ABSTRACT

Introduction: Malignant Peripheral Nerve Sheath Tumor (MPNST) are aggressive soft tissue sarcoma (STS), originally arising from neural cell components. MPNST had a relatively high local recurrence rate of 22% and a disease survival rate of 45 - 60%. In this study, we would like to report a rare case of recurrent MPNST affecting the upper arm region, with a history of previously resected MPNST at the patient’s ipsilateral elbow.

Case Presentation: A 38-years old male patient complained of an enlarging mass in his left anterior axilla Patient had a history of left elbow mass 2 years before and had resected twice. Eight months afterward, a new tumor grew from his left axilla. From the physical examination, the mass was fixated and firm with an oval shape, size 8 x 6 cm. From chest CT scan examination, it appeared a soft tissue mass surrounded with stranding fat had infiltrated his left teres major muscle. The mass was removed successfully and the pathology result revealed a grade 2 MPNST. Post-operative radiotherapy was then scheduled. Among many STS, MPNSTs are notorious for having a high recurrence rate. NF1 mutation, tumors deeper than fascia, large tumors, high-grade tumors, and tumors arising from the trunk, head, and neck are related to poor prognosis in MPNST. Surgeons’ inadequate knowledge, unplanned resections, and their dependency on radiotherapy are other iatrogenic factors for recurrences.

Conclusion: MPNST has high recurrent risk, especially in high-grade tumors, large or deep tumors, surgery with positive resection margins, and NF1 mutations. The primary option for treatment is surgery and radiation therapy.

INTRODUCTION

Soft tissue tumors encompassed a heterogenous group of histologic subtypes. World Health Organization (WHO) had classified soft tissue tumors according to their severity: benign, intermediate (locally aggressive and rarely metastasizing tumors), and malignant. Soft tissue sarcomas (STS) are significantly scarcer and almost 100 times more frequent than benign soft tissue tumors. STS can affect any body part, with 45% affecting extremities (with thighs as their most predilected sites), 38% located in the intraabdominal region, 10% tumors affecting the truncal area, and the remaining affecting the head and neck area.

STS subtypes are differentiated according to their origin, including skeletal muscle, blood vessels, connective tissues, peripheral nerves, lymphatic vessels, and adipose tissues. One of these STS is malignant peripheral nerve sheath tumors (MPNST) which often arise from nerve sheath. MPNST can affect any site, most commonly affecting the lower extremity and retroperitoneal. It is an exceptionally aggressive tumor with a high risk of recurrence and poses risk to metastasize. In this study, we would like to report a rare case of recurrent MPNST affecting the upper arm region, with a history of previously resected MPNST at the patient’s ipsilateral elbow.

CASE PRESENTATION

A 38-year-old male patient came to our clinic with the chief complaint of an enlarging mass in his left anterior axilla, first discovered 2 months before. Within 2 months, the mass gradually increased in size and became significantly noticeable. The mass was not accompanied by other symptoms, such as pain, sensory problems, and any restrictive movements. The patient did not have other medical comorbidities and was not on any medications.

The patient had a history of a similar mass in his left elbow 2 years before encountering his left axilla mass. The tumor had enlarged into a mass sized similar to a golf ball within 3 months. Wide excision of the mass was performed. However, two months afterward, the patient noticed a tumor arising from the surgical site and grew rapidly within 3 months, measuring approximately 5 to 6 cm in diameter. The second resection was performed and tumors were sent for a histopathology examination. A grade-2 MPNST was concluded from the pathology result and free malignant cell margins were achieved with a 0.5 cm margin. The patient then underwent 33 series of postoperative radiation therapy and rehabilitation sessions (Figure 1.)

The patient was then scheduled for follow-up examinations regularly every three months. Eight months after the patient’s last radiation therapy session, a new tumor grew from his left axilla. From...
The patient had a history of a mass in his left elbow 2 years before. From the pathology result, it was concluded as grade 2 MPNST. This photo was taken before the patient underwent resection.

From the physical examination, the mass was fixated and firm with an oval shape, size 8 x 6 cm located in his left axilla extending into his left chest (Figure 2). The patient could freely move his left upper extremity without any difficulties. Incisional biopsy was performed and reported as grade-2 spindle cell sarcoma with myxoid background, tended as MPNST. From the patient's chest CT scan examination, it appeared a soft tissue mass on his left axilla, surrounded with stranding fat and had infiltrated his left teres major muscle, sized approximately 6.8 x 8.3 x 7.8 cm and accompanied by multiple small lymphadenopathies in his left axilla (Figure 3). There were not any signs of metastasis into the patient's lungs and liver. The bone survey was performed to evaluate any signs of bone metastasis, but there were not any. From these results, we concluded that the mass could be entirely and safely resected, thus resection surgery was scheduled.

