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Successful Treatment of Adult Pleomorphic Rhabdomyosarcoma in the Posterior Left Femur: A Case Report

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Abstract

Introduction: Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma, but it represents only a small portion of soft tissue sarcoma in adult population. There is a treatment protocol based on Intergroup Rhabdomyosarcoma Study (IRS) that provides satisfactory results in treating RMS in children, but there is only limited evidence regarding the outcome and prognosis in extrapolating the IRS protocol to treat RMS in adults. We report a case of adult pleomorphic RMS treated with multidisciplinary approach and the results we have obtained. Case presentation: A 48-year-old woman was admitted in February 2011 due to a painful mass on her left thigh. Diagnosis of pleomorphic rhabdomyosarcoma was made by histopathology and immunohistochemistry. After multimodal treatment that includes Trans-Arterial Chemotherapy Infusion, Cryosurgery, and wide excision surgery, our patient remains disease-free as of the latest annual follow up examination on June 2017. Conclusions: The pleomorphic type of Rhabdomyosarcoma is very rare in adults and is often associated with a poor prognosis. In our case, a multidisciplinary approach with multimodal treatment provides excellent result, even after a routine follow up spanning through six years.

Keywords

Rhabdomyosarcoma, Pleomorphic, Adult, Multidisciplinary Approach, Multimodality Treatment, TACI, Cryosurgery, Surgery

1. Introduction

Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma, accounting for more than 50% of all soft tissue sarcomas. In contrast, RMS is exceedingly infrequent in adults. Soft tissue sarcomas constitute less than 1% of all adult malignancies, and RMS accounts for 3% of all soft tissue sarcomas. RMS is a malignant soft tissue tumor with skeletal muscle differentiation. There are 3 main subtypes of RMS—embryonal, alveolar, and pleomorphic. The pleomorphic type RMS is signified by the lack of embryonal or alveolar features in histologic examinations. This type of RMS tends to affect adults, with peak incidence in the fifth decade of life. It most commonly arises in deep soft tissues of the extremities [1] [2].

The Intergroup Rhabdomyosarcoma Study (IRS) was made in 1972 to better understand and improve treatment modalities for children with RMS. The result of this joint effort is better staging and risk stratification, local therapy, and supportive care [3]. The protocols are further improved in 2000 with the inclusion of IRS into Children's Oncology Group—Soft Tissue Sarcoma (COG-STS). Current COG-STS uses risk stratification as the basis for treatment strategy. Older age at the time of diagnosis (more than 10 years old), histological findings (alveolar or pleomorphic type), and higher TNM staging score at diagnosis are considered predictors of worse outcomes [3] [4]. Low and intermediate risk RMS require local therapy such as surgical intervention or localized radiotherapy in addition to systemic chemotherapy to prevent recurrence. High risk RMS treatment protocol uses the same backbone of systemic chemotherapy, but with the addition of novel therapeutic agents such as Cixutumumab, a monoclonal antibody targeted against Insulin-like Growth Factor-I (IGF-I) receptors [4].

The biological behavior and prognosis of adult RMS is still poorly understood. There is not much data in successful treatments using IRS or COG-STS protocol [5]. Multidisciplinary approach comprising several treatment modalities such as surgery, radiation, and chemotherapy are considered more favorable in attempts to cure and maintaining the quality of life [2] [5] [6]. One case of adult Embryonal RMS in Indonesia reported in 2015 was successfully cured through surgical amputation [7]. While it may be considered a success, the loss of a limb would adversely affect the quality of life of the patient.

2. Case Presentation

A 48-year-old woman was admitted to our institution due to painful mass on her left thigh. At the beginning she only felt pain on her left thigh and difficulty to bend her left knee. The mass was rapidly enlarging during the last 8 months, and at the time of admittance, the tumor mass has bulged on the posterior side of her thigh and are tender on palpation (**Figure 1**).

