Case Report

Received : 04-03-16
Review completed : 10-04-16
Accepted : 26-04-16

MPNST: A RARE YET AMBIGUOUS LESION

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ABSTRACT

Malignant Peripheral nerve sheath tumors (MPNSTs) are uncommon, ectomesenchymal in origin, representing about 5% of soft-tissue sarcomas. World Health organization (WHO) coined the term MPNST replacing previous heterogeneous and often confusing terminology, such as malignant schwannoma, malignant neurilemmoma, and neurofibrosarcoma, for tumors of neurogenic origin with similar biological behavior. These tumors may arise from peripheral nerve branches, spontaneously in adult patients in age group of 20-50 years with equal predilection in males and females. Accurate diagnosis of MPNST is important to differentiate between soft tissue sarcomas and other malignant neoplasms as it is a diagnostic dilemma. A combination of clinical presentation, histopathological, and immunohistochemical studies shall be utilized appropriately to arrive at a diagnosis. Surgery is the main stay of treatment of this tumor though they are biologically aggressive in nature. This case report highlights ambiguous nature of the lesion in its clinical presentation with a series of multiple investigations utilized.

KEYWORDS: Malignant peripheral nerve sheath tumor; NF1; Neurofibroma; Neurofibromatosis

INTRODUCTION

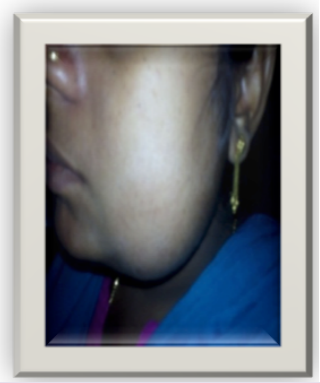
Malignant peripheral nerve sheath tumours (MPNST) are malignant sarcomas that are locally invasive and frequently spread.[2] Peripheral nerve sheath tumors (PNSTs) consists of an array of neoplastic potential ranging from benign neurofibromas and schwannomas to high-grade malignant peripheral nerve sheath tumors (MPNSTs). Enzinger and Weiss gave the term MPNST and is preferred for these tumours because they may retake the appearance of any cell of the Schwann cell and also the perineural fibroblast or fibroblast[2].It is a rare lesion, with an incidence of 1 per 1,00,000 population and which constitutes between 3 to 10% of all soft tissue sarcomas.Presence of the lesion in head and neck region varies 10-12% to 10-15% and are associated with poor prognosis unless wide excision of the tumour is undertaken before local invasion or distant metastasis can occur. An MPNST often is present along with clinical setting of NF1, although sporadic cases do occur The incidence of sporadic MPNSTs is low, with a lifetime risk of 0.001%. The most usual heterologous component in MPNST is rhabdomyoblast differentiation being first reported by Masson in 1932 and named "nerve rhabdomyoma", and later renamed by Woodruff as "malignant triton tumor".[3]

