CASE REPORT

Malignant Peripheral Nerve Sheath Tumour in a 10-year old

Jude-Kennedy C **EMEJULU**[1], Okechukwu H **EKWUNIFE**[2], Titus OG **CHUKWUANUKWU**[3], Ikechukwu V **OKPALIKE**[1], Kodilinye O **IZUORA**[4], Ofodile C **EKWEOGWU**[1], Sylvester O **OBIECHINA**[2], Cyril E **NWACHUKWU**[4]

AFFILIATIONS
[1]Neurosurgery Division
[2]Paediatic Surgery Division
[3]Plastic Surgery Division
Department of Surgery
[4]Dept. of Anaesthesiology

Nnamdi Azikiwe University Teaching Hospital PMB 5025 Nnewi, Anambra State, NIGERIA

CORRESPONDING AUTHOR
Ikechukwu V **OKPALIKE**
Neurosurgery Division
Department of Surgery
Nnamdi Azikiwe University Teaching Hospital PMB 5025 Nnewi, Anambra State NIGERIA

Email: drval011@gmail.com
Phone: +234 806 113 0253

DISCLOSURES:
Authors have no disclosures.

Received: 31st May, 2017
Accepted: 20th June, 2017

ABSTRACT

Malignant peripheral nerve sheath tumours are highly aggressive tumours characterised by a rapid growth with infiltration of surrounding tissue and high incidence of recurrence. In this case report, we present a 10-year old female patient with a recurrent malignant peripheral nerve sheath tumour of the posterior neck. Surgery was the modality of treatment and a near-total tumour excision was done. Immunohistochemistry was not done due to financial constraints. Adjuvant chemotherapy was given with doxorubicin, ifosfamide and mesna combination and the patient is still on follow-up for a possible recurrence, while awaiting adjuvant radiotherapy. We report this case and reviewed the literature by reason of the rarity of this lesion.

Keywords: large and medium sized nerves, rarity, recurrence, sarcoma, Schwann cell,

INTRODUCTION

Malignant peripheral nerve sheath tumour is a sarcoma arising from Schwann cell, perineural fibroblast or endoneural fibroblast of nerves or nerve trunks, usually of the extremities and trunk.[1]

Neurogenic tumours may arise from peripheral nerves or nerve sheaths, or from sympathetic ganglions. They may be malignant, in which case they are variously termed malignant schwannoma, neurogenic sarcoma, or neurofibrosarcoma. However, malignant peripheral nerve sheath tumour (MPNST) is the preferred designation.[2]

The majority of MPNSTs are derived from neurofibroma or they arise *de novo* in normal peripheral nerves. Large and medium-sized nerves are more often involved than small nerves.[2]

Malignant peripheral nerve sheath tumour accounts for approximately 5-10% of all malignant soft-tissue tumours, of which only 8-15% occur in the head and neck.[3] The parotid area and infratemporal fossa are the most common sites.[3]

Malignant peripheral nerve sheath tumours are classified into the following subtypes:

Malignant Triton Tumour (MPNST with Rhabdomyoblastic Differentiation) Glandular MPNST (MPNST with glands) Epithelioid MPNST.[4]

Malignant Triton Tumour shows rhabdomyoblasts scattered throughout an otherwise normal MPNST. The rhabdomyoblasts are often mature with abundant eosinophilic cytoplasm, may show cross-striations, immunoreactive with desmin, myogenin, and myoD1, may also show chondroid, osteoid or epithelial differentiation, and frequently associated with NF-1, with a poor prognosis.[4]

Glandular MPNST shows otherwise normal MPNST with well differentiated glands, cuboidal to columnar cells, usually enteric type, mucin may be present, may contain other heterologous elements, may be confused histologically with biphasic synovial sarcoma, often arises in major nerves, and strong association with NF-1, with a poor prognosis.[4]

Epithelioid MPNST is composed primarily of Schwann cells with a polygonal epithelioid appearance, no association with NF-1, up to 80% show strong diffuse S-100 staining, do not express melanoma markers and only rarely expresses keratins, differentiated from metastatic melanomas or carcinomas by their origination in major nerves or a benign nerve sheath tumour, in cases where this cannot be demonstrated, it may be impossible to make this diagnosis definitively.[4]

Surgical resection with adjuvant radiotherapy even when there is a clear resection margin is the recommended treatment modality due to the tumour's high rate of recurrence, with its poor prognosis.[3] Five-year survival in patients with MPNST is around 33-39%.[5,6] Doorn and co-workers reported median disease-free survival of 14months and median overall survival of 24months.[7]

