Case Report

Malignant Peripheral Nerve Sheath Tumor of the Spinal Accessory Nerve

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Abstract

Background: Malignant peripheral nerve sheath tumors (MPNST) are rare soft tissue sarcomas. They can arise from pre-existing benign nerve tumors, from normal nerves or as secondary neoplasms 10 to 20 years after radiation therapy. They are most commonly found on the extremities and trunk and less often in the head and neck. These tumors are characteristically aggressive, resulting in considerable patient morbidity and generally a poor prognosis. MPNST of the accessory nerve have not yet been described. We highlight a case that occurred at the right base of skull that presented as hypoglossal nerve palsy.

Case Description: A 47 year old male presented with intermittent, multiple cranial nerve palsies and wasting and fasciculation’s of the right tongue. He had a previous Hodgkin’s Lymphoma which was treated with radiotherapy 24 years prior. A CT scan showed a heterogeneous soft tissue density mass within the right superior carotid space. This was avidly enhancing on MRI with extension to the right jugular foramen with local mass effect. Multiple FNA biopsies were non-diagnostic and an excision of the lesion diagnosed a MPNST of the accessory nerve. He was then treated with further radiation therapy after discussion at a multidisciplinary head and neck cancer meeting.

Conclusion: MPNSTs are rare tumors that seldom occur in the head and neck. MPNSTs are staged and treated as malignant soft tissue sarcomas. Because they are rare, there are currently no definitive efficacy trials. In various studies, five-year survival rates range from 34 to 64 percent. We present a case occurring at the jugular foramen which presented with palsies in the relevant cranial nerves.

ABBREVIATIONS

MPNST: Malignant Peripheral Nerve Sheath Tumor; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; FNA: Fine Needle Aspirate

INTRODUCTION

Malignant peripheral nerve sheath tumors (MPNST) are soft tissue sarcomas derived from peripheral nerves demonstrating peripheral nerve differentiation. This term has replaced previous nomenclature such as malignant schwannoma, neurogenic sarcoma, neurofibrosarcoma and malignant neurilemmomas [1,2]. They have also been referred to as malignant triton tumors when coupled with rhabdomyosarcomatous components [3]. MPNST can arise from pre-existing benign tumors (such as from precursor plexiform neurofibromas), from normal nerves or as secondary neoplasms 10 to 20 years after radiation exposure, from either therapeutic radiation therapy or environmental exposure [4,5].

Histopathologically, MPNST arise from differentiated Schwann cells embedded in a varied environment comprising perineurial-like cells, fibroblasts, vascular cells and mast cells. This is in contrast to schwannomas, which do not induce malignancies, but are benign peripheral nerve sheath tumors consisting entirely of Schwann cells. Tumors arising from the epineurium or associated vasculature of peripheral nerves are also not classified as MPNST. Malignant granular cell tumors are another subset of soft tissue tumors of Schwannian origin usually affecting smaller nerve tributaries and should not be confused with MPNST. It is important to define the precise histopathology of nerve sheath tumors as it ultimately guides appropriate management.

CASE PRESENTATION

A 47 year old male presented with intermittent, multiple cranial nerve pareses. He described an intense sensation of gagging and choking as if there were fingers in his throat. This
was associated with right sided tongue deviation, dysarthria, and headache. On examination, there was wasting, fasciculations and right deviation of the tongue, weakness of right palate, minor slurred speech and slight weakness of right sternocleidomastoid muscle. He had a past history of Hodgkin’s Lymphoma which was treated with radiotherapy 24 years prior. A CT scan of the neck showed a heterogeneous soft tissue density mass within the right superior carotid space (Figure 1). This was avidly enhancing on MRI and showed extension to the right jugular foramen with local mass effect (Figure 2). A PET scan showed the mass to have intense FDG uptake (SUV max 14.9) with no lymph node involvement or metastases (Figure 3). A fine needle aspiration (FNA) biopsy/core biopsy was suggestive for a myosarcoma after multiple non-diagnostic FNA. The core biopsy from the right neck mass showed atypical, pleomorphic spindle shaped cells with wavy nuclei with a myxoid background and an area of necrosis. The lesional spindle-shaped cells were positive for S-100 protein. Finally, an excision of the lesion confirmed a MPNST of the accessory nerve of Schwannian origin (Figure 4). The surgical specimen showed a well-circumscribed tumor mass with a thread-like bundle of nerve fibres attached to the lesion (Figure 5A). Microscopic examination revealed a diffuse proliferation of spindle-shaped cells, which had fibrillary cytoplasmic processes and oval to comma-shaped nuclei. The individual tumor cells showed nuclear pleomorphism, hyperchromatism and numerous mitoses including atypical forms was also observed. Well-delineated areas of geographic necrosis were noted (Figure 5B). The lesional cells were positive for S-100 protein (Figure 5C). He was then treated with further radiation therapy after discussion at a multidisciplinary head and neck cancer meeting.

