Misdiagnosis of primary pleomorphic rhabdomyosarcoma of the right thigh in a young adult: A case report

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Abstract. Pleomorphic rhabdomyosarcoma (PRMS) is a rare type of soft tissue tumor accounting for <2% of all adult sarcomas. The present study describes a case of a 28-year-old male patient with primary PRMS of the right thigh. The patient was initially diagnosed with a schwannoma and underwent conservative therapy at a local hospital. At the 6-month follow-up, the patient reported a marked increase in the size of the mass. Finally, the patient underwent fine-needle aspiration and total tumor resection. The tumor measured 11x9x5 cm³ in size and was located in the vastus intermedius muscle. According to histological and immunohistochemical findings, a diagnosis of PRMS was confirmed by an expert pathology consultant. Postoperative follow-up at 3 months revealed no evidence of recurrent disease or residual side effects from therapy. However, it is imperative that such cases are closely monitored following surgery, in order to evaluate the long-term efficacy of the procedure, since misdiagnosis may increase the risk of recurrence and metastasis. The present case is noteworthy due to the misdiagnosis of PRMS, the large size of the mass and the young age of the patient.

Introduction

Rhabdomyosarcoma (RMS) is a highly malignant type of soft tissue tumor with skeletal muscle differentiation. The incidence of RMS is ~43 cases per 10 million each year for individuals under the age of 20 (1). In patients with localized disease, the relapse-free survival rate has improved to 70-80% (2). However, the prognosis for patients with metastases is relatively poor, with a 5-year survival rate of only 30% (3). Diagnostic methods for RMS include clinical and laboratory examination, imaging analysis, pathological diagnosis and immunohistological examination (4). RMS has been divided into 3 main subtypes: Embryonal, alveolar and pleomorphic RMS (PRMS). The most common subtypes are the embryonal and alveolar subtypes (5). Primary PRMS is relatively rare and primarily affects adults, with a peak incidence in the fifth decade of life (6-9). It most commonly arises in the deep soft tissues of the extremities. Due to the similarities in clinical manifestations and imaging features between PRMS and other soft tissue tumors, PRMS is often misdiagnosed (10). The present study presents a case of PRMS that was misdiagnosed as schwannoma. This misdiagnosis resulted in the progression of the mass, and only following fine-needle aspiration and histological and immunohistochemical analysis was the tumor origin confirmed to be the skeletal muscle, and a final diagnosis of PRMS of the right thigh was provided. The present study was approved by the Ethics Review Committee of The First Affiliated Hospital of Nanchang University (Nanchang, China), and written informed consent was obtained from the patient.

Case report

In August 2014, a 28-year-old male patient presented to the Orthopedic Clinic of Taihe County People's Hospital (Ji'an, China) with a chief complaint of swelling in his right thigh for 1 month. According to the local district general hospital radiologist, magnetic resonance imaging (MRI) revealed the presence of a schwannoma and the patient was advised to undergo regular follow-up. However, 6 months later in December 2014, a gradual increase in the size of the mass and pain in the right thigh were noted. The patient was referred to the Department of Orthopedics of The First Affiliated Hospital of Nanchang University for further treatment. No personal or family history of injury or illness was recorded. A general physical examination demonstrated that the passive and active range of motion of the right knee joint was...
normal, with the exception of paresthesia in the right lower extremity. No fever or respiratory embarrassment accompanied the mass, and no history of weight loss or exposure to tuberculosis was reported by the patient.

Additional physical examination revealed a poorly-defined, tender and firm soft tissue mass over the right inner thigh, but no palpable head, neck, supraclavicular, axillary or epitrochlear lymph nodes were identified. Inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein, were within the normal ranges. MRI was performed for the evaluation of the mass. Axial T2-weighted images revealed multiple cystic lesions of varying sizes of high-signal intensity. Fat-suppressed T2-weighted MRI also exhibited high-signal intensity (Fig. 1A and B). In addition, fine-needle aspiration was performed to assess the mass, and cytological diagnosis was consistent with malignant neoplasm; pleomorphic spindle cell neoplasm with marked nuclear atypia and prominent mitotic activity was observed.

Based on the exclusion of surgical contraindications, surgeons affiliated with the Department of Orthopedics, The First Affiliated Hospital of Nanchang University, who specialize in treating bone tumors, performed the surgery. The patient was placed in the supine position, and following the success of epidural anesthesia, sterile drapes were disinfected and paved routinely in the right lower extremity to expose the operative field. First, a medial thigh incision was performed, ~17 cm in length. Next, the subcutaneous tissue, superficial and deep fascia, and vastus intermedius muscle were resected layer by layer, until the femoral artery and vein were observed. The vessels above were intact. The tumor was dark brown and located in the vastus intermedius muscle. The tumor was excised completely with negative margins. Intraoperative tissue samples were extracted for pathological examination. A wound drainage tube was placed and each layer of tissue was sutured strictly following complete hemostasis. The estimated blood loss was 100 ml and no blood transfusion was required during the procedure.