There is little reported in literature on these tumours and little information is available on the clinical management of MPNST occurring in the head and neck area.[3]

The role of chemotherapy in the management of malignant peripheral nerve sheath tumour is unclear. However, good response has been demonstrated in case studies with the use of neoadjuvant doxorubicin and high dose

ifosfamide combination therapy.[8]

Other newer combination therapies like doxorubicin-ifosfamide-etoposide, and ifosfamide-epirubicin, also, exist and are showing promising response. Neoadjuvant and adjuvant chemotherapy is even more important in our environment where there is paucity of radiotherapy facilities.

Encouraging report has been obtained with the use of robotic radiosurgery using CyberKnife.[9] However, the availability is still limited to the developed countries and the cost of such surgeries is still, relatively, prohibitive.

CASE REPORT

A 10-year old right handed female presented to our clinic with a 10-month history of a recurrent bi-occipital and right posterior neck tumour with no systemic symptoms. There was no family history of neurofibromatosis or past history of exposure to radiation. The patient had a preceding 1-year history of a similar, but smaller, swelling at the same location as the index swelling, which was excised at a private hospital at the time, and was said to have been subjected to histologic diagnosis with features suggestive of malignant peripheral nerve sheath tumour.

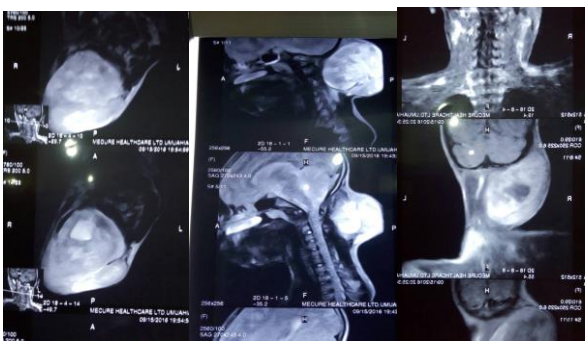
Examination findings revealed an apparently healthy looking young girl with a depressed affect but fully conscious and alert. There were no neurologic deficits and no gait abnormality. However, the patient's neck was slightly tilted to the left due to the mass effect of the tumour, *see Figure 1*.

The tumour measured 18cm x 16cm x 14cm, with a scar at its summit and situated predominantly on the right posterior aspect of the neck with a slight extension to the left posterior side across the posterior mid-line. It was differentially warm and tender, with a mixed consistency (firm and hard), attachment to the overlying skin which has hypopigmented patches, with visible anastomosing vessels, more mobile from side to side, but no palpable cervical or axillary lymph nodes. There were no clinical signs of Neurofibromatosis-1, such as café-au-lait spots, axillary freckling, multiple cutaneous neurofibromas or Lisch nodules.

Figure 1. Pre-operative images of the patient

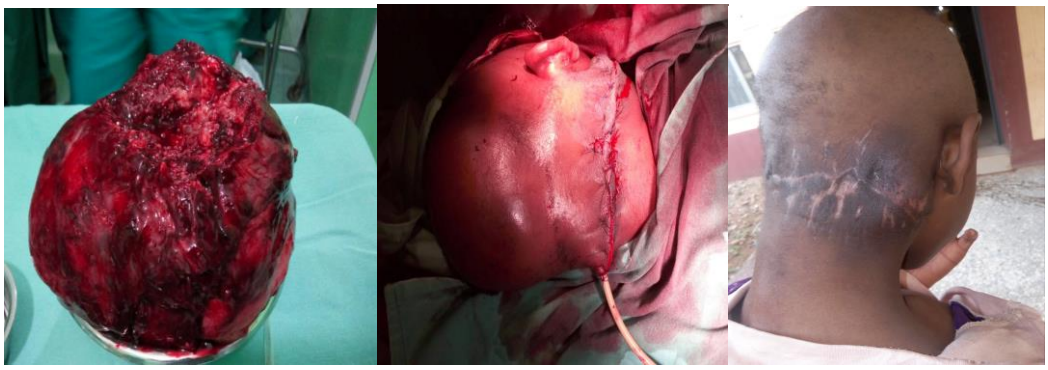
The patient was worked up for excision biopsy in conjunction with the paediatric surgery, plastic surgery and anaesthesiology teams, and the pre-operative laboratory investigations were within normal ranges. Cervical spine magnetic resonance imaging (MRI) showed a huge well circumscribed hyperintense mass in the right aspect of the posterior neck with extension to the left posterior neck and a core of hypointensity suggestive of tumour necrosis. The mass appeared to have a stalk arising from the C1 and C2 spinal nerves, *see Figure 2*.

