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Case Report

Intraosseous malignant peripheral nerve sheath tumor of maxilla: A case report with review of the literature

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ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST), the principle malignancy of peripheral nerve origin, though rare in the general population, occurs with excessive frequency among patients with neurofibromatosis. This tumor always arises in soft-tissues, usually found in the lower extremities and only 10-12% of all lesions occur in the head and neck region, which makes it a rare entity. The primary intraosseous MPNST is rare and has been reported most frequently in the mandible. This article discusses a case report of MPNST of the left maxilla without a history of benign nerve tissue tumor and the diagnostic difficulties associated with MPNST.

Key Words: *De novo*, intraosseous, malignant peripheral nerve sheath tumor, S-100

INTRODUCTION

Malignant peripheral nerve sheath tumor (MPNST) is a rare variety of soft-tissue sarcoma of ectomesenchymal origin.[1] World Health Organization coined the term MPNST replacing previous heterogeneous and often confusing terminology, such as malignant schwannoma, malignant neurilemmoma and neurofibrosarcoma, for tumors of neurogenic origin and similar biological behavior.[2] These tumors often create diagnostic problems because of their cellular origin and histopathological similarities with other spindle cell sarcomas.[3] MPNSTs are usually seen in the extremities, trunk and their occurrence in the head and neck region is very rare.[4] A case of MPNST of maxilla has been described in this article, which was clinically and histopathologically non-specific and it was diagnosed with immunohistochemical techniques.

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CASE REPORT

A 65-year-old male patient presented with a swelling and partial numbness of the upper left side of the jaw. The swelling was first noticed 9-10 months back, which slowly increased to the present size. There was also mild, intermittent, dull aching pain along with a discomfort during the mastication.

The family history of patient was non-contributory. On physical examination, he was healthy and hematological findings were within the normal limits.

Extra-oral examination showed an oval-shaped well-defined swelling on the left middle-third of the face extending from the ala of the nose to the zygomatic arch antero-posteriorly and from the infra-orbital margin to the alveolar process superoinferiorly. The overlying skin was stretched and surrounding tissues appeared normal. On palpation, there was no local rise in temperature. The swelling was non-tender, firm in consistency, non-fluctuant, non-reducible and non-compressible. None of the lymph nodes were palpable.

On intraoral examination, an intraosseous growth [Figure 1] was noticed, measuring around approximately 3 cm × 5 cm in dimensions and extending from the distal of left maxillary canine region to the maxillary tuberosity area along with palatal extension in relation with missing 24, 25, 26, and 27. There was an evidence of paresthesia on the affected site and the overlying mucosa appeared normal.

The panoramic radiograph showed an oval radiolucent lesion extending from the distal of left maxillary canine to the maxillary tuberosity with an ill-defined margin. Computed tomography (CT) scan [Figure 2] showed an irregular destructive soft-tissue mass within the left maxilla.

Based on the history, clinical findings and radiographic examination a provisional diagnosis of ossifying fibroma, odontogenic tumor and aggressive malignant neoplasm was given.

The incisional biopsy from the left alveolar ridge and palate was performed. A macroscopic examination showed multiple bits of soft-tissue specimens, which were irregular in shape and soft in consistency. Nerve tissue was also identified during the examination, which was white in color, firm in consistency, solid tube like in appearance, but unfortunately, grossing photographs were unavailable.

Microscopic examination of H and E stained section showed highly cellular lesional tissue consisting of numerous malignant spindle shape cells with wavy nuclei, showing fascicles, whorls and a palisaded arrangement. At many places herringbone pattern [Figure 3] was also evident. These cells showed hyperchromatic nuclei with

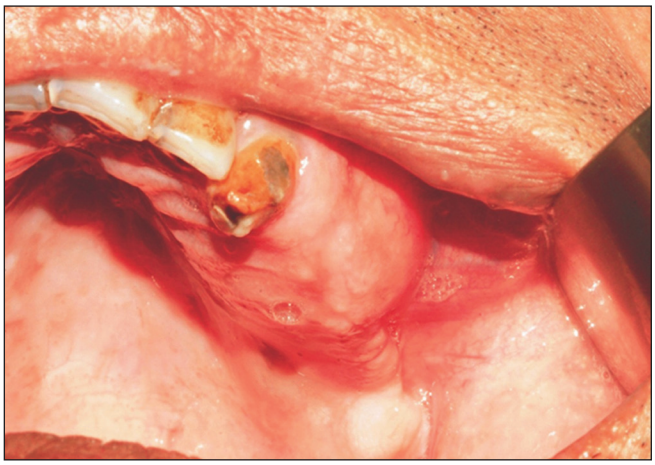

Figure 1: Intraoral photograph shows intraosseous growth with a normally appearing overlying mucosa on the left side of maxilla