Surgical Intervention

A right neck dissection and excision of the tumor was performed. A tracheostomy was placed and a mandibulotomy was performed to gain access to the tumor at the base of the skull. A right parotidectomy was performed as part of the neck dissection. The accessory nerve was sacrificed as it was engulfed by the tumor at the jugular foramen.

Outcome

There were no perioperative complications. Although the accessory nerve was sacrificed, the patient had reasonable strength in the right sternocleidomastoid and trapezius muscles. After discussion at a multidisciplinary head and neck cancer meeting, he was given a course of radiation therapy. It was felt that chemotherapy would not be beneficial as there is insufficient evidence in the literature to support its role in MPNST. At 2 years follow up, his shoulder shrug remained strong, there were no more symptoms and signs of glossopharyngeal, vagal or hypoglossal nerve palsies and there was also mild improvement in the right tongue wasting.

DISCUSSION

MPNST arise from peripheral nerves and show variable differentiation toward one of the cellular components of the nerve sheath (Schwann cells, fibroblasts and perineurial cells). They form a group of neoplasms with a range of morphology and are frequently destructive tumors with a propensity to recur and metastasise.

Epidemiology

MPNST are rare and accounts for approximately 2% of all sarcomas [6]. It affects 5 million people annually [7]. It has an incidence of 1/100,000 in the general population [3]. Neurofibromatosis (NF) type 1, an autosomal dominant condition resulting in formation of multiple neurofibromas, is associated with half of all MPNST [1]. There is only a weak association between MPNST and NF2 [8] and both sexes are affected equally. MPNST present earlier than most other genomically complex sarcomas, which tend to present after 60 years of age [9]. The median age of diagnosis for sporadic MPNST is between 30 to...
60 years and those that are associated with NF-1 present earlier between 20 and 40 years. MPNST have been documented to occur in childhood in very rare cases [10,11].

**Clinical presentation**

Patients with MPNST may present with a rapidly growing mass that may cause local pain or neurological symptoms. It may also cause a mass effect with compression of nearby structures. New onset pain or expansion of a neurofibroma in a NF1 patient should always be carefully investigated for suspicion of development of MPNST. NF1 patients have a risk of 4.6% to 13% of developing a MPNST in their lifetime [13,14]. At presentation, most MPNST are greater than 5cm and up to half of patients already have advanced disease with metastases to the lungs. The nerve roots and bundles in the trunk and upper and lower extremities, in particular the sciatric nerve, are common sites of involvement [12]. Head and neck MPNST are rare with only 16 cases reported in the literature [13,14]. We describe the first case of a MPNST of the hypoglossal nerve.

**Investigation**

The most useful imaging modality for surgical planning and for anatomical evaluation is magnetic resonance imaging (MRI). They appear isointense to muscle on T1-weighted images and typically hyperintense on T2-weighted images with fasicular appearance [15]. Differentiation between benign and malignant tumors may be difficult with MRI and hence CT is useful to look for bony erosion as a sign of malignancy [16]. MPNST on CT have low attenuation, possibly due to fat entrapment, high lipid content of Schwann cell myelin and cystic areas due to haemorrhage or necrosis [15]. There is a small role for Fluorodeoxyglucose-positron emission tomography (FDG-PET) in the investigation of MPNST as one study has shown that it can reliably differentiate benign neurofibromas from MPNST in NF1 patients [17]. However, these results are yet to be demonstrated in other studies. The gold standard of diagnosis requires pathological analysis of biopsy specimens. Diagnosis of MPNST can be challenging as it can be histologically varied and because of morphological overlap with a variety of other sarcomas [18]. Pathologically, MPNST are characteristically composed of spindle cells arranged in a fascicular growth pattern and mitotic rate and extent of tumors necrosis is variable [19]. It lacks specific immunochemical markers and there are currently no distinct or widely reproducible molecular prognosticators.