Figure 2. MRI images



Excision biopsy was done under general endotracheal anaesthesia and the briskly haemorrhagic, excised tumour showed a roughly ovoid shaped, grey to tan mixed consistency (firm and soft) with partial encapsulation, and a dehiscence measuring 10cm in its widest diameter; *see Figure 3.* The stalk of the tumour was ligated and incompletely resected due to difficulty with accessing the entire extent of the tumour stalk. Two units of whole blood were transfused, intra-operatively.

Figure 3. Excised tumour, with the post-operative wound closure and wound healing by primary intention



The tumour measured 15cm x 15cm x 12cm and weighed 2100grams. Cut sections showed a central area that was producing an amber coloured gelatinous material from small cystic cavities. Microscopy showed malignant spindle cell neoplasm composed of pleomorphic spindle cells disposed in alternate hypocellular and hypercellular areas, with the neoplastic cells arranged partly in herring-bone and storiform patterns. There were zones of geographic necrosis and haemangiopericytoma-like vascular channels and tumour giant cells with brisk mitosis.

Features were those of high grade sarcoma, more likely a malignant peripheral nerve sheath tumour. Immunohistochemistry was strongly advised and was requested but, was not done due to a lack of the facility in our centre and those around us, with attendant financial constraints to conduct in a distant centre with the facility.

The patient was commenced on adjuvant chemotherapy on the 18th post-operative day and has received the 1st cycle of 3courses of chemotherapy with doxorubicin, ifosfamide and mesna, and discharged home. Radiotherapy is still being delayed due to the long queues in the few centres with functional facilities in the country.

DISCUSSION

According to the World Health Organisation (WHO) definition, MPNSTs are malignant tumours arising from a peripheral nerve or extraneural soft tissue with nerve sheath differentiation.[11] They are a very rare disease, with the overall incidence of 0.001%.[11] There is a paucity of data on their demographics or treatment, especially in a paediatric population. Only 10-20% of MPNSTs arise in the first two decades of life.[11]

Although approximately 25% of all neurofibromas are found in the head and neck region, fewer than 10% of MPNSTs affect this anatomic area. In this region, the neck is most frequently (40-60%) involved which is not surprising why the index patient had a right posterior neck tumour.[12]

It is estimated that 8-13% of neurofibromatosis type 1-associated neurofibromas eventually become malignant, usually after a latency of 10-20years. Irradiation and long-standing plexiform types have been recognised risk factors.[12]

Clinically, MPNST presents as a rapidly enlarging mass that may give rise to neurologic complaints, and the proximal extremities are the most common locations of these tumours.[13] Our index patient had a rapidly enlarging tumour even though there were no neurologic complaints at the time of presentation. A family or personal history of NF-1 is helpful in making the correct diagnosis, though this was absent in this case.

Grossly, MPNST is a firm tumour and may either appear pseudoencapsulated or have ill-defined margins. The tumour may grow along adjacent nerves or infiltrate nearby soft tissue, and the foci of haemorrhage or necrosis may be seen as was seen in the index patient. Our case appears to show these characteristics.

However, the diagnosis of MPNST requires a combination of clinical information and histomorphological features with supportive immunostains. We missed the immunochemical diagnostic component on account the current socioeconomic challenges that are being faced by all sections of the Nigerian state.

Curative treatment of MPNSTs is difficult. Every effort should be made to perform *en bloc* resection with tumour-free margins, and this was almost attained by our surgical technique, save for the epineural stalk that enmeshed the two spinal nerves that most likely gave origin to the tumour.[14,15] A prophylactic neck dissection is not warranted because lymphatic spread is rare.

Adjuvant radiotherapy is recommended whether tumour-free margins can be obtained or not.[12] This is because of the high rate of recurrence (50%) of the tumour even with tumour-free margin resections.[15] Our patient is, yet, to receive radiotherapy because only one public health facility in Nigeria currently has a functional facility for radiation treatment.

The role of systemic chemotherapy remains controversial. However, in Nigeria, where access to radiotherapy is very limited, chemotherapy still has a big role to play in reducing the chances of recurrence in these patients.

