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CASE REPORT

Malignant peripheral nerve cell tumour

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Abstract Malignant Peripheral Nerve Sheath Tumour (MPNST) also termed as spindle cell malignancy of the peripheral nerve schwann cell or neurogenic sarcoma represents 10% of all soft tissue sarcomas. The tumour is usually found in lower extremities and only 10% to 20% of all lesions occur in head and neck region thus making it a rare entity. Central involvement, particularly in the jaw bones is quite unusual. Neurofibroma is one of the common nerve sheath tumours occurring in the soft tissues and generally appears in neurofibromatosis I (NF-I or von recklinghausen's disease). MPNST are uncommon sarcomas that almost always arise in the soft tissues. Here we report a case of intraosseous peripheral nerve sheath tumour occurring in the mandible and discuss the surgical management with adjuvant and neoadjuvant treatment plan.

Keywords Neurilemmoma · Nerve sheath tumour · Neurofibromatosis-I · Malignant triton tumours · Sarcoma/bone neoplasms

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Introduction

Malignant peripheral nerve cell tumour or malignant neurilemmoma is a form of cancer of the connective tissues surrounding nerves. Given its origin and behavior it is classified as a sarcoma [1,2]. About half the cases are diagnosed in people with neurofibromatosis; the lifetime risk for an MPNST in patients with neurofibromatosis type I is 8% to 13% [2].

MPNST with rhabdomyoblastomatosis component are called malignant triton tumours. According to Enzinger and Weiss 1993, the term MPNST is preferred for these tumours because they may recapitulate the appearance of any cell of the Schwann cell and also the perineural fibroblast [3]. This tumour is usually found in lower extremities and retroperitonium and is rare in head and neck area [4–9]. The intraosseous localization of MPNST is very rare in literature [10]: Dahlin and Krishanan [11] reported 10 cases, Wirth and Bray [12] 31 cases, Bullock et al. [13] 18 cases, and De la Monte et al. [14] presented 60 histologically documented cases. The diagnosis of MPNST has also been complicated by unclear criteria for determining the malignancy of a tumour originating in the nerve [15]. Since Harkin et al. (1978) first reported plexiform schwannoma [16]; several authors have reported plexiform schwannoma unassociated with Von-Reckling Hausen's disease, which usually show benign histological features (Lee et al. 2001); (Woodruff et al. 1983); (Barbosa and Hansen 1984); and (Guarino 1993) (6,17–20). Here we report a case of intra-osseous malignant peripheral nerve sheath tumour of mandible in an 18-year-old female patient.

Clinical report

An 18-year-old female patient reported to the department of faciomaxillary surgery with a chief complaint of a large lower jaw swelling, which was increasing in nature, associated with pain, difficulty in speech and mastication. History of presenting illness revealed that the swelling associated with the left side of mandible was insidious in nature and has been gradually increasing in size over a period of 8 years to the present state, there was history of associated moderate intermittent pain, occasional intra-oral pus discharge, difficulty in speech and mastication.

On clinical examination the swelling extending from left ascending ramus, angle and across the midline to right hemimandible, measuring about 45cm, there was no extra-oral sinus or discharge and no paresthesia.

On palpation the growth was firm, non-fluctuant with no mobility, moderately tender with wide expansion of lower cortex. Bilaterally palpable, mobile submandibular lymph nodes were present.

Intra-oral examination revealed inflammation and soft tissue hyperplasia in relation to left retromolar area, with missing first molar and second premolar (history of extraction), the swelling was hard, non fluctuant and tender to palpation with expansion of both buccal and lingual plates, floor of mouth and tongue was raised, there was pus discharge in relation to left canine area, and no mobility of associated teeth.

Panoramic radiograph showed a large radiolytic lesion (multi-locular irregular radiolucency) extending and involving almost the entire left side of the mandible with expansion of mandibular canal, and extending to the right body/angle of the mandible.

