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Advanced Metastatic Malignant Triton Tumor in Neurofibromatosis Type 1: A Case Report and Management Challenges

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Abstract

Background/Aim: A malignant Triton tumor (MTT) is a rare and aggressive soft tissue sarcoma associated with poor prognosis and with no established treatment protocol.

Case Report: A 38-year-old man presented with severe right thigh pain and limited hip motion. Since childhood, the patient had a mass on their thigh, accompanied by café-au-lait spots. Upon admission, a biopsy confirmed MTT that had metastasized to the lungs. Preoperative radiation therapy was administered to reduce the tumor size; however, the tumor did not shrink. Extensive resection was not feasible because of the tumor size and location, prompting a decision to perform volume reduction surgery aimed at alleviating the patient's pain and improving mobility. Although the surgery provided temporary relief from the symptoms, the patient died two weeks later.

Conclusion: MTT requires a multidisciplinary approach that includes surgery, chemotherapy, and radiation therapy; however, in advanced cases such as this one, palliative measures may be more appropriate. This case underscores the challenges in managing MTT and highlights the potential role of volume reduction surgery in improving the quality of life of patients with significant symptoms. Despite the poor prognosis, symptom palliation during the two weeks leading up to the patient's death was significant, illustrating the importance of addressing pain and mobility issues while considering overall treatment strategies in such complex cases. These findings emphasize the need for further research on effective management options for MTT to improve patient outcomes.

Keywords: Malignant triton tumor, palliative therapy, surgery, chemotherapy, radiation therapy.

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) represent 3-5% of all soft tissue sarcomas (1). A notable subtype of MPNSTs is malignant Triton tumors (MTTs), distinguished by the presence of rhabdomyosarcomatous differentiation (1). MTTs are relatively rare and aggressive

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and are characteristically composed of malignant schwannoma cells and malignant rhabdomyoblasts (2). MTTs have been reported to occur in the head and neck, as well as in the extremities and trunk (3). To date, approximately 200 cases of MTT have been reported; however, no standard treatment has been established (4). Although multidisciplinary treatment combining surgery, chemotherapy, and radiotherapy is used, patient prognosis remains extremely poor (5). Here, we describe a case of a patient with MTT treated with local preoperative radiotherapy and tumor reduction surgery.

Case Report

The patient was a 38-year-old male with a primary complaint of right thigh pain and limited range of hip motion. The patient was born with mild intellectual disabilities and had neurofibromatosis type 1 (NF1) since childhood. Recently, they experienced worsening right thigh pain and visited their local physician, who referred them to our department with a suspected malignant soft tissue tumor. During the examination, a café-au-lait spot was noted on the patient's trunk. Additionally, multiple cutaneous and subcutaneous nodules were observed, predominantly on the trunk. Blood test results indicated an elevated C-reactive protein concentration of 18.01 mg/ml, white blood cell count of 11,100/µl, and platelet count of 61.0×10^4/µl, suggesting increased inflammation. The tumor in the right thigh measured 20×19×18 cm. The patient experienced severe immobility and pain in the right hip. Magnetic resonance imaging (MRI) revealed a T1 hypointense (Figure 1A) and T2 hyperintense (Figure 1B). Computed tomography (CT) further indicated pelvic invasion (Figure 1C). The tumor was determined to have originated from a branch of the obturator nerve based on its anatomical location. A needle biopsy indicated necrotic tissue (Figure 2A) with dense proliferation of irregularly shaped dysplastic cells and enlarged heterotypic nuclei (Figure 2B). Rhabdomyoblastic change was also observed (Figure 2C). Immunohistochemistry showed that only the large cells were positive for desmin (Figure 2D) and transducin-like enhancer of split 1 (TLE-1) (Figure 2E), whereas tri-methylation of lysine 27 on histone H3 protein (H3K27me3) was absent (data not shown). SOX-10 and S-100 staining was also negative (data not shown).