The tumor was large, smooth-surfaced and dark brown upon gross examination. The irregular tissue mass measured ~11x9x5 cm³ in size (Fig. 2A). The resected tumor tissue was fixed in 10% formalin, embedded in paraffin and cut into 5-µm sections using a microtome. The sections were subsequently stained with hematoxylin and eosin and visualized under a microscope. Microscopic examination revealed a tumor composed of interconnected bundles of atypical, spindled, pleomorphic and giant cells with high-grade atypical nuclear features. Numerous abnormal and multinucleated giant cells were observed, and the majority of cells exhibited prominent nucleoli and abundant eosinophilic cytoplasmic granules. Immunohistochemistry, tissue sections were incubated at 25˚C for 60 min with monoclonal mouse antibodies against desmin (catalog no., kit-0023) and myogenic differentiation 1 (MyoD1; catalog no., MAB-0119) (dilution, 1:1,000; Fuzhou Maixin Biotech Co., Ltd., Fuzhou, China). Immunohistochemical analysis revealed that the cells were positive for actin, MyoD1 and desmin, and negative for human melanoma black 45, calponin and melan-A (Fig. 2C and D). Based on these findings, a diagnosis of PRMS of the right thigh was provided.

The patient was discharged without any complications 1 week following surgery. The patient was administered 6 cycles of chemotherapy as follows: Doxorubicin, 90 mg/day for 3 days; 14 days off followed by ifosfamide 3.8 g/day for 5 days, followed by 14 days off prior to the next treatment cycle. At the 3-month follow up, which consisted of plain radiography and MRI, the patient was symptom-free and able to return to work. At present, the patient is currently alive and well. However, in cases like the present one, it is necessary for patients to be closely monitored, due to the high rate of recurrence and metastasis associated with misdiagnosed PRMS.
RMS is a highly malignant type of soft tissue tumor that arises from striated muscle cells, exhibits skeletal muscle differentiation and is associated with early and widespread metastasis (11,12). RMS is divided into 3 main subtypes: Embryonal and alveolar RMS and PRMS, according to the 2002 World Health Organization Classification of Soft Tissue and Bone Neoplasms (5). The embryonal and alveolar subtypes are the most common, and the most frequent sites of origin of RMS include the head and neck, extremities and soft tissues. The disease has a male predominance, with a male-to-female ratio of 1.3:1 (13). PRMS was first described by Stout in 1946 (14). Primary PRMS is relatively rare and primarily affects adults in the fifth decade of life (15). Its occurrence in young adults, as in the present case, is extremely rare. Notably, PRMS is often misdiagnosed or missed entirely, since its clinical manifestations and imaging features are similar to those of other soft tissue tumors, including fibrous histiocytoma and schwannoma (9). In the present study, the patient was misdiagnosed with schwannoma, which led to the progression of the disease for half a year; therefore, fine-needle aspiration is crucial to the diagnosis of soft tissue masses.

The histological manifestations of RMS widely vary, and the histopathological diagnosis is based on morphological, immunohistochemical and ultrastructural findings that reveal a skeletal muscle phenotype (16,17). PRMS is histologically distinguished from the two more common subtypes (embryonal and alveolar) by the haphazard arrangement of cells that are composed of large, pleomorphic nuclei and eosinophilic cytoplasm. PRMS cells may also be arranged in fascicles, which resembles the cell pattern observed in leiomyosarcoma (18). Histological subtyping is crucial, due to the various prognoses and therapeutic approaches used in PRMS as opposed to other soft tissue tumors. Immunohistochemistry is considered valuable for the diagnosis of PRMS, as a series of markers with a range of specificity and sensitivity is available. The primary markers of PRMS are MyoD1, desmin, sarcomeric actin and myosin (19,20).

Surgical excision of PRMS is considered to be the preferred treatment, since it relieves swelling and allows for the final diagnosis to be confirmed histologically. The ideal surgical management involves complete tumor resection with negative microscopic margins (21). By contrast, RMS has particular sensitivity to external beam radiation; thus complete resection may be delayed following size reduction by radiotherapy. Certain studies have reported that RMS has an 85% overall response rate to chemotherapy (22,23), in contrast to PRMS, which Ferrari et al (11) have reported a lower response rate of 6.25%. PRMS predominance in adults, as well as its resistance to chemotherapy, has led to PRMS being often considered as a distinct entity from other subtypes of RMS.

In conclusion, the present case describes a 28-year-old male patient who suffered from primary PRMS of the right thigh. Fine-needle aspiration and total tumor resection was performed, and at the 3-month follow-up, the patient had no evidence of recurrent disease or residual side effects from therapy. The performance of laboratory tests and imaging examination is particularly important in the differential diagnosis of patients presenting with soft-tissue tumors. Although the follow-up time of the current patient was relatively short, in consideration of the high risk of recurrence.

Figure 2. Pathological examination confirming pleomorphic rhabdomyosarcoma. (A) Gross appearance of the resected tumor, measuring ~1x9x5 cm³ in size. (B) Hematoxylin and eosin staining revealed spindled, pleomorphic cells arranged in a fascicular pattern. The majority of cells exhibited prominent nucleoli and abundant eosinophilic cytoplasm. (C and D) Immunohistochemical staining revealing positivity for (C) myogenic differentiation 1 and (D) desmin. (Magnification, x200).
and metastasis in misdiagnosed PRMS, long-term follow-ups are often recommended in such cases.

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