A Benign Tumor Masquerading Malignant Behavior
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Abstract
Intra-osseous Schwannomas are rare primary tumors, accounting for 1% of all primary tumors seen in the maxillofacial region. Schwannomas commonly manifest as well-encapsulated, asymptomatic, slow-growing lesions with late evidence of cortical expansion. Radiographically, intra-osseous Schwannomas present as well-defined unilocular radiolucent lesions with no pathognomonic radiological features. Here an unusual case of a 30 years old female patient with a diffuse swelling in the left malar region has been reported. On histopathological analysis it was diagnosed as a case of benign aggressive Schwannoma. Routine radiological examination along with computed tomography and Magnetic resonance imaging revealed extensive involvement of the bone with intra-cranial extension. The rare occurrence of intra-osseous Schwannoma with clinical presentation mimicking various other lesions makes diagnosis of this lesion a challenge.

Key Words: Neural; Neurinoma; Neurilemmoma; Schwann Cells; Nerve Sheath Neoplasms; Intraosseous; Neoplasms; Nerve Tissue.

Introduction
Schwannomas were first established as a pathologic entity in 1910 by Verocay who called them neurinomas. The terms Schwannoma and neurilemomas presently describe solitary encapsulated nerve tumors of ectodermal origin arising from peri-neural Schwann cells of the nerve. Schwannomas are seen as slow-growing neural tumors that have a predilection for the head and neck region with an abundant number of cases reported from the flexor surfaces of the upper and lower extremities. Intra-orally, these tumors occur most commonly on the tongue followed by the palate, floor mouth, oral mucosa, gingivae, lip and buccal mucosa.

Intra-osseous Schwannomas are rare primary neural tumors representing less than 1% of benign primary tumors of the bones. The sites most commonly involved are the mandible and the sacrum. Intra-osseous Schwannoma of the maxilla is exceptionally rare. The radiographic features of these lesions, further, are non-pathognomonic that makes their diagnosis even more difficult. Recent studies have shown a substantial increase in the number of the cases reported of intra-osseous Schwannomas with preponderance for the women and patients in the second, third and fourth decades being more commonly affected. The malignant transformation of Schwannoma is extremely rare. Herein we are presenting an unusual case report of a benign aggressive Schwannoma of the fifth cranial nerve with involvement of the maxillary division which presented as a slow growing lesion in the form of a swelling in relation to the left side of the face that was successfully managed in our institutional set-up.

Case-report
A 30 years old female patient reported to Department of Oral Medicine and Radiology, Government Dental College and Research Institute, Bangalore, Karnataka, India presenting with swelling since one year in relation to the left side of face. Swelling was insidious in onset, beginning in the left malar region from about a year and gradually progressed to involve the whole left side of the face. The patient gave a history of pain that followed the swelling four months ago in left upper posterior tooth region. The pain was vague, dull aching in nature, continuous with no temporal variations and poorly localized. There was no history suggestive of radiation, reference or its shifting and migratory nature. Patient had visited a dental surgeon regarding the same complaint and was advised and subsequently underwent extraction in relation to left upper back tooth region one month ago because of tooth mobility and mal-position.
Patient did not reveal a significant, past medical history. All vital parameters were also found to be within normal range. The general physical examination of the patient did not reveal any sign of a pathological state associated with other systems. On examination of face, gross asymmetry of face due to a roughly semi-spherical, ill-defined swelling in relation to left side of face measuring about 6 to 8 cm in greatest dimensions, was noted. Overlying skin was stretched but normal in appearance (Fig 1). A slight ptosis and epiphora in relation to the left eye were the only additional signs in the face that were prominent. There was no evidence noted in the form of discharge or ulceration in relation to the lesion.

Intra-oral soft tissue examination revealed an ill-defined, sessile swelling in relation to the upper left buccal vestibule region with distinct buccal vestibule obliteration and grade one mobility in relation to the premolars. The maxillary molars in the region were missing. The posterior aspect of the swelling could not be traced out well. Swelling was non-tender and non-fluctuant. On the basis of these findings, a provisional diagnosis of an aggressive giant cell granuloma was arrived at and the patient was subjected to routine blood investigations followed by a conventional radiologic examination and an incisional biopsy. Patient's blood investigations reports came out to be within the normal range while orthopantomograph (Fig 2a) and paranasal sinus view (Fig 2b) of the patient revealed an extensive bone involvement in the affected region, the posterior extent of which could not well be appreciated.