The patient had taken an MRI examination on another hospital prior to admittance into our hospital. The MRI on her left thigh revealed a hypervascular mass sized 12.51 × 10.61 × 21.11 cm with inhomogeneous enhancement, with

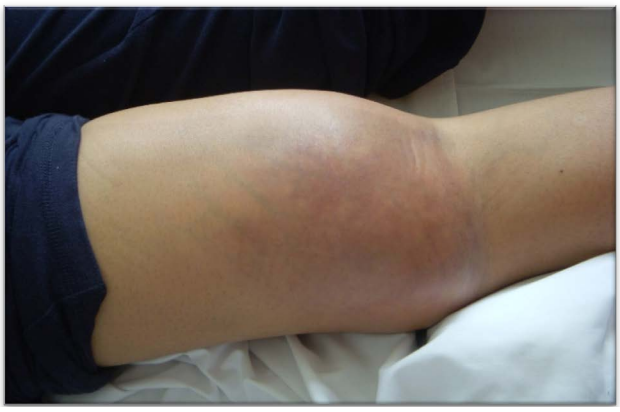

Figure 1. Clinical Presentation of RMS of the Left Thigh: a rapidly enlarging and painful mass in the left thigh that is tender on palpation.

feeding arteries from the left superficial and deep femoral artery, as seen on **Figure 2**. This radiologic finding leaves an impression of a well-defined solid mass that are highly suspicious of a Rhabdomyosarcoma.

The case was brought to a Tumor Board discussion in our hospital. Through the discussion, we decided to perform TACI (Trans Arterial Chemotherapy Infusion) twice, on Feb 9th, 2011 (Cisplatin 15 mg + Farmorubicin 7 mg) and Mar 7th, 2011 (Carboplatin 50 mg). After two TACI treatments we perform another MRI, and it revealed a malignant, contrast-enhanced solid mass at distal left femur involving two compartments within the biceps, semitendinosus, semimembranosus, and left adductor magnus muscles, 10.8 × 14.3 × 20.6 cm large, highly suspicious of a sarcoma with necrotic area within. The result of the second MRI examination can be seen on **Figure 3**.

We decided to perform cryosurgery on seven areas on the left femur with 6 - 7 cm depth and temperature of −160˚C to −180˚C. During cryosurgery we also took a biopsy sample, and the histopathologic finding was an undifferentiated sarcoma. We performed another cryosurgery on eight areas on the lower third part of the femur with temperature −160˚C to −168˚C for 6 minutes and afterwards we gradually increase the temperature to 8˚C to 11˚C. Two weeks after the second cryosurgery we evaluate the progress through MRI and found that the mass on the patient's left thigh was smaller, with an enlarging necrotic area within the mass (**Figure 4**).

We decided to perform another cryosurgery, with the same cryosurgery protocol. After the general condition of the patient has improved and the tumor was considered operable, a wide excision surgery was scheduled on May 27th, 2011. The surgery was performed with longitudinal excision on the posterior side of the femoral region, followed by excision of the entire firm quadriceps muscle that was involved (**Figure 5** and **Figure 6**). After the excision we continued with another cryosurgery on the tumor bed and the upper border of the surgical site (**Figure 7** and **Figure 8**).

