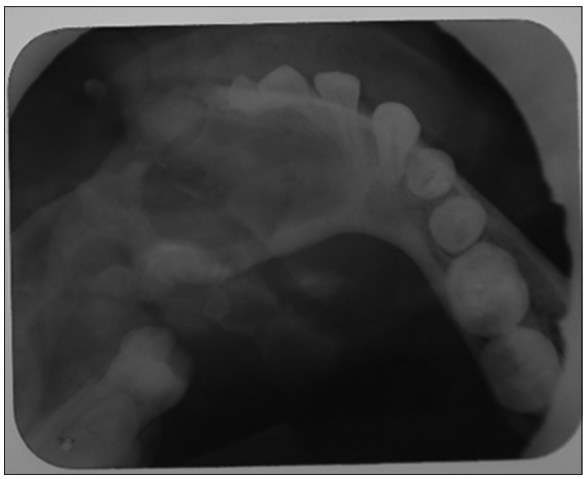

Figure 4: Marked expansion of labial, buccal, and lingual cortical plates with osteolysis and soft-tissue shadow of the mass. Displacement of 41, 31, 72, and 35 was evident

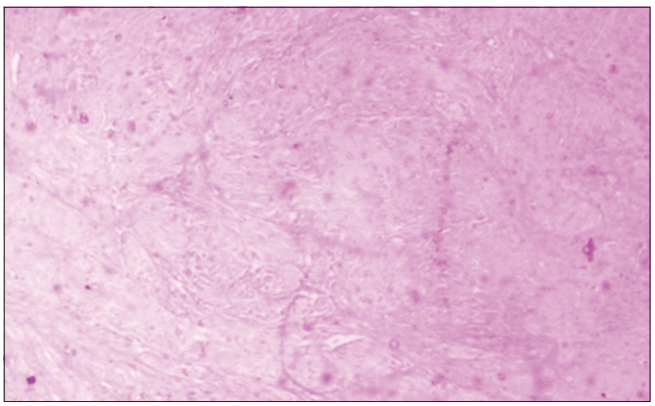

Figure 6: Photomicrograph revealing histopathological findings of H and E-stained sections with ×10 view of the lesion

The etiologic factor is unknown although it is believed to develop as a spontaneous growth to external injury, chronic irritation, or irradiation. Frameshift mutations and deletions result in truncated protein concerning the NF2 gene at 22q12.2, which is a tumor suppressor gene coding for schwannomin protein. Functional loss of this protein involved in intracellular signaling pathways and in the linkage of cell membrane, and the cytoskeleton is linked to the disease expression in NF2. SMARCB1/INI1 mutation was also seen in some cases.[10]

Mandibular schwannomas occurred in the age range of 8–72 years (average age being 34 years) with a peak prevalence in the second and third decades of life and a female predilection (1.6: 1).[5,9] Clinically, neurilemmoma is a slow-growing tumor that may be present for years before being symptomatic, the duration being from few months to few years.[2] The present case was a 12-year-old girl which was younger than the mean age.

Swelling is the most common presentation, but pain and paresthesia are not uncommon occurring in about 50% of the cases and all these were seen in the present case also.[9] Although of neural origin, schwannomas are generally painless producing pressure on the adjacent nerves other than nerve of origin and may present with paresthesia of the area of trigeminal sensory distribution.[10] The size of the tumor ranged from 1 to 9.5 cm with a mean diameter of 6.2 cm.[11] The present case was also around 9.0 cm in size.

Radiological differential diagnosis

Radiographic findings of an intraosseous mandibular schwannoma are nonspecific but otherwise suggestive of a benign process such as odontogenic keratocyst or ameloblastoma.[12] The present case also displayed nonspecific features, for which the following radiological differential diagnoses were given.

Odontogenic keratocyst occurs in all age groups affecting males and is located in the mandible. It is often unicystic but sometimes has scalloped borders frequently occurring with a multilocular appearance.[13]

The ameloblastic fibroma develops under 20 years of age with no sex preference and the majority occur in the premolar–molar region of the mandible. It is not associated with an unerupted tooth and appears as a unilocular or multilocular lesion.[13]

Central giant cell granuloma occurs under 30 years of age affecting females with the mandible being the most common site. Majority of the tumors are located anterior to the second molar with the lesion often crossing the midline. Quite commonly, the lesion presents with a radiolucent, multilocular, honeycombed appearance and ill-defined and granular septae. At times, there is marked expansion with thinning of the cortical plates, perforation, tooth displacement, and root resorption.[13]

Odontogenic myxoma may occur with a concomitant missing tooth and is seen in the age group of 10–50 years. It affects the females with the mandible being the most affected site. These tumors tend to grow along the bone and are not expansile. They present with honeycomb, soap bubble, wispy, or tennis-racket appearance radiographically. The septae are typically thin, sharp, and straight and meet each other at a sharp angle (tennis racket).[14]

Schwannomas (though not considered in the present case) quite commonly are situated within an expanded inferior mandibular canal, posterior to the mental foramen. Pain if present typically develops at the site of the tumor; when paresthesia develops, it is felt anterior to the tumor. The internal structure is uniformly radiolucent. These lesions have a scalloping outline giving a false impression of a multilocular pattern.[14]

The typical presentation is that of a unilocular radiolucency with a well-defined thin, sclerotic border. Other rare features are root divergence (expansive growth), external root resorption only in teeth contacting the lesion, cortical thinning/erosion, spotty calcification/focal radiopacity, multilocularity, cortical expansion, peripheral scalloping, and distension of the mandibular canal, indicating peripheral nervous system lesion.[5] During surgery, a direct association with a neurovascular bundle was noted in the present case as was seen in many instances (10%–50%).[5] The present case revealed bicortical expansion with unilocular radiolucency, peripheral scalloping, and root divergence with difficulty in tracing mandibular canal within the lesion.