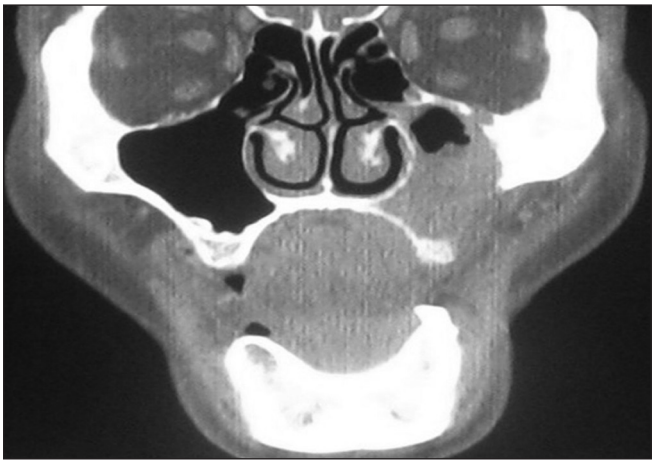

Figure 2: Coronal computed tomography scan showing an irregular destructive soft-tissue mass in the left maxilla

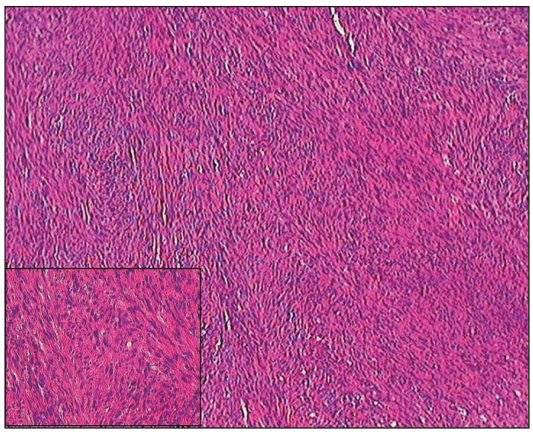

Figure 3: Herringbone pattern of malignant spindle shape cells (H and E, original magnification ×10) (cells in a malignant peripheral nerve sheath tumor having irregular, buckled shape with wavy nuclei under higher magnification [inset])

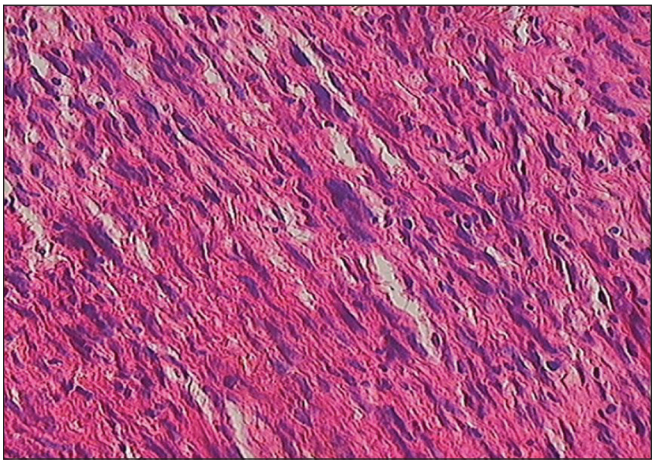

Figure 4: Malignant spindle shaped cells showing large pleomorphism with enlarged nuclei (H and E, original magnification ×40)

mitotic figures [Figure 4] with xanthomatous change around irregularly arranged neoplastic cells [Figure 5]. Few areas of necrosis were observed [Figure 6] and transverse sections of nerve bundles were also evident with perineural invasion [Figure 7]. Few areas showed perimucsular invasion [Figure 8] and at places the tumor appear to herniated into the lumen of vessels [Figure 9]. The histopathological findings were suggestive of MPNST. Immunohistochemical stain helped to confirm the diagnosis as the mesenchymal component stained intensely and focally with S-100 [Figure 10]. Correlating the radiological, histopathological and immunohistochemical investigation, a final diagnosis of MPNST was given.

Patient was referred to the "Tata Memorial Hospital and Cancer Research Center" for further evaluation and management and advised post-operative short term and long-term follow-up visits.