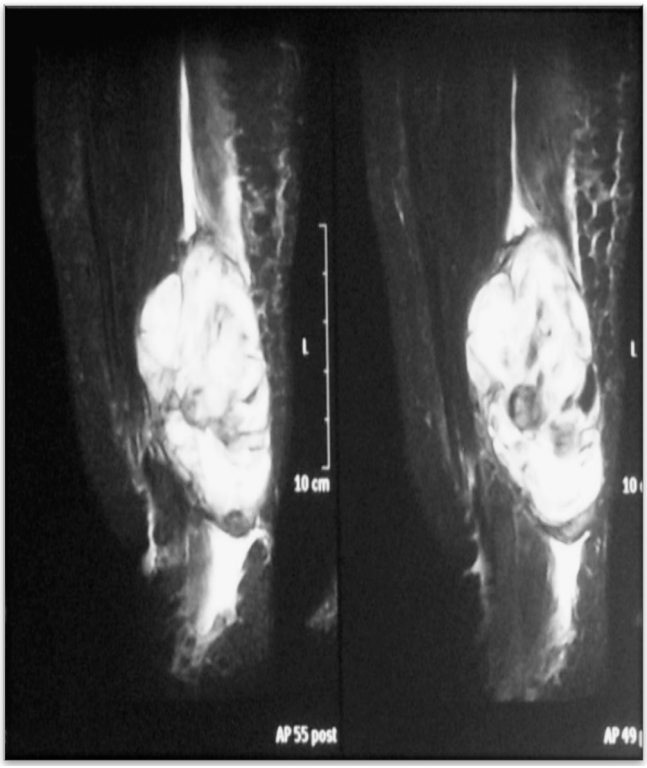

Figure 2. MRI examination of the large mass on the left thigh before treatment course.

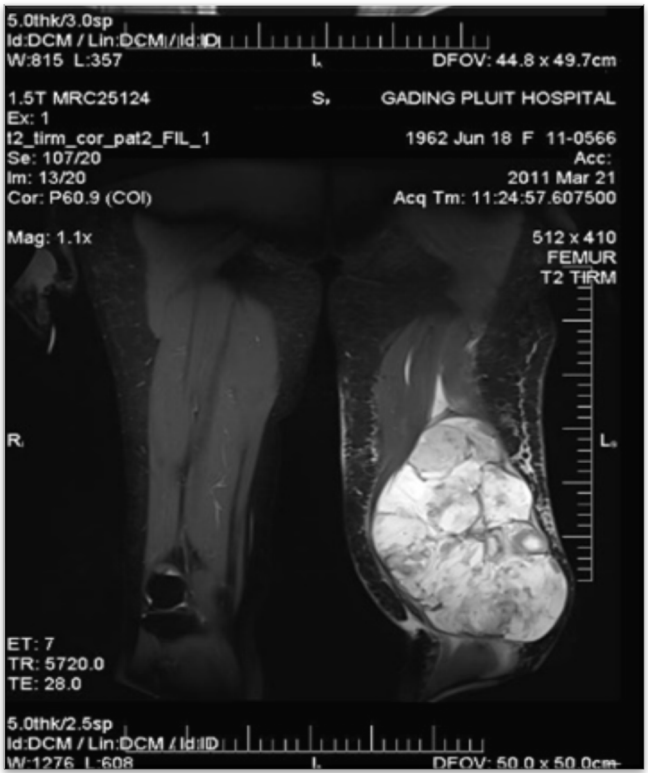

Figure 3. MRI examination of the large mass on the left thigh after two TACI therapy.

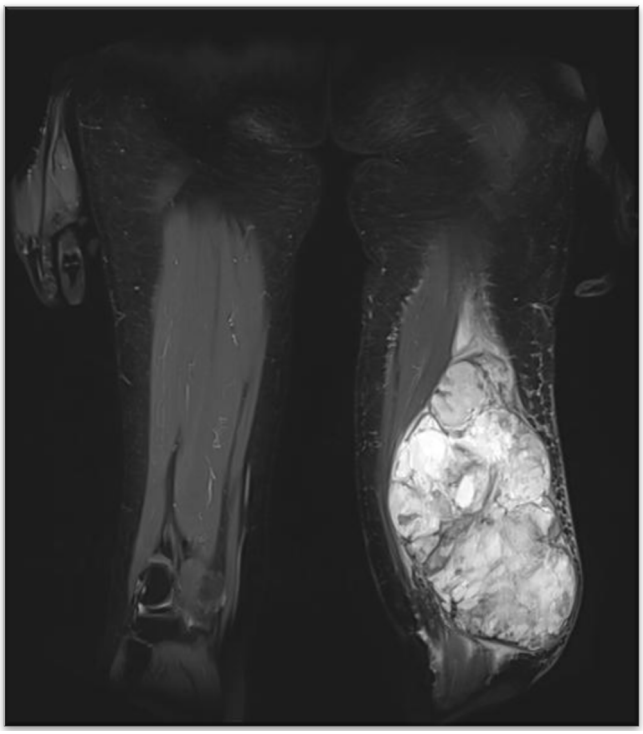

Figure 4. MRI examination of the large mass on the left thigh after two Cryosurgeries.