CASE REPORT

A 40 year old female patient named Ashwini

reported to the Department of oral medicine and radiology with a chief complaint of swelling in Lower right face region from 2 months(Figure 1 and 2).The history revealed that the Patient was apparently normal 2 months back until she noticed a swelling on the lower right face region. Swelling was progressive in onset and progressed to attain the present size. No history of pain bleeding, pus discharge and any surface changes were noticed.Patient gives a history increase in size of swelling with hot fermentation. Patient gives a history of tobacco consumption and reduced mouth opening from 2 months(Figure 3). Patient visited a private dental practitioner for the same where extraction of lower third molars was advised and underwent.Swelling did not reduce even after the extractiom for which the patient was advised on panoramic radsiograph and was given antibiotics.Patient was referred to Rajarajeswari Dental College and Hospital.Her Past Medical History, Dental History, Family History and Personal History were non-contrubutory towards the findings.On General Physical Examination patient was moderately built and well coordinated gait and upright posture with all vital signs in normal limits.Extraoral Examination revealed**,** Gross Facial asymmetry was noted on right side. Solitary well defined swelling is seen over the right middle and lower third of the face measuring 4*4 cms in size extending anteroposteriorly from the corner of the lip to the tragus of the ear and superoinferiorly from the ala tragus line to 1cm below the lower border of the mandible. skin over the swelling appears normal. The surrounding area does not reveal any abnormality. Mouth opening was noted 23 mm. On palpation all inspectory findings are confirmed. Swelling is non tender and firm to hard in consistency. No localized rise in temperature present and no regional lymphadenopathy. On intraoral examination of the lesion proper general findings were supragingival calculus and dental caries irt 26. Examination of the lesion proper revealed buccal vestibular obliteration and tenderness irt 46,47,48. Diffuse swelling was noted on the right retromolar region measuring about 1*1 cm in size extending from the distal aspect of 46 to distal aspect of 47 and superoinferiorly from line of occlusion to buccal vestibule. Swelling is firm to hard in consistency and non-tender. Clinically missing irt 48.Tenderness present on extraction site irt 48.Thus,based on the history and clinical findings a Provisional diagnosis of Ameloblastoma was a given and a Differential diagnosis of Dentigerous cyst was considered. Patient was subjected to Radiographic Investigations. Panoramic radiograph revealed a partial loss of body of the mandible on the right side extending from 44 till ramus and superoinferiorly from the alveolar crest to the lower border of mandible. A diffuse ill-defined radiolucency radiolucency seen on the right ramus of mandible with loss of internal structure extending from 2cm inferior to sigmoid notch to the lower border of the mandible superoinferiorly and from the right medial to lateral border of the mandible anteroposteriorly. Radiographic features were suggestive of ameloblastoma undergoing malignant changes and osteosarcoma of mandible. CBCT was advised to assess the size,extent and dimension of the lesion as it gives a detailed 3D overview of the lesion proper. The findings revealed osteolytic area with well defined borders and floating tooth appearance irt 47 in the reformatted panoramic view. Expansion of buccal cortical plate seen on axial section. Mixed radiolucent radiopaque areas seen near the right angle and body of the ramus in all 3 sections(Figure 4 and 5). Sigmoid Notch is intact and posterior and anteriuor border of ramus is lost in all 3 sections. Which revealed intraosseous malignancy involving right mandible.The blood investigations were within the normal limits. For further understanding the lesuion better It was sent for Histopathologic investigations, as the Hematoxylin and eosin stained sections revealed a connective tissue specimen consisting of spindle shaped cells which vary in size and shape(Figure 6). These cells have scanty cytoplasm with indistinct cell borders with little amount of collagen fibers. In some areas the nuclei are spindle shaped and vary in nature.The overall feature was suggestive of a diagnosis of malignant spindle cell neoplasm.Further IHC markers were required to arrive at a specific diagnosis.The Immunohistochemistry was done and the report revealed the tumour markers S100,CD 56 and CD 131.Which were elevated . S 100 revealed that lesion is of nervous origin and CD 56 showed that it is a proliferative growth and CD 131 revealed that the lesion is Malignant Peripheral Nerve sheath tumour. Which suggested that the lesion was malignant peripheral nerve sheath tumour. And complete excision of the tumour was done(Figure 7).