DISCUSSION

MPNST consists of malignant proliferation of any cell of the nerve sheath; schwann cell, peripheral fibroblast or endoneural fibroblast.[5] The schwann cell is thought to be the major contributor to the formation of benign as well as malignant neoplasms of the nerve sheath.[6]

Its development is thought to be a multistep and multigene process with an etiology due to loss of chromosomal arm 17q sequence including complete inactivation of neurofibromatosis-1 (NF-1) gene.[7] About 40-50% of MPNST are associated with a family history of NF-1.[8] Since the patient had denied previous benign pathology that may have been likened to be a NF, a *de novo* origin may be thought of for the present case.

Intraosseous peripheral nerve sheath tumors are rare and usually benign.[9] These are most commonly solitary

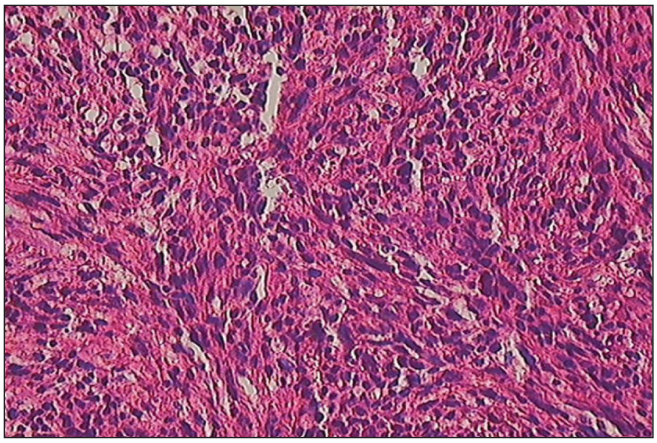

Figure 5: Xanthomatous change is evident with irregularly arranged neoplastic cells (H and E, original magnification ×40)

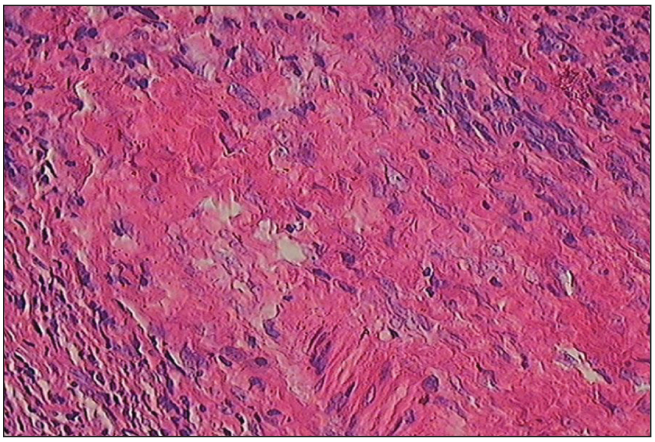

Figure 6: Areas of necrosis within the connective tissue stroma (H and E, original magnification ×40)

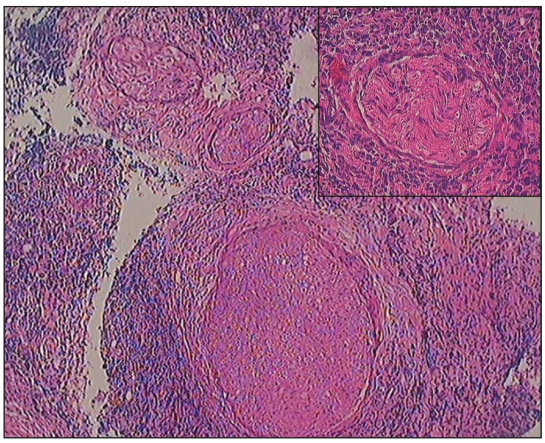

Figure 7: Perineural invasion (H and E, original magnification ×10) (Another area showed perineural invasion under higher magnification [inset])

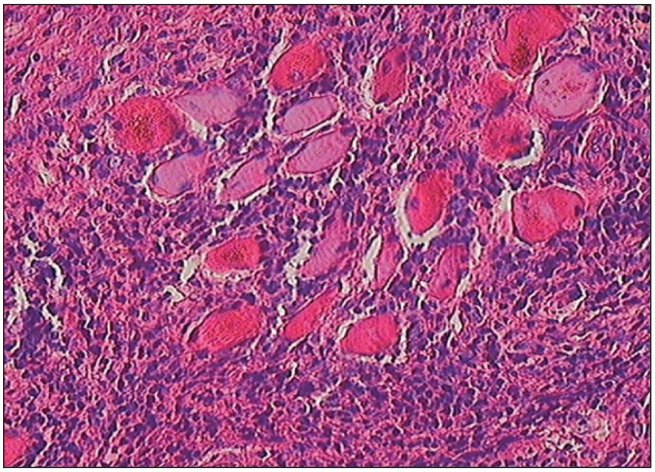

Figure 8: Perimuscular invasion (H and E, original magnification ×40)