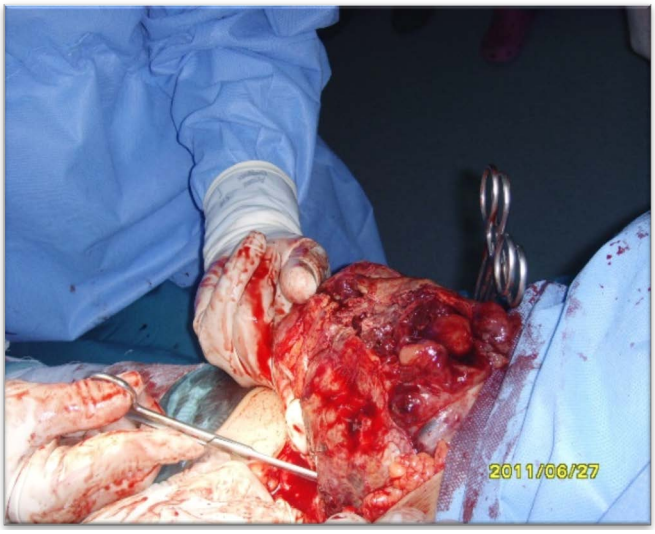

Figure 5. Wide excision surgery of the tumor mass on the left thigh.

The histopathology report of the excised tissues revealed a sarcoma with differential diagnosis of a rhabdomyosarcoma with free-of-tumor area on the upper border of the excised tissue. According to the immunohistochemistry results which can be seen on **Figure 9** and **Figure 10**, it was a pleomorphic type Rhabdomyosarcoma. We conducted follow-up examinations at 3 months, 6 months, and then annually for 6 years post-therapy. On the follow-up at the 3rd month we

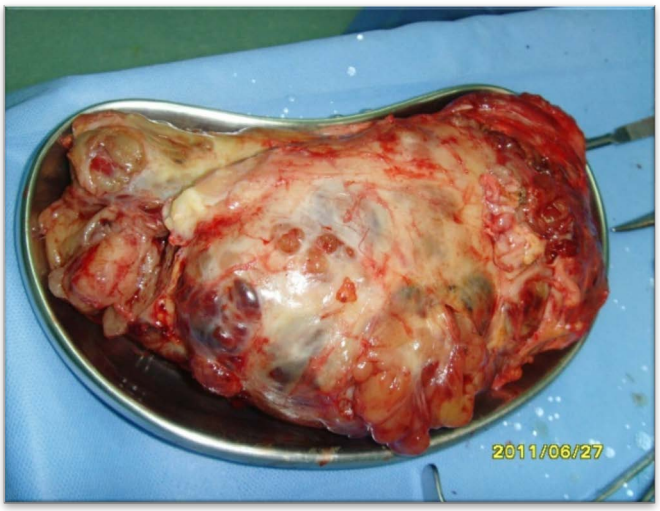

Figure 6. The tumor mass successfully excised from the patient's left thigh.