CONCLUSION

Malignant peripheral nerve sheath tumours are very rare and rapidly growing and have a very high incidence of local recurrence despite apparently complete tumour resections.

Adjuvant radiotherapy plays a major role in the reduction of the risk of recurrence. Robotic radiosurgery has shown promising results in ensuring complete and precise tumour excision with reduced risk of recurrence and minimal damage to surrounding tissues but with a prohibitive cost and very limited access.

Chemotherapy may still play in environments where access to radiotherapy is not readily available.

More research is needed on malignant peripheral nerve sheath tumours to develop a generally acceptable and affordable management guideline.

REFERENCES

1. Masood Hasan Khan, Kausar J Khwaja, Nasir Ahmed Salati, Minhaj Anwar. Malignant peripheral nerve sheath tumor of mandible in a young female - A case Report. *Annals of Dental Specialty* 2014 Oct-Dec; 2 (4): 155-157.
2. Ruay-Sheng Lai, Shong-Ling Lin, Shu-Shong Hsu, Min-Ting Wu. Intrathoracic paraspinal malignant peripheral nerve sheath tumour. *J Chin Med Assoc* 2006 Jan; 69(1): 37-41.
3. Guler Berkiten, Muhlis Bal, Yavuz Atar, Ziya Salturk, Onder Dogan, Caglar Cakir. Malignant peripheral nerve sheath tumor of the neck. *Otolaryngology Online Journal* 2014; 4(1):1-7.
4. Louis D.N, Ohgaki H, Wiestler OD, Cavenee WK (Eds). WHO Classification of tumours of the Central Nervous System, Fourth Edition. IARC Press: Lyon 2004; 11-14.
5. deCou JM, Rao BN, Parham DM, et al. Malignant peripheral nerve sheath tumors: the St. Jude Children's Research Hospital experience. *Ann Surg Oncol* 1995; 2: 524-529.
6. Vege DS, Chinoy RF, Ganesh B, Parikh DM. Malignant peripheral nerve sheath tumors of the head and neck: a clinicopathological study. *J Surg Oncol* 1994; 55:100-103.
7. Doorn PF, Molenaar WM, Buter J, Hoekstra HJ. Malignant peripheral nerve sheath tumors in patients with and without neurofibromatosis. *Eur J Surg Oncol* 1995; 21:78-82.
8. Kroep JR, et al. First-line chemotherapy for malignant peripheral nerve sheath tumour (MPNST) versus other histological soft tissue sarcoma subtypes and as a prognostic factor for MPNST: an EORTC soft tissue and bone sarcoma group study. *Ann Oncol* 2011, Jan 01; 22(1): 207-214.
9. Alexander Muacevic, Berndt Wowra, Christian Drexler, et al. C5 Malignant peripheral nerve sheath tumor. Europarsches Cyberknife Zentrum Munchen-Grobhadem. 2007 Accuracy Inc; 1-4.
10. Pei-I Chung, Chang-Lin Chen, Yun-Ting Chang, Han-Nan Liu. Malignant peripheral nerve sheath tumor arising from solitary neurofibroma. *Dermatologica Sinica* 2014; 32: 164-168.
11. James E Bates, Carl R Peterson, Sughosh Dhakal, et al. Malignant peripheral nerve sheath tumors(MPNST): A SEER Analysis of incidence across the age spectrum and therapeutic interventions in the pediatric population. *Pedtiatr Blood Cancer* 2014; 61: 1955-1960.
12. Han-Ju Chen, Huan-Sen Chen, Yen-Liang Chang, Yi-Yiing Wu. Malignant peripheral nerve sheath tumor of the neck: Transformation from a recurrent neurofibroma in a patient without neurofibromatosis. *TZU CHI MED J*; 2010 Dec; Vol 22(4): 195-199.
13. Christopher J Stasik, Ossama Tawfik. Malignant peripheral nerve sheath tumor with rhabdomyosarcomatous differentiation (Malignant Triton Tumor). *Arch Pathol Lab Med* 2006 Dec; 130:1878-1881.
14. Minovi A, Basten O, Hunter B, et al. Malignant peripheral nerve sheath tumors of the head and neck: management of 10 cases and literature review. *Head Neck* 2007; 29: 439-445.
15. Bailet JW, Abemayor E, Andrews JC, et al. Malignant nerve sheath tumors of the head and neck: a combined experience from two university hospitals. *Laryngoscope* 1991; 101: 1044-1049.