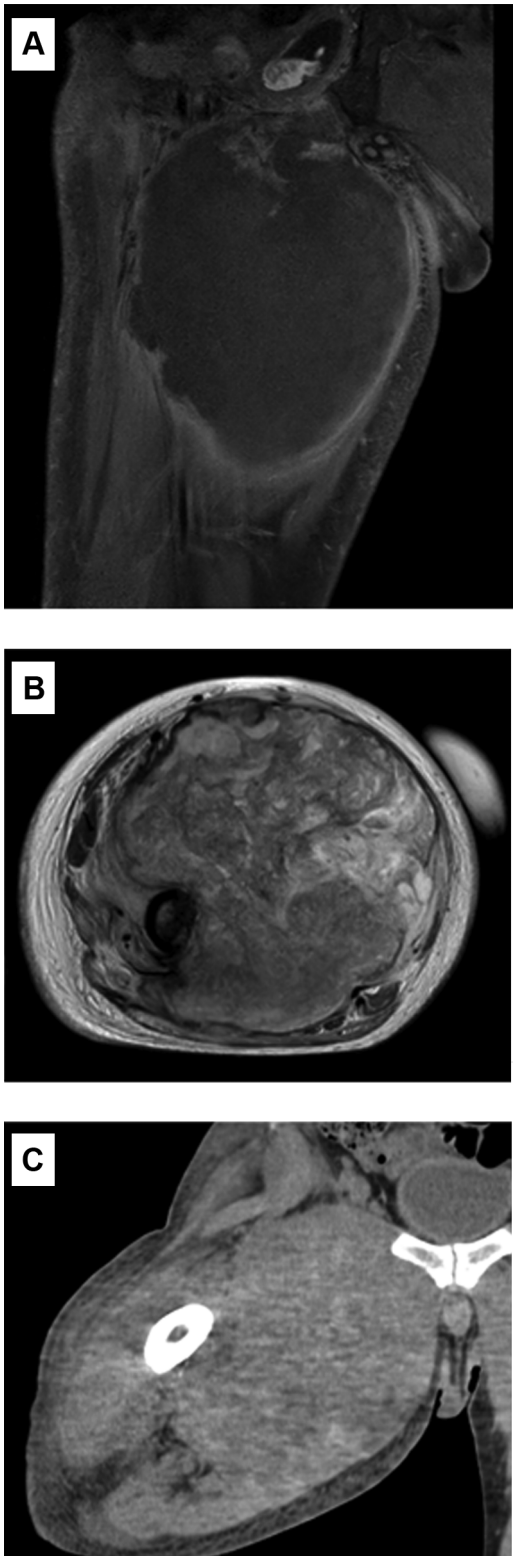
A diagnosis of MTT was confirmed through comprehensive histopathological evaluation. At the time of diagnosis, CT revealed multiple lung metastases (Figure 3A). Radiotherapy (2 Gy × 25) was administered as palliative treatment. However, as the tumor did not shrink and the patient's pain was only slightly alleviated, tumor reduction surgery was performed (Figure 3B and C). Pathological analysis of the excised specimen pathology showed predominance of necrotic tissue (Figure 4A). Dense proliferation of irregularly shaped atypical cells with enlarged atypical nuclei was observed (Figure 4B). Immunostaining was positive for desmin (Figure 4C). Cytokeratin, Multi (AE1/AE3), vimentin, and glial fibrillary acidic protein (GFAP) were negative (data not shown). Postoperatively, the pain and limited range of motion of the hip were relieved. However, the patient died two weeks after surgery. Consent for publication was obtained from the patient and their father.

Discussion

In 1932, Masson and Martin first reported a case of MTT (6). It was clinically named in 1973 by Woodruff *et al.* (7), who suggested that MTT was a peripheral nerve tumor with rhabdomyosarcomatous differentiation. More than half of MTT cases are associated with NF1 (5), such as the present case.