**Prognosis**

MPNST have a high metastatic potential and generally a poor prognosis. The lungs, soft tissues, bone, liver and brain are all documented sites of haematogenous metastases [1,8,12,16]. Local recurrence rates range from 30% to 60% and have been reported to recur even in cases where there was complete resection [8,20]. MPNSTs are classified between grades 2 and 4 by the World Health Organization, but there is no prognostic correlation between grade and survival [8,21]. 5 year survival rates vary among many centers ranging between 15 to 52% [1,22]. The most reliably determined adverse prognostic factor across all studies is large tumor size at presentation [19,23,24]. Other reported factors include tumor grade, surgical margin status, local recurrence, truncal location and heterologous rhabdomyoblastic differentiation.

There is controversy with the true prognostic influence of NF1 syndrome in MPNST. Several large, single institution series describe NF1 patients with MPNST to have significantly worse outcomes with poor responses to chemotherapy and lower 5 year survival rates (up to 50% worse) compared with sporadic MPNST. However, a more recent meta-analysis showed that the poorer prognostic impact on survival in NF1 associated MPNST was abolished in patients diagnosed after the year 2000. This is most likely due to improved overall surveillance with better imaging and diagnostic techniques and prompt early intervention [25].

**Treatment**

Localized soft tissue sarcomas such as MPNST are treated with complete surgical resection and clear margins [14]. Involved margins and local recurrence result in poorer outcomes as suggested by multiple retrospective series. This proves difficult for MPNST arising from the trunk as gross, extensive total resections would result in significant morbidity. Likewise, intracranial tumors require individual assessment and work up to plan access and avoidance of important nearby structures. We were fortunate in resection of the described MPNST in this study as there was only a small extension of the tumor into the jugular foramen and adequate access was achieved via the neck with a mandibulotomy.

Adjuvant radiation therapy is advocated to decrease rates of recurrence, especially for large, high grade sarcomas. Its use has been debated but is implicated as it can increase rates of tumor control and long-term survival [1,8,26]. This requires comprehensive risk-benefit counseling with the patient as
radiation therapy itself can increase the risk of further developing a radiation-induced sarcoma. Despite this known cause, adjuvant radiation therapy is the usual recommended treatment following surgery, (even if it is completely resected) due to the aggressive nature of MPNST [14]. Currently, there is little evidence showing a benefit for the role of chemotherapy specifically for MPNST. Most sarcomas are not responsive to current regimes of chemotherapy and further research is required to define its role. It may perhaps be considered in cases where there are metastases or systemic pathology, where surgery or radiation therapy alone might offer limited symptomatic control. Although there are currently several preclinical and clinical studies being conducted, there are no effective targeted therapies for MPNST to date [18].

Current Case

We were fortunate to obtain complete margins of the MPNST dissection which gives our patient a better prognosis for survival. Histopathologically, the MPNST was of Schwannian origin, which unfortunately, has a poorer prognosis than MPNST derived from perineurial cells [21]. There were no signs of tumor recurrence at 6, 12, 18 and 24 month follow up thus far. Of interesting mention is the unexpected preservation of sternocleidomastoid and trapezius muscle strength after accessory nerve sacrifice. This is most likely due to significant contributions of the descendens trapezius muscle strength after accessory nerve sacrifice. This is the unexpected preservation of sternocleidomastoid and trapezius muscles which have been previously described in both live and cadaveric cases and studies [27,28].

CONCLUSION

Head and Neck MPNST are a rare heterogenous group of nerve tumors, with no cases yet described in the accessory nerve. Patients with cranial nerve MPNST present with a variety of clinical symptoms depending on which nerve is affected. MPNST should be managed in a multidisciplinary fashion as long term survival is best achieved with a combination of surgery and radiation therapy due to the highly infiltrative nature of these tumors.

REFERENCES