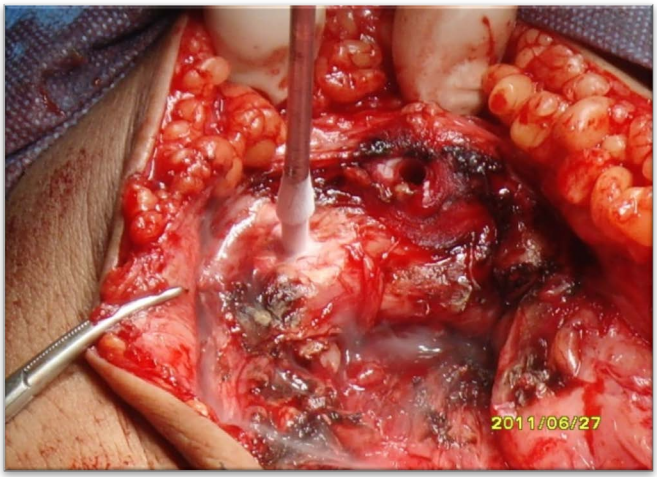

Figure 7. Cryosurgery probe freezing tissues on the tumor bed.

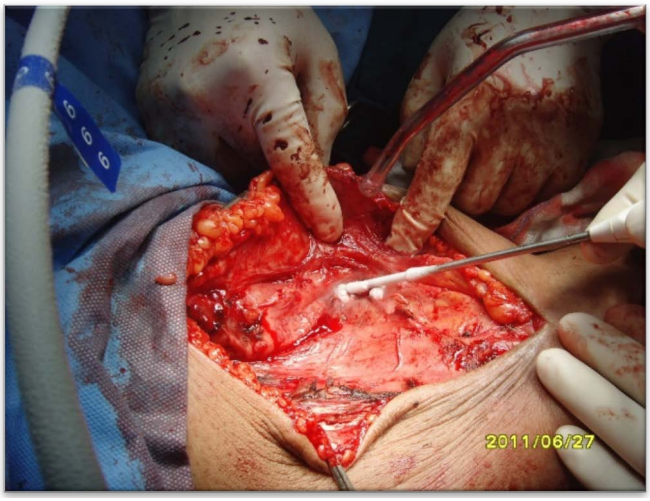

Figure 8. Cryosurgery on the upper borders of the surgical site.

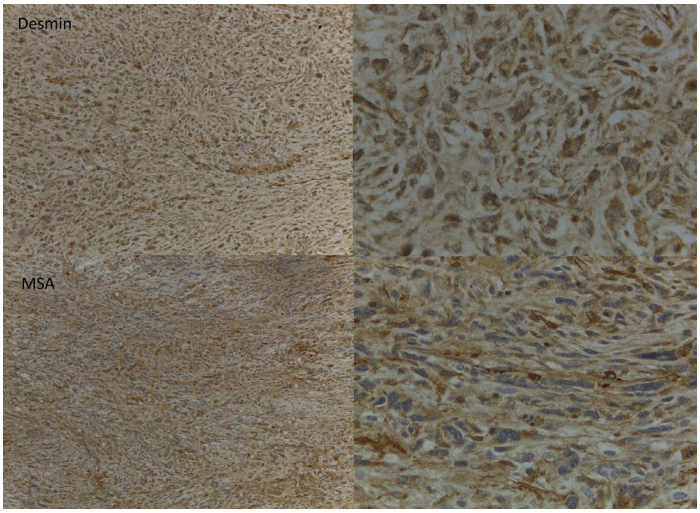

Figure 9. Desmin and Muscle-specific Actin (MSA) staining of the tissue samples obtained from the excised mass.

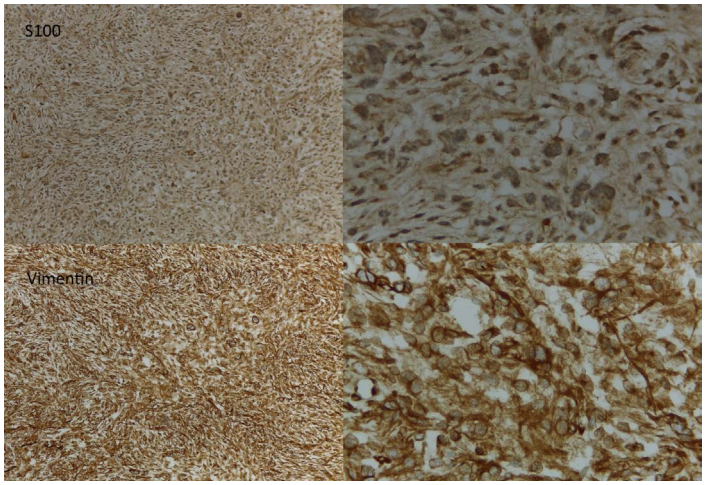

Figure 10. S100 and Vimentin staining of the tissue samples obtained from the excised mass.