Generally, the pathological findings of hematoxylin and eosin-stained MTT reveal fascicles of spindle-shaped cells, frequently exhibiting a hemangiopericytoma-like vascular pattern with alternating hypercellular and hypocellular areas (1). In addition, regions with geographic necrosis and prominent mitotic figures are often observed. Notably, MTTs are characterized by skeletal muscle differentiation (1).

In the current case, most of the tumor tissue was necrotic, likely because of the excessive size of the tumor, causing inadequate blood flow. Positive desmin staining



and loss of H3K27me3 indicated differentiation into rhabdo-myoblasts, leading to the diagnosis of MTT. Diagnosis of MTT requires immunostaining to confirm the expression of desmin, myoblast determination protein 1, and myogenin, which indicate differentiation into rhabdomyosarcoma (8, 9). Furthermore, there is a high probability of complete loss of H3K27me3 in the MTTs (10, 11).

Genetic analysis has identified a frameshift mutation in the tuberous sclerosis complex 2 gene in patients with MTT, potentially enhancing diagnostic accuracy (12).

When MPNSTs occur in peripheral nerves, they most frequently involve the sciatic nerve (1). Complete resection has been reported as an effective treatment for MTT (13, 14). The role of postoperative adjuvant therapies, such as radiation therapy and chemotherapy, is not well defined, and these therapies have not been proven effective (1, 2, 7). However, several reports demonstrate prolonged survival in patients with recurrent MTT treated with repeated resection combined with chemotherapy and/or radiation therapy (13, 15). Other studies have combined surgery, adjuvant chemotherapy, and adjuvant radiation therapy to treat MTT with favorable results (16).

Chemotherapy with doxorubicin and ifosfamide is often used to treat MTT (16, 17). Other reported treatment regimens include combined vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide (VDC/IE); combined mesna, doxorubicin, ifosfamide, and dacarbazine (MAID); and combined ifosfamide, carboplatin, and etoposide (ICE) (18, 19). Additionally, radiation therapy at a dose of 40–70 Gy can effectively reduce tumor size and improve survival rates for patients with MTT (3, 20).

Figure 1. *Imaging results. (A) Magnetic resonance imaging findings: T1-weighted imaging reveals a hypointense tumor in the proximal right thigh. (B) T2-weighted imaging shows a hyperintense. (C) Computed tomography imaging indicates partial tumor invasion into the pelvis.*