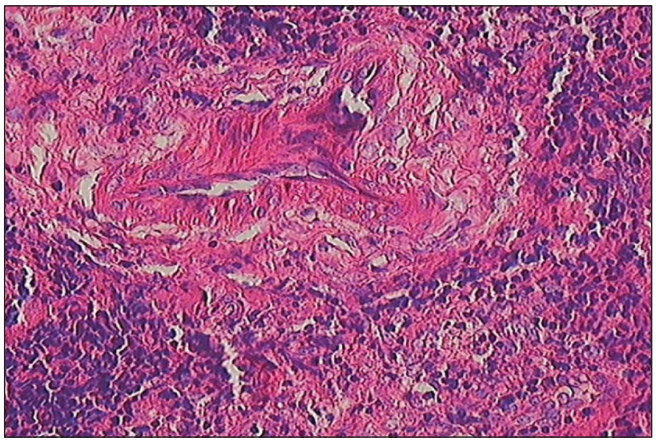

Figure 9: the tumor appears to herniated into the lumen of vessels (H and E, original magnification ×40)

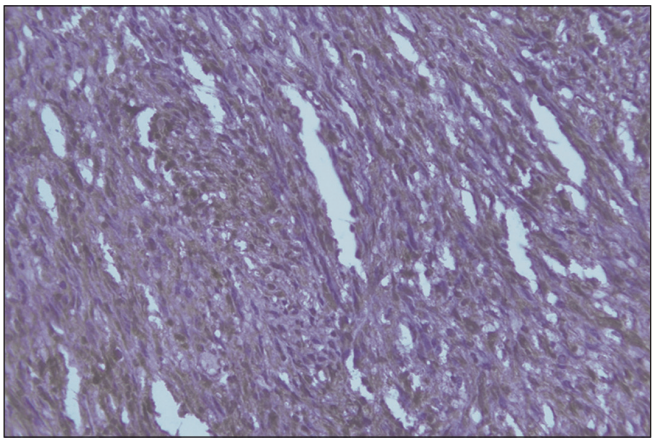

Figure 10: Mesenchymal malignant spindle cells showing diffuse and intense positivity with S-100 (immunohistochemical stain, original magnification ×40)

lesions that arise in the mandible[7] and are most often not associated with NF-1.[10] The present case comprises an extremely rare presentation of this malignancy owing to its involvement within the maxilla, extending into the maxillary sinus and nasal cavity. This tumor occurs in the age group of 20-50 years,[7] with equal frequency in males and females and some series have shown a female preponderance.[2] However in our case, it was associated with 65 years male patient.

Only 29 cases of intraosseous MPNSTs have been reported [Table 1],[5,7,9,11-16] 20 of which have occurred in the mandible or maxilla. There have been three reported cases involving the femur. Sternum, sacrum, humerus and palate each have shown a single case along with two cases of ulna. To the best of our knowledge, only one case of intraosseous MPNST of maxilla in a male patient has been published.

Clinically, it tends to grow slowly, which was seen in our case, but sometimes may exhibit rapid growth.[7] This tumor can spread through direct extension, hematogenous extension and by perineural spread. Lymph node metastasis is rare.[4]

Radiographic examination of intraosseous tumor of the oral cavity will show a complete destructive pattern with bony expansion, erosion and tooth mobility. The present case showed edentulous jaw due to the lesional tissue.[7] On CT, MPNSTs present as a hypo dense, non-homogenous mass due to areas of degeneration and areas of varying cellular density.[12] These similar findings were observed in our case.

The difficulty in demonstrating the origin from a nerve is usually demonstrated in 61% of cases.[5] However, in our case, nerve tissue could be identified on gross examination as well as histopathologically. Myelinated nerve fibers have been documented within the bone in humans, thus; it is possible that MPNST may arise from these intraosseous nerves.[9] The pathological features of MPNST reveal irregular fusiform or globoid mass associated with a nerve and features of malignancy such as palisading arrangement, nuclear atypia, bizarre mitotic figures, giant cells, hemorrhage.[17] As the tumor was showing malignant spindle shaped cells with herringbone pattern, fibrosarcoma and fibroblastic variant of osteosarcoma were also considered histologically. As there was no osteoid tissue in the lesional tissue,[4] the diagnosis of fibroblastic variant of osteosarcoma was ruled out. Intraosseous fibrosarcoma is a very rare entity and fibrosarcoma shows symmetrically spindled cells with fascicular patterns; therefore, fibrosarcoma was also ruled out. The term MPNST replaces the earlier terms malignant schwannoma, neurofibrosarcoma and neurogenic sarcoma because MPNSTs recapitulate the appearance of various cells of the nerve sheath, they range in appearance from tumors that resemble a neurofibroma to those resembling a fibrosarcoma.[18]