The histopathological examination of the incisional specimen suggested the tumor to be of neural origin revealing the tumor cells with parallel nuclei and palisading Antoni A appearance alternating with homogeneous acellular zones composed of small hyaline structures known as Verocay bodies, (Fig 3), characteristic of Schwannoma.

Patient was then subjected to advanced imaging modalities including computed tomography (CT) and Magnetic resonance imaging (MRI) evaluation to find the exact extent of involvement of the subjacent structures by the lesion along with the extent of neural involvement. CT of the face with brain (Fig 4) revealed the lesion in the left maxillary posterior region with evidence of extensive bony erosion. The report predicted the lesion as large, ill-defined, heterogeneously enhancing soft tissue attenuation with non-enhancing areas in the center suggestive of focal areas of necrosis. A few cystic areas predominantly in the left infra-temporal region were also suggested. The lesion was seen extending superiorly by widening of the pterygo-maxillary fissure and left superior orbital fissure causing compression of the sphenoid sinus and leading to the involvement of the cavernous sinus.

The lesion was extending intra-cranially up to the level of the inferior temporal lobe however the dura appeared to be intact. Medially, the lesion was seen to be extending into the posterior nasopharyngeal area and involving the anterior ethmoidal air cells. Lytic destruction of the greater wing of the sphenoid bone on left side with thinning and displacement of the left squamous temporal bone was also noted. Major extracranial vessels, however, appeared to be intact. The inferior extension of the lesion involved the left mandibular angle area with compression of the soft part of maxilla and presenting with thinning and displacement of the superior, lateral and medial walls while lytic destruction of inferior wall of the maxillary sinus.

The MRI of brain with plain and contrast, revealed a lesion that was iso-echoic on T1 and hyper-echoic on T2 weighted images. The lesion was predominantly extra cranial in origin with a small intracranial component, in the medial temporal region (extra-dural) with extension into the left maxillary, ethmoid and sphenoid sinuses and left orbital involvement (Fig 5). Lesion was hypo-on T1 and iso-echoic to hyper-echoic on T2 weighted images on contrast MRI suggesting the possibility of a neural tumor.

Patient was then referred to the Department of Neurosurgery, National Institute of Mental Health and Sciences, Bangalore, for further evaluation and needful; where she was subjected to left lateral facial incision with zygomatic osteotomy and total surgical decompression of the infra-temporal tumor using trans-zygomatic infra-temporal approach. After the tumor was surgically removed, the field was inspected for bleeding and hemostasis achieved. Peroperatively, the tumor presented with a well-defined capsule, soft-to-firm in consistency with focal areas of yellowish discoloration (Fig 6). The patient was subjected to
excisional biopsy and an advanced histopathological investigation. Postoperative period was uneventful and the patient was discharged to be followed after a period of three months.

The preoperative frontal view of the patient reveals gross asymmetry with roughly hemi-spherical, ill-defined swelling in relation to the left side of the face (Figure 1). The radiographs (Figure 2) showing cropped orthopantomograph (a) and paranasal sinus (b) images having extensive bone involvement in relation to left posterior maxilla.

The photomicrograph (Hematoxylin and eosin 10X) reveals tumor cells with parallel nuclei and palisading Antoni A appearance alternating with homogeneous acellular zones composed of small hyaline structures known as Verocay bodies (Figure 3). The axial view CT of the face with brain reveals the lesion in the left maxillary posterior region with evidence of extensive bony erosion (Figure 4). The axial view MRI brain reveals the lesion, predominantly extra-cranial, with a small intracranial component, in the medial temporal region (extra-dural) and with extension into the left maxillary, ethmoidal and sphenoidal sinuses (Figure 5).

Gross excised specimen reveals a tumor mass soft-to-firm in consistency with evidence of ulceration and granulation tissue (Figure 6). The photomicrograph reveals dense brown nuclear staining for S-100, a neural crest marker, which is highly supportive of Schwannoma (Figure 7). A three-dimensional CT of the head reveals the lesion in the left posterior maxillary region with evidence of extensive bony erosion (Figure 8).
Immunohistochemistry demonstrated strong nuclear staining for S-100 protein revealing negative S-100 alpha and positive S-100 beta subunits typical of normal Schwann cells (Fig. 7). This further helped us to differentiate our lesion from other typical S-100 protein negative tumors including malignant fibrous histiocytoma, fibrosarcoma and synovial cell sarcomas. Thus, histological architecture along with immunohistochemistry led to the final diagnosis of intraosseous Schwannoma.