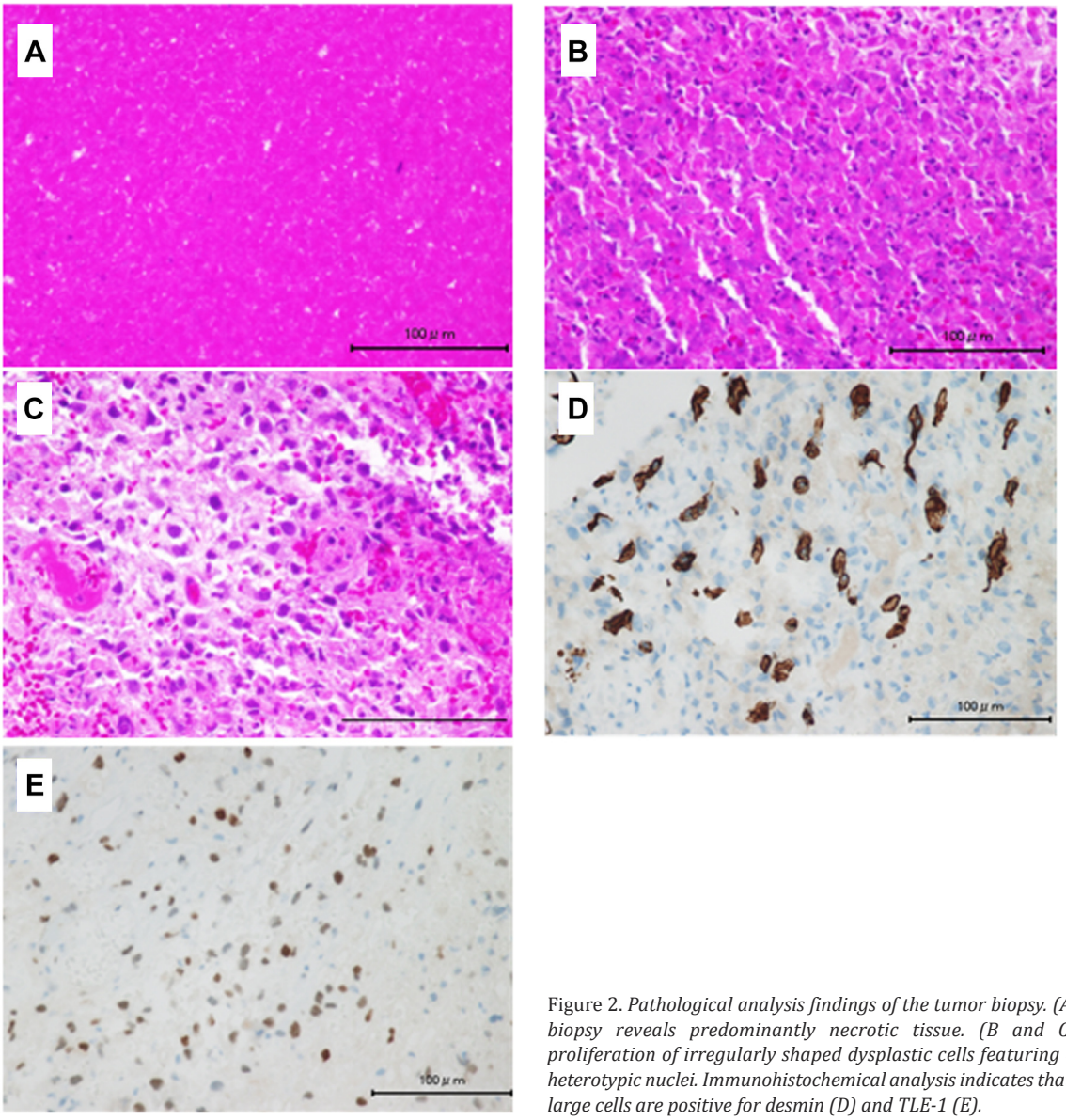


Figure 2. *Pathological analysis findings of the tumor biopsy. (A) Needle biopsy reveals predominantly necrotic tissue. (B and C) Dense proliferation of irregularly shaped dysplastic cells featuring enlarged heterotypic nuclei. Immunohistochemical analysis indicates that only the large cells are positive for desmin (D) and TLE-1 (E).*

The patient in this case had intellectual disabilities, and the care team determined that they would not be able to tolerate chemotherapy. Initially, the patient was treated with preoperative radiotherapy to reduce tumor size and activity. Subsequently, partial resection of the tumor was performed to reduce tumor volume. Postoperative pain and range of motion of the hip joint improved after partial tumor resection, and the tumor size remained the same. Even with multidisciplinary treatment, the 5-year survival rate of patients with MTT is approximately 13% (20, 21). In addition, patients with an elevated inflammatory response in preoperative blood tests, as in this case, have a poor prognosis (22, 23). Although this patient died two weeks after surgery, we believe that the palliation of symptoms leading up to their death was significant.