Fig 1 : Extraoral Photograph



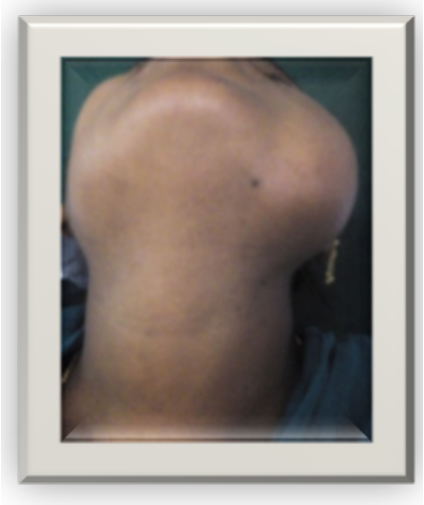


Fig 2 : Extraoral Photograph

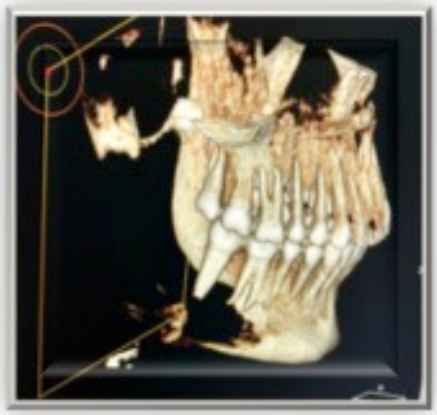


Fig 5 : CT Image

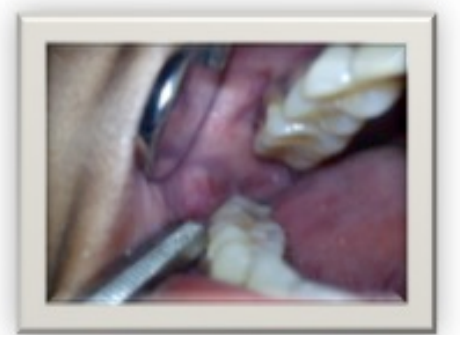


Fig 3 : Reveals diffuse swelling on right retromolar region and buccal vestibular obliteration