found that the post-operative wound healing was excellent. **Figure 11** is the photo taken during this follow-up examination. The limb function was preserved, and the patient was able to walk with minimal impairment. PET-CT Scan evaluation taken at 6 years post-therapy shows no sign of disease recurrence (**Figure 12**).

3. Discussion

Adult RMS is a very rare case. Approximately only 350 new cases diagnosed with RMS in United States each year, and mostly children under 20 years. Adult RMS differs from childhood RMS in terms of natural history, behavior, poor response to treatment, prognosis, and outcome [1]. In children and adolescents, embryonal and alveolar subtypes of RMS predominate. While in adults the pleomorphic subtype is the most common [8]. Adult RMS has high propensity of

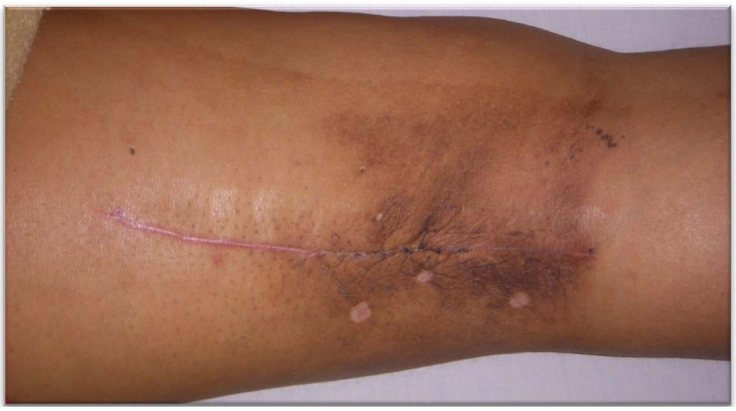

Figure 11. Excellent post-operative wound recovery on the patient's left thigh, 3 months after surgical excision and cryosurgery.

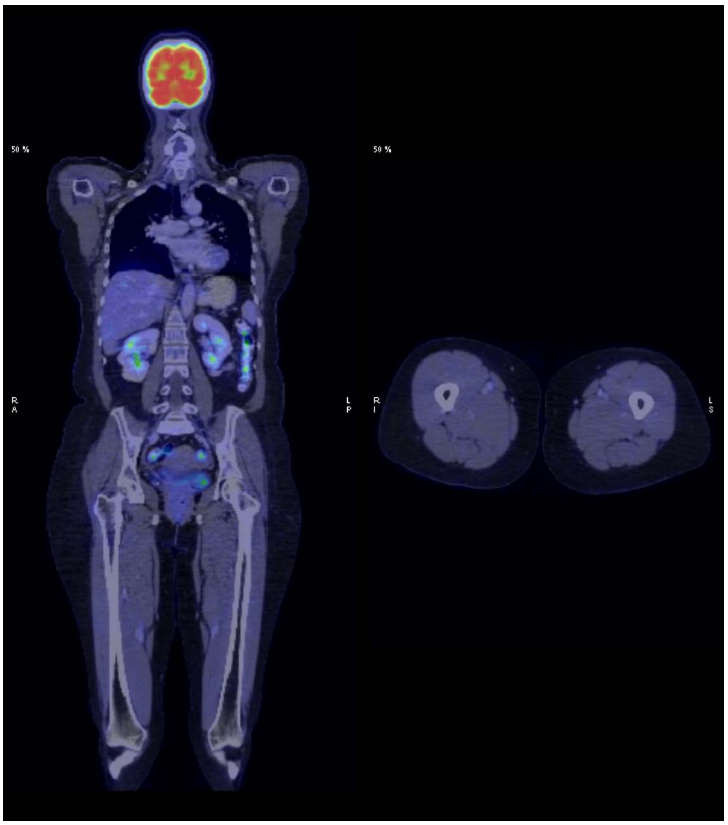

Figure 12. Follow-up PET-CT Scan imaging on May 2017 shows no recurrence of RMS.