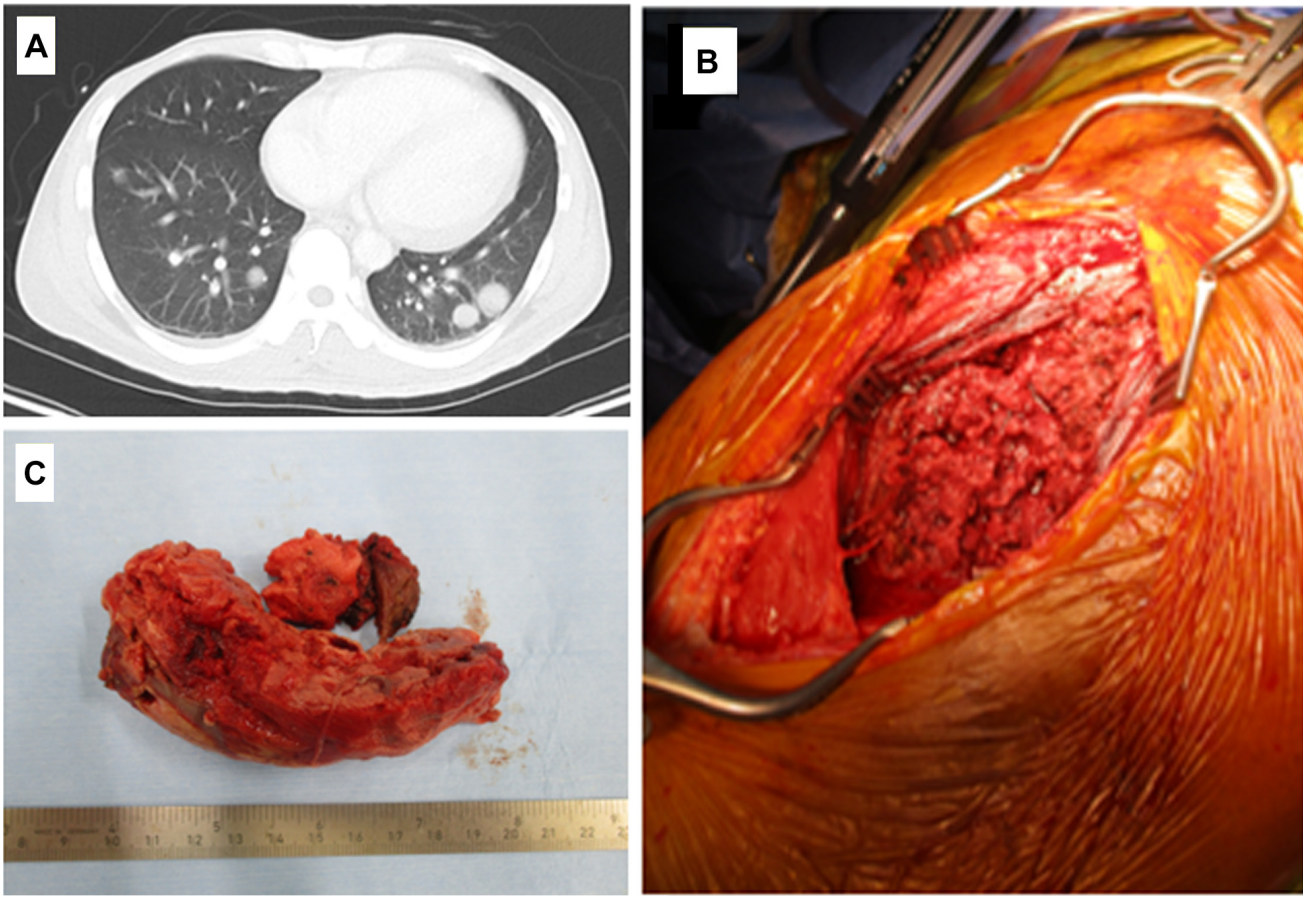


Figure 3. *Surgical removal of tumor. (A) Computed tomography imaging shows multiple metastases in the bilateral lung fields. (B) Gross anatomy of the surgical field showing piecemeal resection performed using Cuiser and Ruel forceps. (C) Gross examination of the excised specimen reveals a reddish-black, elastic, hard tumor.*

Palliative surgery may be a viable option for MTT, particularly when pain management is challenging.