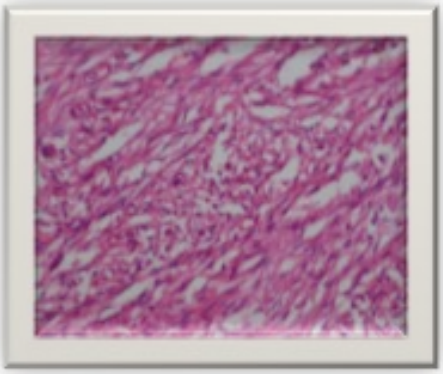


Fig 6 : H & E Stain

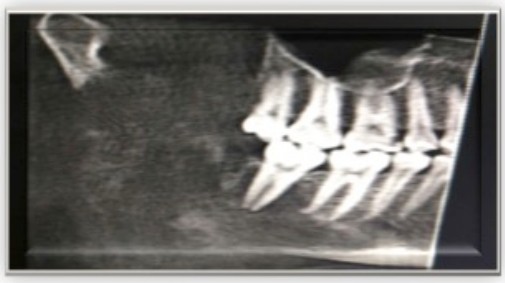


Fig 4 : Panoramic Radiograph

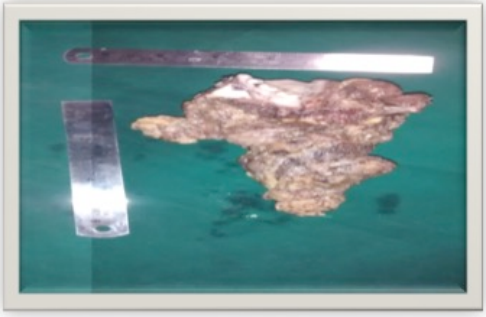


Fig 7 : Excised Lesion

DISCUSSION

MPNST is also known as malignant schwannoma, neurofibrosarcoma, malignant neurilemmoma and neurogenic sarcoma.[2] It is an aggressive sarcoma of neural origin showing a close association with peripheral nerve or neurofiboma or may show features of neural differentiation.[2]Neurogenic tumors include malignant and benign variants; benign group constitute neurofibroma, schwannoma, neuroma peripheral nerve sheath tumors .[4] Previously, various terminologies like neurogenic sarcoma, neurilemmosarcoma, malignant fibrosarcoma and malignant neurilemmoma had been used, but World Health Organization (WHO) has recently adopted the term 'malignant peripheral nerve sheath tumor.[4] MPNST are sarcomas with one of the following features: (1) arising from a peripheral nerve (2) arising from a pre-existing benign nerve sheath tumor (3) which demonstrate schwann cell differentiation on histologic examination.[5] Its occurrence in the oral cavity is extremely rare and the most common sites being mandible, lips and buccal mucosa.[4]Around 40-50% of MPNSTs are associated with a family history of neurofibromatosis-1 (NF-1)[4]. MPNSTs occur in about 2–5% of NF1 patients compared with an incidence of 0.001% in the general population. Etiology for MPNST is thought to be multistep and multigene process with loss of chromosome arm 17q sequence including complete inactivation of neurofibromatosis-1 gene.[5] Common occurance is in the age group between 20-50 years with an equal male and female predilection .[5] MPNSTs are found in the extremities and the trunk generally on the body.[6] It can occur anywhere on the oral cavity with the most common sites being-mandible, lips, buccal mucosa, tongue and palate.[2] It mostly appears as a bosselated, sessile, circumscribed submucosal mass associated with pain or parasthesia or muscle weakness and atrophy.[2] it may occur as a slow enlarging mass which sometimes may exhibit rapid growth. The tumour may also occur centrally within the jaws or as a deep soft tissue malignancy.[2] Soft tissues (MPNST) are fleshy in consistency and are confluent with adjacent tissues.[2] Two thirds of the lesions are larger than 5 cms at the time of diagnosis.[2] MPNST presents as a rapidly enlarging mass that may give rise to neurologic complaints. A family or personal history of NF1 is helpful in making the correct diagnosis.[7] Sometimes it shows slow growth because of this slow growth ,despite being a malignant lesion it radiographically showed a sclerotic border.[5] When associated with major nerve trunks, projecting pain, paresthesia, and weakness are the common symptoms. This tumor can metastasize by hematogenous and perineural spreads. Rarely, is lymph node metastasis noted.[5] Radiographic examination of intraosseous tumour of the oral cavity will show a complete destructive pattern with bony expansion, erosion and tooth mobility.[2] Intraosseous tumour of mandible will show widening of the mandibular canal.[2] CT is used in assessing the tumor extension and eventual metastasis[6]. Magnetic resonance imaging (MRI) can be used to evaluate the nerve of origin, and it is more accurate in assessing topographical relationship of the tumor with the neighboring structures, especially the vascular and muscular structures and fat planes involvement. Thereby, MRI distinguishes the lesion from the fat tissue better than CT, whose dislocation and thinning of the fat tissue thickness has a critical importance in localizing the space of origin of a neck lesion.Another investigation that is, Fine needle aspiration, a biopsy method employed to obtain individual cells for cytologic review. It can be performed with a very small needle, which is more easily tolerated by the patient and is often useful to establish the presence of malignant cells.[6] Microscopically, it is noted that the tumour consists of spindle cells with a high mitotic rate and indistinct cytoplasmic borders arranged in bundles or fascicles.[4] The diagnosis of MPNST is tricky and elusive in the soft tissue disease due to lack of standardization. It is not always simple to demonstrate the origin from a nerve, especially when it arises from a small peripheral branch.[5]In most cases,the tumors display fascicles of spindle cells woven into herringbone pattern with varying degrees of mitosis and necrosis[1]. Immunohistochemistry plays a vital role in the diagnosis, with tumor cells showing specific positivity for S-100.[4] Some neural markers, such as S-100, CD56 and protein gene product 9.5 (PGP 9.5),nestin are considered sensitive markers for peripheral nerve sheath tumors. S-100, which is traditionally regarded as the best marker for MPNST, has limited diagnostic utility and is positive in only about 50-90% of the tumors .[3] MPNSTs per se lack sufficiently specific and sensitive immunohistochemical marker .[3] S-100, Leu-7 and myelin basic protein can be used to identify nerve sheath differentiation and they are immunoreactive for Vimentin and not immunoreactive for HMB-45. S-100 immunoreactivity is focal and scattered in 50-90% of MPNST.[2] Differential diagnosis includes leiomyosarcoma, fibrosarcoma, and monophasic synovial sarcoma. MPSNT should be differentiated from these lesions by characteristic histological features, special stains, and IHC.[4,5] Most common routes of spread are through direct extension, hematogenous extension and by perineural spread whereas Lymph node metastasis is rarely seen[4]. Treatment is predominantly