recurrence even after complete response to therapy [2]. The typical presentation of patients with pleomorphic RMS is one of a rapidly enlarging mass in the extremities over the course of several months. This type of RMS usually happens between the 4th to 6th decade of life [9]. This corresponds to our case, an enlarging mass in the lower extremity of a 48-year old female over the course of 8 months. Our case is also typical of adult RMS since the enlarging mass was found in the most frequent site: the deep musculature of the thigh. This presen-

tation is different with RMS case in childhood which can occur anywhere in the body [10]. Due to the very small number of adult RMS cases, there is lack of information about the management and prognosis of the patient. The treatment strategies for RMS in adults are extrapolated from the IRS or COG-STS. An important thing to note is that the IRS and COG-STS protocols are designed for RMS cases in children.

Morphologically, RMS is similar to other small round blue cell tumors that involve the bone and soft tissue, such as lymphoma, small cell osteosarcoma, mesenchymal chondrosarcoma, and the Ewing sarcoma family of tumors. As a group, these tumors often pose difficult diagnostic problems, and advanced immunohistochemistry, molecular genetics, or ultrastructural techniques may be necessary to precisely establish the diagnosis. Most of the time cytologic material from fine needle aspiration biopsy is inadequate. For diagnosis we need an adequate amount of tissue samples for routine light microscopy, immunohistochemistry, cytogenetics, and molecular genetic studies. These samples should be obtained at the time of biopsy or initial resection [11]. Separate categories have been established for "sarcoma, not otherwise specified" (NOS) tumors that could not be classified into a specific subtype, and for diffusely anaplastic sarcomas, which were previously included as pleomorphic sarcomas in older classifications and associated with a poor prognosis [10]. Gross pathology often shows prominent necrosis with focal hemorrhage. Histopathologic examinations of the excised tissue in our case shows inconsistent and disordered growth pattern, with prominent spindle and eosinophilic, pleomorphic cell within a dense lymphohistiocytic infiltrate which corresponds to the pleomorphic subtype of RMS. Immunohistochemical and/or ultrastructural evaluation of sarcomeric differentiation are mandatory in making this diagnosis.

Treatment of adult with RMS is very limited, and compared to children, adults have an inferior outcome. Whereas the five-year overall survival rates of RMS in the pediatric population have improved in recent years to around 70%, the survival of adult populations with RMS is consistently lower with 5-year overall survival rates ranging from 40% - 54% [2] [5] [12]. The poorer prognosis in adults may in part reflect the inadequacy of primary treatment. One retrospective analysis in 2015 shows the 5-year overall survival rate of RMS in adult was 45% and local control 53% [1]. In another study from 171 patients over age 19, 5-year disease free and overall survival rates were 28% and 40% based upon modern treatment guidelines for pediatric RMS [13]. Adults with RMS can be treated with the same principle for children and the best way are to integrate surgery, radiation, and chemotherapy for patients [6] [12] [13].

For this patient we opted to use multidisciplinary approach as the result of our Tumor Board discussion. The strategy is based on the principle of localized treatment, combined effort to preserve the functional aspects of the limb, in order to achieve cure and also to maintain the quality of life of the patient. Before scheduling the patient for the definitive surgery, we performed TACI twice

followed by cryosurgery with the aim of lessening the tumor mass, and thus facilitating the surgery for better removal of the tumor mass. Cryosurgery was also used after surgical excision to prevent further tumor spread and chance of recurrence. Every treatment approach for this patient was observed, monitored and discussed in the Tumor Board discussions.