Discussion
Schwannomas or, neurilemmomas were first described by Verocay in 1910 who called them as neurinomas. In 1935, Stout used the term neurilemmoma to describe the lesion.\textsuperscript{10} Schwannomas or, neurilemmomas (neurinoma, perineural fibroblastoma) and neurofibromas are the major benign neoplasms of neuroectodermal origin. A central Schwannoma or, neurilemma is a tumor of neuroectodermal origin arising from the Schwann cells that make up the inner layer of the peripheral nerves.

Presenting as a relatively slow growing lesion, the tumor occasionally presents a relatively rapid course of development (an aggressive clinical behavior), may arise at any age, cases having been reported during the first year of life and without a specific sex predilection. Despite the fact that these tumors arise from the nerve tissue, they are usually painless until and unless they exert pressure on the adjacent nerves rather than on the nerve of origin. The presenting symptom in majority of the patients is only the presence of a tumor mass seen in the form of a slow growing swelling, initially asymptomatic but later coming to notice because of an obvious asymmetry of the involved tissue or, associated pain because of pressure effects on the adjacent nerves.\textsuperscript{5,3}

Schwannomas have been reported as central lesions within the bone, chiefly, mandible apparently arising from the mandibular nerve.\textsuperscript{4} The soft tissue lesion is usually a single, well-circumscribed lesion of varying sizes that presents no pathognomonic features. It may resemble any of a number of benign odontogenic or, non-odontogenic tumors. The central lesion in bone may occasionally lead to considerable destruction of the bone with expansion of the cortical plates, thus, resembling a more serious lesion.\textsuperscript{2} Pain and paraesthesia may accompany in the later stages of the lesion.\textsuperscript{1}

The histopathological picture of Schwannomas is however characteristic and can seldom be confused with that of other lesions. The tumor is classically described as being composed of two types of tissues: Antoni type A and Antoni type B. Antoni type A tissue is composed of cells with elongated or spindle shaped nuclei aligned to form a characteristic palisading pattern with the inter-cellular fibers aligned in a parallel fashion between the rows of cells and nuclei. These fibers in some planes give the impression of occurring in the form of whorls or swirls. Antoni type B tissue does not exhibit the characteristic palisading pattern revealed in the former type of the tissue but rather presents a disorderly arrangement of cells and fibers with areas of what appears to be edema fluid and with the formation of micro-cysts. Small hyaline structures seen in the form of Verocay bodies are also characteristically present in the tumor.\textsuperscript{1} Of great importance is the fact that in nearly all instances, the tumor is well encapsulated.\textsuperscript{10}

Immunohistochemical markers such as S-100 protein, leucine 7 and myelin basic protein are used to differentiate Schwannomas from other spindle cell lesions and tumors. S-100 protein came out to be positive in our case revealing negative S-100 alpha and positive S-100 beta subunits typical of normal Schwann cells which further helped us to differentiate our lesion from other typical S-100 protein negative tumors including malignant fibrous histiocytoma, fibro- and synovial cell sarcomas.\textsuperscript{11,12}

Like other tumors of neural origin, Schwannomas are not radio-sensitive. Treatment of Schwannomas lies with surgical excision of the tumors. Since, Schwannomas are well encapsulated tumors of Schwann cell origin, little difficulty, if any, is encountered during its surgical removal although occasionally, preservation of nerve may not be possible. Complete surgical excision, many a times, is not feasible owing to a need for extensive sacrifice of the subjacent structures resulting in structural and functional compromise. Recurrence, however, is highly unlikely. Also, Schwannomas do not undergo malignant transformation as may neurofibromas after numerous episodes of surgical tempering.\textsuperscript{5}
Conclusion
Despite recurrence being highly unlikely and the lesion with almost negligible chances of undergoing malignant transformation, an early diagnosis of Schwannomas is of utmost clinical relevance as it helps save unnecessary delay in treatment and resultant severe structural and functional compromise on the part of the patient left with significant morbidity especially in case the lesion displays an aggressive clinical behavior (Fig 8).

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Ethical declaration
The manuscript has been prepared by taking full consideration of the ethical standards laid down in the 1964 declaration of Helsinki and its later amendments after a written informed consent of the patient for the publication of the manuscript for the sake of academic interest. Details that might disclose the identity of the patient have been omitted.

References

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