Case Report

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Two-Year Local and Distant Control of Malignant Peripheral Nerve Sheath Tumor (MPNST) in NF1 Patients after Multiple Recurrences: A Case Report

Mostafa Farzin, Fatemeh Jafari*, Ava Yousefi

Department of Radiation Oncology, Cancer Institute, Imam Khomeini Hospital complex, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Malignant peripheral nerve sheath tumors (MPNSTs) are rare, biologically high-grade sarcomas that tend to recur and metastasize. The known risk factors for MPNSTs include neurofibromatosis type 1, highly aggressive MPNSTs, and dismal survival outcomes. Multimodality therapies, including surgical resection, radiotherapy, chemotherapy, targeted therapy, and combination therapy, are available. This case report describes a young woman with NF1 who was referred to us with a history of three local recurrences of MPNSTs in the proximal part of her left thigh after several surgical attempts. Successful local and distant control was achieved via preoperative radiotherapy and chemotherapy prior to the latest surgery. With preoperative RT and chemotherapy, more long-term and successful local and distant control was achieved, particularly in high-risk NF1-associated MPNST patients with a history of recurrence. Trials with larger sample sizes may show improvements in local control (LC), disease-free survival (DFS), and overall survival (OS) with neoadjuvant interventions in such patients.

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are rare varieties of soft tissue sarcomas of mesenchymal origin, with an expected incidence of one per million per year [1,2]. The association between MPNSTs and neurofibromatosis type-1 (NF1), an autosomal dominant disorder, is well known, as 20–25% of patients with MPNSTs also have NF1. Therefore, clinicians and patients need to be aware of the symptoms of malignant changes in a neurofibroma, such as pain and rapid growth. Positron emission tomography (PET) facilitates the early diagnosis of MPNSTs [3,4]. Compared with sporadic MPNSTs, NF1-associated MPNSTs have worse survival outcomes because of their larger size, truncal location, and lower rate of negative surgical margins [2].

Multimodality therapies, including surgical resection and postoperative radiotherapy, chemotherapy, and targeted therapy, in combination or alone, are available [5,6]. The importance of negative margin

*** Corresponding Author:**
Fatemeh Jafari
Address: *Department of Radiation Oncology, Cancer Institute, Imam Khomeini Hospital complex, Tehran University of Medical Sciences, Tehran, Iran.*
E-mail: *fatemeh.jafari92@yahoo.com*

resection is paramount because it is a determinant of local control and disease-specific outcomes. RT in combination with R0/R1 resection is associated with improved local control. Chemotherapy is administered more often to patients with advanced disease (unresectable or metastatic) [5]. Investigations have shown the superiority of doxorubicin and ifosfamide combination regimens, with an overall response rate of 26% and a median overall survival (OS) of 51 weeks [7]. Targeted inhibitors, such as erlotinib, sorafenib, and imatinib, have been used in MPNSTs with minimal observed responses [5]. In this study, we report successful local and distant control with multimodality therapy in a case of NF1-associated MPNST after three local recurrences.

Case presentation

A 30-year-old female patient was referred to the Radiation Oncology Department by an onco-surgeon colleague following several instances of MPNSTs located in the proximal part of her left thigh, resections, and recurrences after each surgical attempt over six months for adjuvant radiotherapy.

The patient was of low socioeconomic status and did not have a documented personal or familial history of any disease, as she reported. However, physical examination revealed several café au lait macules, with the greatest dimension over 15 mm, all over her body. Additionally, freckles were observed in the right axillary and inguinal regions. She seemed to be undiagnosed with NF1. Her chief complaint was a mass in her left buttock 7-8 years ago, probably a neurofibroma, which had become much larger and painful in the last 3 months. On the first MR image, a mass-like lesion measuring 104 × 80 × 67 mm in the posterior portion of the left thigh was reported. Metastasis evaluation via a chest CT scan with intravenous contrast agent was negative. The mass was resected, and the pathologist described it as a high-grade malignant peripheral nerve sheath tumor. Surgical margins could not be evaluated during the first surgical resection. The patient presented with local recurrence three months later, and surgical resection was performed according to the same pathological report. Two months later, another local recurrence occurred, and the same management was used for the second recurrence.

Following the second episode of local recurrence, the patient was referred to the Radiation Oncology Department and considered a candidate for postoperative radiotherapy. In the duration between the last resection and starting RT (approximately 15 days), the patient returned with the complaint of rising solid masses in the same location. A necrotic solid mass measuring 83 × 67 mm in the posterior portion of the left thigh with hamstring muscle involvement and at least seven superficial masses (greatest dimension, 52 mm) were reported in a magnetic resonance imaging (MRI) study. Radiotherapy was initiated at a total dose of 70 Gy in 35 fractions (2 Gy/fraction) as soon as possible. The treatment plan was continued with chemotherapy (MAID regimen) for 4 cycles. In further response evaluations, no progression was reported, and the masses were stable in size and count. Therefore, the patient underwent surgery, and all masses were resected. Thereafter, the team started to follow her every month with physical examination and every 3 months during the first 2 years, a left thigh MRI study and a chest CT scan were performed. Currently, having passed local and distant controls for more than two years, the follow-up duration has increased to every six months.

Discussion

The incidence rate of MPNSTs is 4.6% in individuals with NF1 and 0.001% in the general population, and approximately 52% of patients with NF1 present with MPNSTs [8]. The unfavorable outcome of NF1-associated MPNSTs is related mainly to the development of larger tumors. This feature, which is a key determinant of local control and disease-specific outcomes, makes margin-free resection more difficult [1,2,5]. Additionally, patients who present with local recurrences have worse outcomes and a 2.5-fold greater risk of mortality from the disease [2]. MPNSTs are high-grade sarcomas that tend to recur (40–65%) and metastasize (40–80%), mostly to the lungs [7]. Most local recurrences occur within 2 years after resection [1]. Resection of the tumor is the definitive treatment for MPNSTs, and effective adjuvant and neoadjuvant therapies have not been fully investigated [8]. Some trials have shown that RT in combination with R0/R1 resection is associated with better local control [1,2]. Few trials have investigated the role of chemotherapy in advanced and metastatic patients with MPNSTs. Most chemotherapy regimens prescribed for patients with MPNSTs are based on evidence of soft tissue sarcoma (STS) sensitivity. The most active chemotherapeutic agents for unresectable and metastatic STS are ifosfamide and doxorubicin. Retrospective data from pediatric patients in a small series revealed that neoadjuvant chemotherapy in patients with unresectable MPNSTs reduced the tumor size and facilitated R0 resection [7].

As we mentioned, because of the nature of our patient's disease, NF1-associated MPNST, and the history of several recurrences in a short duration,

the incidence of morbidity and mortality was high, especially within 2 years after the latest surgery. However, after more than 2 years of follow-up, no local or distant findings were reported in the physical examination or imaging studies in this case. Acceptable local and distant control of this type of sarcoma may be a possible result of the addition of neoadjuvant RT and chemotherapy prior to the latest resection. Neoadjuvant chemotherapy may play a role in preventing metastasis, in addition to reducing the size of inoperable MPNSTs and improving disease-free survival and OS.

Conclusion

Randomized clinical trials with adequate sample sizes are necessary to investigate the role of neoadjuvant radiotherapy and chemotherapy in identifying high-risk features of MPNSTs, such as NF1-associated MPNSTs and patients who present with multiple recurrences. Preoperative interventions may improve LC, DFS, and OS in MPNST patients with poor outcomes.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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