Transcatheter intraarterial therapies are image-guided local-regional therapies for treatment of patients with primary and metastatic tumors. The goal is to deliver anticancer treatment such as chemotherapy to the arterial supply of the tumor to inflict lethal insult. Trans Arterial Chemotherapy Infusion therapy involves local and targeted delivery of high concentrations of chemotherapeutic drugs directly to the tumor and this therapy appear to have some role in palliative measures and providing survival benefit. The role of these therapies has been established in the past decade. The rationale is to maximize chemotherapy drug concentrations in the tumor, while minimizing systemic toxicity [14].

Modern treatment such as chemotherapy is important for primary cytoreduction and eradication of metastatic disease. Surgery approach are recommended on tumors of less risk or can be considered as a treatment option in tumors with higher risks after radiation therapy or chemotherapy to control microscopic local residual disease. Specific treatment regimen depends on the estimated risk of disease recurrence, prognostic factor and approach termed risk adapted therapy. In case of RMS, complete excision for localized disease as long as functional or cosmetic results are acceptable the evidence is grade 1A. For difficult areas where surgery is not feasible, an initial diagnostic biopsy followed by induction (neoadjuvant) chemotherapy followed by definitive local therapy (*i.e.* radiotherapy) is advised [15]. In our case, due to the location of the tumor and no signs of lymph node involvement, surgical treatment is still considered a feasible option.

Cryosurgery is considered an experimental or alternative method of surgical treatment that often used as an adjunct to standard surgical procedures, even though the history of the cryosurgery itself goes far back to the 1960s. This surgical technique is quite similar to cauterization but it uses extremely cold temperatures instead of heat or electrical current to induce cell death in the applied tissue. It utilizes either liquid nitrogen or cooling probes to freeze a tumor cavity, with the goal of causing cell death by controlled, direct exposure to the sub-zero degrees temperature. Combined with excisional surgery, this procedure can be used to eliminate tumor cells for debulking (by direct application to the tumor cavity) and to reduce the possibility of tumor recurrence (by freezing the surgical site borders and/or adjacent tissues) [16]. Therefore the Tumor Board opted to use cryosurgery as means both to reduce the size of the tumor in this patient, and also after the wide excision surgery to decrease the likelihood of metastasis and recurrence of RMS. The cryosurgery procedure was performed according to the protocol, and by a trained surgeon to minimize tissue damage that could adversely affect wound healing.

We performed PET-CT Scan to evaluate the response to the treatment plan. We planned to continue the therapy with radiotherapy or systemic chemotherapy if a local residue of the tumor or a distant metastasis was found in the PET-CT Scan examination. Since we found no residue or metastasis in the PET-CT Scan, only routine monitoring follow-up examinations were scheduled. The patient responded well to the multimodality treatment, the wound healing process is excellent, and after brief physiotherapy exercises the patient can walk with little to no impairment. We still could not find any signs of recurrence of RMS even after 6 years of routine follow-up examinations.

4. Conclusion

RMS is uncommonly found in adults and is associated with worse outcomes compared to the RMS in children. There is still limited data in extrapolating treatment protocols that are made for RMS cases in children to treat adult RMS patients. Multidisciplinary approach with multimodal treatments has been used to treat adult RMS with satisfactory results. In our case, the combined treatment approach of TACI, wide excision surgery, and Cryosurgery granted us a very favorable outcome. Limb functions are preserved and the patient can walk with minor impairment, so there are no major impacts in the patient's quality of life. During the routine follow up examinations for the last 6 years, there are no signs of recurrence of Rhabdomyosarcoma. This is the longest evidence of a disease-free period we can gather as a case report. We consider that multidisciplinary approach with multimodal treatment to be a viable strategy to improve treatment outcomes in cases of adult RMS.

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Conflict of Interest

None of the authors has conflict of interest with this submission.

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