A clinical impression/differential diagnosis was that of an aggressive odontogenic tumour such as odontogenic myxoma or ameloblastoma. Also considered were fibrosarcoma, malignant

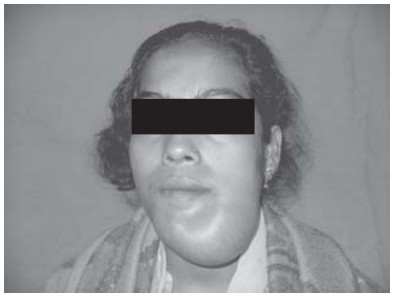

Fig. 1 Extra-oral view

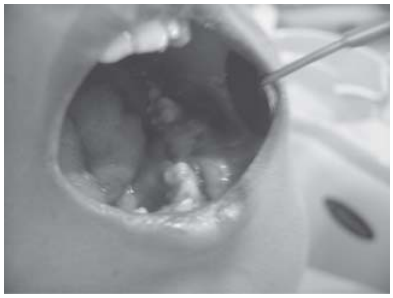

Fig. 2 Intra-oral view

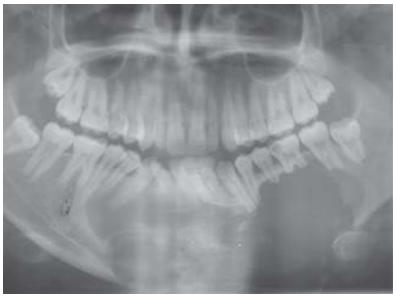

Fig. 3 Panoramic radiograph

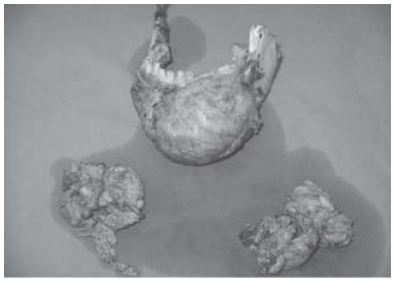

Fig. 4 Resected specimen

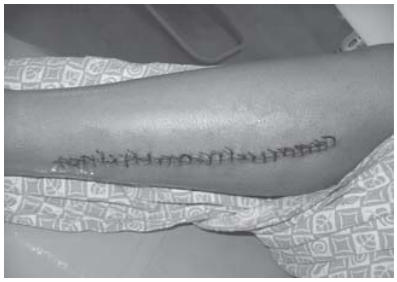

Fig. 5 Closure lower limb

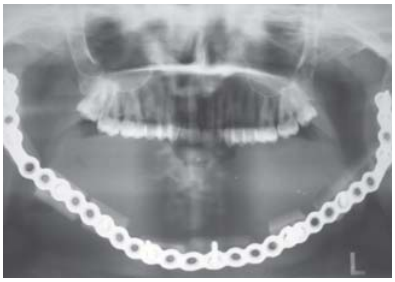

Fig. 6 Mandible reconstruction

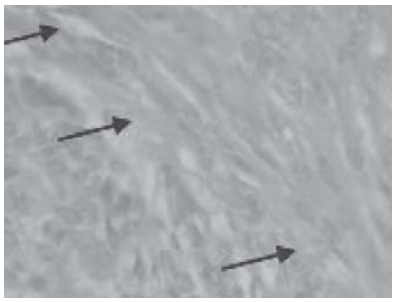

Fig. 7 Microscopic view (Arrow indicating dense fascicles of spindle cells)

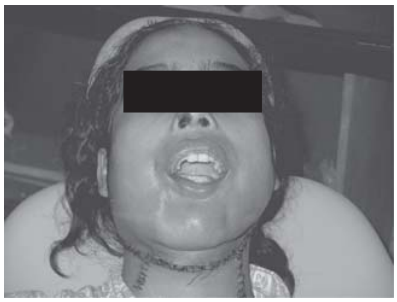

Fig. 8 Post surgery

fibrous histiocytoma and osteo-sarcoma. Both extra-oral and intra-oral aspiration with a wide bore needle did not yield any clinically significant material.

An intra-oral deep incisional biopsy in the region of left retromolar area was performed under local anesthesia, which confirmed the lesion as malignant peripheral nerve cell tumour.