surgical[5]. Complete surgical excision of the tumor with negative margins gives the best outcome when it comes to local recurrence and distant metastases. Anatomic location of the tumor determines the resectably rate primarily. [4].Radiation therapy has been tried in preoperative, intraoperative, and postoperative settings. With the addition of postoperative radiation therapy there is a statistically significant reduction in the rates of local disease recurrence, but not in overall survival. Chemotherapy is usually considered for patients with large tumor size (> 5 cm), unresectability or metastatic disease.[4]. Its local recurrence rate ranges from 40% to 42%. Mainly metastatizes to lungs, followed in decreasing order of frequency by soft tissue and bone [4]. MPNST has been reported to have a 5-year survival rate of 34–39% [5]. The malignant transformation of a neurofibroma has an extremely poor prognosis with prevalent recurrences and distant metastasis[4]. Favourable prognostic factors include tumor size < 5 cm, lack of local recurrence, low histologic grade and extremity location[4]

CONCLUSION

Malignant peripheral nerve sheath tumor (MPNST) of the mandible is an uncommon tumor that develops either from a preexisting neurofibroma or *de novo*. MPNSTs are sarcomas that originate from peripheral nerves or from cells associated with the nerve sheath, such as Schwann cells, perineural cells or from fibroblasts. Because MPNSTs can arise from multiple cell types, the overall appearance can vary greatly from one case to the next. A combination of clinical, pathological and immunohistochemistry helps in diagnosing these tumors. Although a multimodality therapy, including surgical resection and adjuvant radiotherapy, is available, the prognosis remains dismal. Modern clinical studies and the development of effective targeted chemotherapy are needed to gain control of the disease.

BIBLIOGRAPHY

1. M Kar, SV Suryanarayana Deo, NK Shukla, A Malik, SD Gupta, B Kumar Mohanti, S Thulkar.Malignant peripheral nerve sheath tumors (MPNST) – Clinicopathological study and treatment outcome of twenty-four cases.World Journal of Surgical Oncology. 2006, 4:55 doi:10.1186/1477-7819-4-55.
2. Patil K, Mahima VG , Ambika L. Malignant peripheral nerve sheath tumour: An elusive diagnosis. Indian J Dent Res 2007;18:19-22.
3. A Guo, A Liu*, L Wei, X Song. Malignant Peripheral Nerve Sheath Tumors: Differentiation Patterns and Immunohistochemical Features - A Mini-Review and Our New Findings. Journal of Cancer. 2012; 3: 303-309. doi: 10.7150/jca.4179.
4. R A Kannan, K Koushik, U Muniyappa, R Harjani, and A Murthy, "Malignant Peripheral Nerve Sheath Tumor of Buccal Mucosa: An Oncological Surprise." American Journal of Medical Case Reports, vol. 2, no. 10 (2014): 222-224. doi: 10.12691/ajmcr-2-10-6.
5. Bagalad BS, Ananthaneni A, Guduru VS, Kuberappa PH. Intramandibular malignant peripheral nerve sheath tumor: A case report.Saudi J Oral Sci 2016;3:49-52.
6. US Yaga, R Shivakumar, M. A Kumar, and Sathyaprakash. Malignant peripheral nerve sheath tumor: A rarity.Indian J Dent 2015;6:53-6.
7. C J. Stasik,O Tawfik. Malignant Peripheral Nerve Sheath Tumor With Rhabdomyosarcomatous Differentiation (Malignant Triton Tumor). Arch Pathol Lab Med. 2006;130:1878–1881.

CONFLICT OF INTEREST & SOURCE OF FUNDING

The author declares that there is no source of funding and no conflict of interest among all authors.