Immunohistochemistry (IHC) plays a crucial role in determining the diagnosis. Hence, prior to IHC, routine microscopic diagnosis of MPNST was difficult.[5] The suggested IHC markers used for MPNST are S-100, glial fibrillar acidic protein, Leu-7, myelin basic protein, neuron specific enolase and neurofilament. The most widely used antigen, S-100 protein is known to be observed in 50-90% of MPNSTs cases. Although Leu-7 and myelin basic protein are found in 50% and 40% of them, respectively,[11] recent

Table 1: Summary of reported cases of intraosseous malignant peripheral nerve sheath tumor[5,7,9,11–16]

References	Sex/age	Cancer site	NF–1	Follow–up
Peers 1934	M/55	Ulna	No	Resected, well at 20 months
Bell 1936	F/65	Mandible	No	–
Guthert 1952	M/20	Humerus	No	–
Millard and Busser 1952	F/42	Mandible	No	Died of disease
De Larue 1959	M/30	Mandible	–	–
Devore and Waldron 1961	M/65	Mandible	No	Radiation, resection, recurrence
Ingram 1962	F/4½	Mandible	–	–
Bose *et al*. 1970	M/28	Ulna	No	–
Cernea *et al*. 1974	M/–	Mandible	–	–
Glass and Livingstone 1984	F/11	Mandible	No	Resected, well at 6 months
Kitamura *et al*. 1985	F/–	Mandible	–	–
Shirasuna *et al*. 1986	F/76	Mandible	No	–
Kameyama *et al*. 1987	F/61	Maxilla	No	–
Punyasingh *et al*. 1987	F/6	Mandible	No	Resected, chemotherapy, well at 3 years
Urade *et al*. 1990	F/47	Maxilla	No	Resected, radiation, chemotherapy, died at 22 months
Bailet *et al*. 1991	M/50	Mandible	No	Radiation, died of disease at 1 year
Bullock *et al*. 1995	M/28	Femur	No	Resected, lung metastases at presentation
Mirra *et al*. 1989	–	Sternum	Yes	–
Terry *et al*. 1998[9]	M/26	Femur	Yes	Resected, radiation, died of disease
Che *et al*. 2006[11]	F/13	Maxilla	No	Resected
Che *et al*. 2006[11]	F/15	Mandible	No	Resected
Lesic *et al*. 2006[12]	M/45	Femur	No	Resected
Patil *et al*. 2007[7]	M/45	Maxilla	No	–
Kumar *et al*. 2010[5]	F/32	Maxilla	No	Resected
Lin *et al*. 2007[13]	F/65	Sacrum	No	Resected
Salla *et al*. 2009[14]	M/45	Palate	No	–
Salla *et al*. 2009[14]	M/45	Mandible	No	–
Janardhanan *et al*. 2011[15]	M/40	Maxilla	Yes	Died of disease
Ali *et al*. 2011[16]	M/50	Maxilla	–	Resected

NF–1: Neurofibromatosis–1; M: Male; F: Female

studies suggest that nestin, which is an intermediate filament protein, is more sensitive for MPNST than other neural neural markers (S-100, CD56 and protein gene product 9.5) and immunostains for nestin in combination with other markers could be useful in the diagnosis of MPNST.[19] In the present case, lesional tissue showed positivity for S-100.

MPNSTs have been reported to be highly aggressive and have a high propensity to metastasize to distant sites.[20] In addition, they tend to recur locally despite aggressive surgical approaches. A positive margin is known to be the primary and single factor for predicting a local recurrence. Therefore, treatment requires a block resection and sometimes even radiation therapy has been recommended.[11]

Prognosis of MPNST is poor and survival is found to be influenced by tumor location, size and association with NF-1. Survival rate is worse for patients with NF.[20] Overall survival rate is 40-75%.[7]

CONCLUSION

MPNSTs constitute a small fraction of peripheral nerve tumors. In the present case, it was appreciated that a *de novo* maxillary intraosseous MPNST can also arise, which was a highly aggressive tumor and very difficult to treat. Their site of origin, routine as well as immunohistochemical staining pattern were thought to indicate a schwannian origin; however, the histogenesis of the tumor remains controversial. Despite the substantial progress in treatment modalities available in the present era, the wide spreading nature of this tumor has a strong hold in determining the prognosis. The effects of environmental carcinogens are still unclear. Early detection of this aggressive tumor may help reduce morbidity.

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