Excision of the tumour was done under general anesthesia. A visor flap access approach in bilateral neck crease was utilized to reach and expose the entire tumour and the jaw margin; meticulous dissection of the tumour for wide margins and bilateral subcondylar osteotomy was performed. Segmental mandibulectomy and tumour resection with wide margins was achieved. A bilateral comprehensive Functional Neck Dissection (FND III) with adequate nodal clearance and submandibular/sublingual gland excision was done.

The large existing jaw defect was adequately reconstructed with a free osseous fibular bone graft harvested by Gilbert lateral approach from the ipsilateral leg. Multiple osteotomies were performed in the osseous bone graft to achieve the contour of the previously existing mandible, which was then adapted and rigidly secured to the distal jaw bone segments bilaterally using AO mandibular reconstruction plate with 2.5/10mm screws.

Complete haemostasis was achieved, drains placed and both the neck incisions and leg wound closed in layers.

Postoperative wound healing was uneventful and patient was adequately mobilized on 5th postoperative day.

Postoperative histopathological report confirmed the lesion as malignant nerve sheath tumour, stated H and E section showing cells, which are plump spindle shaped with vesiculated nuclei and arranged in bundles. Areas showing nuclear palisading arrangement, hyalinised nodular areas. Cells showing whorled pattern with evident mitosis. The neck margins were free of malignancy. Patient was reviewed twice at three months interval (6 months) and after 1 year 5 months for any recurrences. Clinically there was no evidence of any recurrence.

Discussion

MPNST is also known as malignant schwannoma, neurofibrosarcoma, neurolemmoma and neurogenic sarcoma [5,6,21,22]. Malignant peripheral nerve sheath tumour (MPNST) is the coined term used by the WHO and corresponds to the malignant proliferation of any cell of the nerve sheath: Schwann cell, perineural fibroblast or endoneural fibroblast [3,23,24]. The tumour represents 10% of all soft tissue sarcomas and 8% to 16% in head and neck region [23,25]. Its development is thought to be a multi step and multi gene process with an etiology of loss of chromosomal arm 17q sequence including complete inactivation of neurofibromatosis-1 gene [5,7,26]. This tumour occurs in the age group of 20 to 50 years with an equal male and female predilection [5,6,9,27]. Inspite of being uncommon, MPNST have been described in different locations of the body, occasionally associated or not with Neurofibromatosis type-I [28]. Isolated cases in the orbit [29], neck [30], para-pharyngeal region [6] have also been reported. On occasions the existence of the tumour is related to the presence of Neurofibromatosis or Von-Reckling-

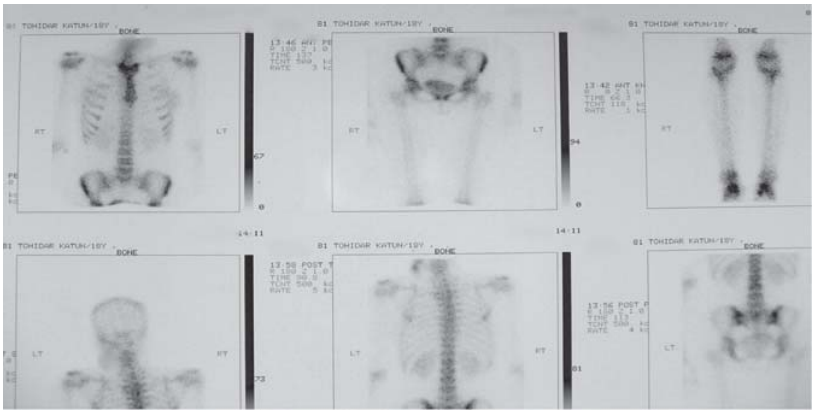

Fig. 9 Bone scan to rule out spread (Post-surgery-18 months)