The surgery was performed in Prof Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali with a team consisting of oncology and general surgeons. The incision design was made according to tumor margins, which were 10 mm around the tumor. We carefully separated the tumor from adjacent structures and discovered that the tumor had adhered to the patient's left pectoralis major muscle, left teres major muscle, and had encased his left axillary vein. The whole tumor and its adjacent structures were entirely removed en bloc. We took the patient's great saphenous vein and performed end-to-end anastomosis to maintain the axillary vein's flow (Figure 4). We inserted a 16-F drain and the defect could be closed primarily.

The patient stayed for 7 days after surgery. During his hospitalization, the patient was monitored closely. We observed the patient's left arm movement, vascularization, and motoric and sensory functions. The surgical drain was removed 4 days after surgery and the patient started to light exercise his left arm. With no other postoperative complications, the patient was safely discharged home. Histopathology results revealed the same conclusion as his biopsy result, which was grade 2 MPNST. It consists
As one of the aggressive tumors, MPNST occurred MPNST in the upper extremity. Aged between 30 to 39 years and the lower than 25% of MPNST tumor patients are neurofibromatosis type 1 (NF1). Between 8 to 13% of all patients with population, with incidence ranging are relatively uncommon in the general peripheral nerve sheath tumor. MPNSTs a previously existing benign form of components, usually originating from neural cell that originally arise from neural cell mass occur MPNST in the upper extremity.

Although MPNST is relatively prone to form local recurrence, to our knowledge there was only one study that reported MPNST cases with multiple recurrences with different multiple sites. The reasons why STS masses tend to re-occur are multifactorial. Some patients underestimate these masses, due to their small size and thought of these as benign tumors. Numerous patients neglect and delay STS until they become large and take shape, which increases their risk to re-occur even after they were removed. STS, if it’s diagnosed at an early stage, has a more promising prognosis, which is why early diagnosis and treatment are strongly recommended and advised to all patients.

Other factors related to STS recurrence are iatrogenic issues. Surgeons’ inadequate knowledge and experience with dealing with STS, unplanned and unprofessional resections, and their dependency on radiotherapy are examples. Based on National Comprehensive Cancer Network (NCCN) guidelines concerning STS, close margins are preferred to protect and preserve vital structures nearby. However these guidelines did not mention specifically how wide does it require. In a study by Bilgeri et al in 2020, they reported a similar conclusion, where positive resection margins in high-grade STS could worsen local recurrence-free survival (LRFS) and patient’s overall survival (OS). They also concluded that a margin < 1 mm did not significantly improve OS and LRFS compared to a positive margin and a margin > 10 mm did not improve prognosis. Five millimeters margin is considered to be sufficient.

Radiation therapy became one of the routine management of STS. It can be administered before or after the operation and it depends on the surgical outcomes. Based on NCCN guidelines, post-operative radiation therapy should not be administered in R0 patients unless local recurrence in the future will cause significant morbidity. Particularly in MPNST, surgery, and radiotherapy combined are the main treatments for localized and resectable tumors. In a study by Bishop et al in 2016, surgery and radiation on MPNST had an 84% of 5-year local control rate and 62% disease-free survival rate. In a meta-analysis by Albertsmeier in 2017, external beam radiation reduced STS local recurrence risk in any body part (OR: 0.47 – 0.49, p: 0.001). For these reasons, we planned radiation therapy sessions in our patient, because another recurrent tumor in the future can be disastrous.

What we are afraid of from recurrent STS is that patients with recurrent tumors tend to have a higher histological grade, are highly associated with metastasis risk, and lead to more complicated surgery. Among many STS, MPNSTs are notorious for having a high recurrence rate. In a study by Bergamaschi et al, they reported an 86.7% of local recurrence rate in 73 MPNST patients. In a meta-analysis by Zhenyu et al in 2020, NF1 mutation, tumors deeper than fascia, large tumors, high-grade tumors, and tumors arising from the trunk, head, and neck are related to poor prognosis in MPNST. Reflecting on our case, our patients do tend to have poor outcomes, keep in mind that our patient had already experienced multiple recurrences. Systemic therapy and palliative options will be considered if recurrence or metastasis occurs in the future.

CONCLUSION
MPNST is one of the STS which has aggressive nature and has a high risk for recurrence. The risk factor for MPNST recurrences is high-grade tumors, large or deep tumors, surgery with positive resection margins, and NF1 mutations. The primary option for treatment is surgery and radiation therapy, especially for those with locally recurrent MPNST. Systemic therapy such as chemotherapy can be considered in MPNST with high risk or any evidence of metastasis.

CONFLICT-OF-INTEREST
None to declare

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ETHICAL STATEMENT
The patient already gave consent regarding data and information in this study to be published.

AUTHOR CONTRIBUTION
The author contributed fully to this study.

REFERENCES