Conclusion

For massive MTT, in addition to multidisciplinary treatment, localized symptom palliation should be considered. Specifically, introducing aggressive palliative therapy for symptoms such as pain and limited joint range of motion is important to help patients reduce their suffering and lead a more comfortable life. Moreover, the development of an individualized treatment plan based on the patient's condition and preferences may lead to an improved prognosis.

Conflicts of Interest

The Authors declare that they have no conflicts of interest to report regarding the present study.

Authors' Contributions

Conceptualization: K.H., S.N., K.G.; methodology: K.H., S.N.; software: K.H., S.N.; validation: K.H., S.N., K.G.; formal analysis: K.H., S.N., K.G.; investigation: K.H., S.N.; writing the original draft preparation: K.H.; writing the review and editing: K.H., S.N., K.G.; All Authors have read and agreed to the published version of the manuscript.

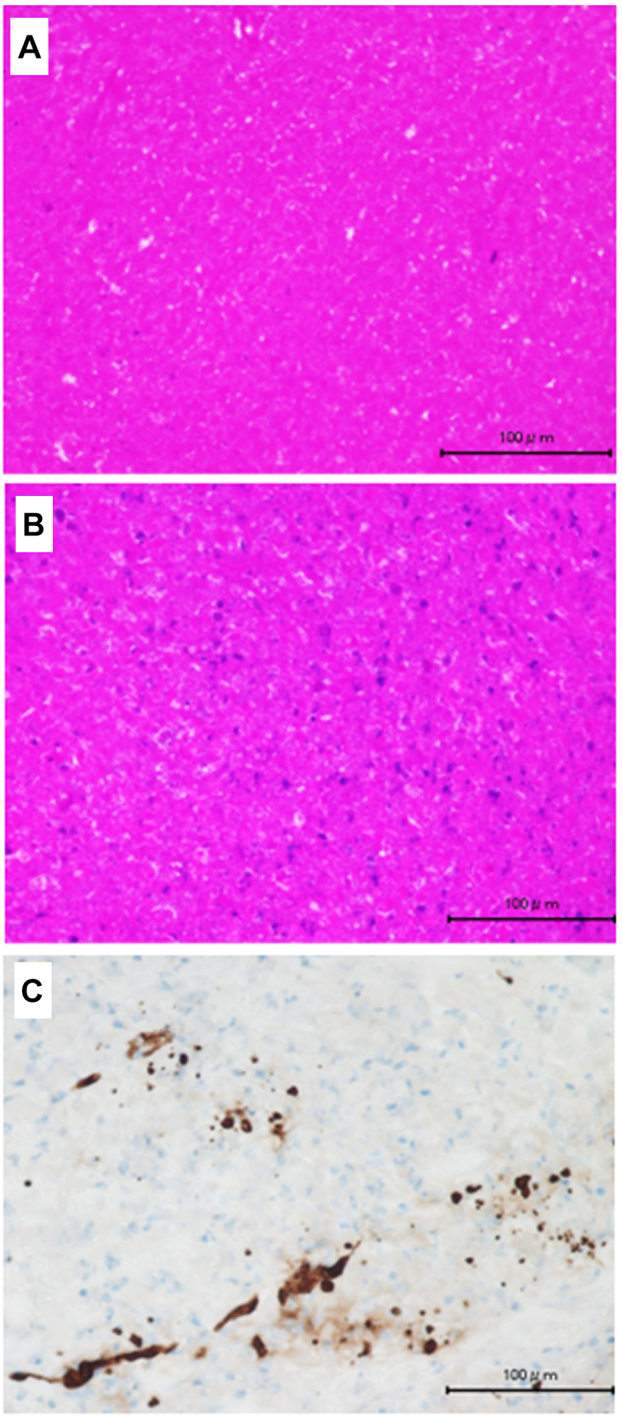


Figure 4. *Pathological analysis findings of the excised tumor. (A) The pathology of the excised specimen was primarily characterized by necrotic tissue. (B) Dense proliferation of irregularly shaped atypical cells with enlarged, abnormal nuclei. (C) Immunostaining was positive for desmin.*

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