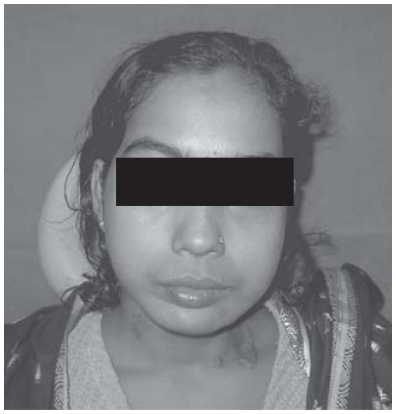

Fig. 10 Review after 18 months

Immuno-histochemistry

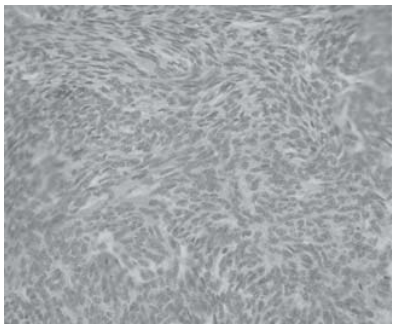

Fig. 11 S-100 profile

Fig. 12 Cyto-keratin profile (negative)

Fig. 13 CD68 profile - 70% possitivity

hausen's disease with described cases located in the bladder, thorax, orbit, mediastinum and prostate [28]. Two series of MPNST of head and neck region have been presented, Loree et al. [31] informed of 17 cases in 9 men and 8 women whose mean survival in 5 years was 52%. Vege et al. [32] presented 27 patients with the average age of 42 years and survival within 5 years was 33%. Primary MPNST in bone are exceptionally rare [13].

The tumour appears as a bosselated, sessile, circumscribed submucosal mass associated with pain or paresthesia or muscle weakness and atrophy [6,7,26]. This slow enlarging mass exhibits rapid growth [8] and 2/3rds of the lesions are more than 5cm at the time of diagnosis. Neurilemmomata can affect bone by 3 different mechanisms [10].

1. The tumour tissue can be localized extraosseously, eroding into the bone secondarily.
2. It can develop within a nutrient canal primarily, involving the bone secondarily.
3. Primarily arise within the central medullary canal.

These tumours can spread through direct extension, hematogenous or by perineural spread. Lymph node metastasis is rare (5). The definitive diagnosis of MPNST is histopathological. Two different cell patterns can usually be recognized on microscopy:

Antoni type A: like pattern with spindle cells in a palisade formation, surrounded by an interstitial substance that forms verocay bodies.

Antoni type B: like pattern with irregular cells and a myxoid component [10]. Although Antoni A and B arrangements are commonly described in benign schwannoma [10] the long duration and slow growth of low grade MPNSTs can lead to similar histological characteristics. The presence of verocay bodies is pathognomic of neurilemomma [10,33].

Immuno-histochemistry plays an important part in the diagnosis and differential diagnosis of MPNSTs: excluding, fibrosarcoma, synovial sarcoma, fibrous histocytoma, adenoid cystic carcinoma, neurogenic sarcoma, and chondrosarcoma.

Immuno-histochemically the tumour cells show immune-reactivity to the S-100 protein and vimentin, with focal positivity to CD68 and negativity to keratin [34,35].

50% to 70% of MPNSTs are S-100 immuno-possitive. Although S-100 expression is not exclusive of MPNST, it is indicative of neural differentiation [23]. Other proteins such as Glial Fibrillary Acidic Protein (GFAP), Leu-7, Myelin basic protein, Neuron Specific Enolase (NSE) and neurofilament may be evaluated in the diagnosis of MPNSTs [23,36].

Radiographic examination of intraosseous tumour of the jaws will show a complete destructive pattern with bony expansion, erosion, and tooth-mobility, widening of the mandibular canal [27,26] or mental foramen with or without irregular destruction of surrounding bone [8]. On CT MPNSTs present a hypodense, non-homogenous mass due to areas of degeneration and areas of varying cellular density [10].

The treatment of MPNSTs of jaws is wide surgical excision but local recurrence is common. Hematogenous metastasis occurs in atleast half the cases [5,6,26]. Patient's survival is correlated to the size of lesion, adequacy of margins, association or not with neurofibromatosis-I and immunohistochemical findings. Over all survival rate is 40% to 70% [6,7]. Prognosis is generally poor.

Conclusion

MPNST is a highly aggressive tumour, which could be difficult to treat, despite substantial progress in treatment modalities available in present era. The wide spreading nature of this tumour has a strong hold in determining the prognosis. Early detection of this aggressive tumour may help reduce morbidity. Although chemotherapy (high dose of doxorubicin) and often radiotherapy are done as adjuvant/neoadjuvant treatments, their role is questionable.

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