Intramandibular schwannomas are hard to differentiate from other bone tumors such as ameloblastoma, myxoma, fibrous dysplasia, neurofibromas, central giant cell lesion, or periapical lesions.[6]

Despite computerized tomography and magnetic resonance imaging (MRI) images, it was concluded that definitive diagnosis was difficult to make on the basis of radiography alone, and histopathological examination is usually mandatory.[9] MRI is of great value as it helps in differentiating solid mass (schwannoma) from purely cystic lesions (dentigerous cyst, periodontal cyst, etc.). MRI can not only depict the tumor and the capsule but also depict, at times, the nerve from which it has originated.[1] However, it is quite hard to distinguish schwannoma from other solid tumors, for instance, ameloblastoma and neurofibroma. Adding, the inferior alveolar canal which is encased by tumor cells or in contact with tumor cells is not visible or shows characteristic destructive changes. In a case reported, in addition to the ameloblastoma-like features, the wall of the inferior alveolar canal was obliterated which helped in distinguishing schwannoma from ameloblastoma radiographically. Furthermore, ameloblastoma shows the displacement of the canal and does not present with paresthesia.[14]

MRI would have been more appropriate in the present case also.

The diagnosis of schwannoma is made by histopathological analysis and specific immunohistochemistry staining. Histological examination establishes the benign nature of the tumor.[15]

The features considered to be characteristic of schwannomas are encapsulation, Verocay bodies, palisading nuclei, and Antoni A and B tissues.

Histologically, six types of schwannoma have been described: classical, cellular, plexiform, epitheloid, ancient, and melanotic schwannomas.[5]

Plexiform (multinodular) schwannoma is an anatomically exclusive variant characterized grossly and/or microscopically by intraneural plexiform and often multinodular growth/pattern. Vera-Sempere in 2010 reported the first case of intraosseous plexiform schwannoma of the mandible, an extremely rare benign neurogenic tumor.[16] The following year another case was reported.[17] Plexiform variant is more cellular than the classic type.[5]

Schwannoma versus neurofibroma

It is vital to differentiate histologically between neurofibroma and schwannoma as neurofibromas have the potential to recur and malignant transformation might be a manifestation of neurofibromatosis.[9] Only 4% of neurofibromas are encapsulated. Although neurofibromas may exhibit Antoni B-like tissue, they do not exhibit Antoni A areas.[5] Generally, neurofibromas lack Antoni A, Antoni B patterns, and Verocay bodies. Furthermore, the presence of mast cells is one of the most useful features in neurofibromas.[4] Adding, neurofibroma is difficult to remove surgically.[1,2] In the mandibular canal, schwannomas become rounded unlike neurofibromas which invariably grow within the canal and appear ovoid shaped.[9]

Immunohistochemical studies

S-100 protein schwannomas steadily show positive staining in a greater number of the tumor cells with the staining intensity more in cells in the Antoni A tissue compared with that seen in the Antoni B tissue, while neurofibromas showed fewer S-100 positive cells.

Epithelial membrane antigen

Staining for epithelial membrane antigen (EMA) was observed only in the capsular tissues of schwannomas, whereas scattered EMA-positive cells were evident within tumor tissue in a minority of neurofibromas.

Factor XIIIa

In schwannomas, positively stained dendritic/spindle cells were located in capsular tissues of many tumors. Many XIIIa-positive cells were detected in a majority of neurofibromas and some in a perivascular distribution.

CD34

Antoni B tissue and capsules demonstrated CD34-positive cells in almost all schwannomas unlike the Antoni A zones, which were consistently negative for CD34. Neurofibromas showed a significant inter-tumor variability of CD34. Many CD34-positive dendritic/spindle cells were found in the connective tissue surrounding the lesions.

Type IV collagen

Schwannomas exhibited immunoreactivity for collagen IV in connotation with the capsule, and most of the tumor cells with the Antoni B tissue showed weaker staining than Antoni A tissue. Most lesions had positive cell-associated staining with the presence of axons (silver stain) in neurofibromas though some variabilities were noted.[18]

Focal positivity for synaptophysin, glial fibrillary acid protein, and neuron-specific enolase has also been reported.[19]

The above-mentioned markers were not used to confirm the diagnosis in the present case. This is a shortcoming of our case.

Schwannomas can recur if the excision is inadequate and is resistant to radiotherapy.[11] As it is a well-encapsulated lesion, the treatment of choice is conservative surgical enucleation with periodic follow-up.[5] It is apt to remove the involved nerve to reduce the risk of recurrence.[8,4]

In a case reported, during the surgery, the tumor was removed with the inferior alveolar canal, as it was encased by the tumor.[20]

It is very important to inform the patient regarding the risk of postoperative anesthesia or paresthesia of a part of the lower lip as a result of the surgery.[15]

Schwannoma seldom undergoes malignant transformation and its not been described in an intrabony schwannoma.[15]

CONCLUSION

Intraosseous schwannoma although extremely rare, one should be well acquainted with the clinical, radiological, and microscopic features, as apt diagnosis and suitable treatment of the lesion is imperative. Schwannoma often copies various odontogenic cysts and tumors, but a concomitant widening of the mandibular canal sometimes observed in intramandibular schwannomas may provide a clue. This rare case corroborates the significance of schwannoma and hints at the addition of this tumor in the differential diagnosis of cysts and benign odontogenic and nonodontogenic tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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