Case Report

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Alveolar rhabdomyosarcoma of the vulva in an adult: a case report and literature review

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Abstract

Rhabdomyosarcoma (RMS) is a common soft tissue tumor in children, but it is rare in adults. Alveolar rhabdomyosarcoma (ARMS) is a subtype of RMS and is extremely rare in adults, especially concerning the genital tract. We report a case of a 20-year-old woman who was admitted to and treated in our hospital for an RMS of the vulva. The patient presented with local recurrence and bone metastasis during chemotherapy after surgery and died within 1 year of diagnosis. Based on a literature review, the prognosis of ARMS in adults is poor. The treatment strategy for ARMS is not well established yet. The lungs and bone are two common sites of metastasis of ARMS.

Keywords

Adult, alveolar rhabdomyosarcoma (ARMS), vulva, genital tract, bone metastasis, soft tissue tumor

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Introduction

Rhabdomyosarcoma (RMS) is a type of malignant soft tissue sarcoma that is derived from rhabdomyoblasts.[1] RMS is common in children and adolescents, but it is rare in adults.[2] Soft tissue sarcomas account for less than 1% of all adult solid tumor malignancies, while RMS represents only 3% of all adult soft tissue sarcomas.[3] The predilection sites of RMS are different for children and adult patients. Among children and adolescent patients with RMS, the genitourinary tract is the most common primary site for RMS (21%), followed by the extremities (20%), parameningeal area

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(14%), head and neck (13%), and orbit (10%).[4] However, for adult patients, the genitourinary tract is the third most common primary site, secondary to the head and neck and extremities.[3,5–7] Therefore, RMS originating from the adult female genital tract is extremely rare. Currently, understanding of RMS in the adult female genital tract is largely based on case reports and small case studies.

RMS is classified into four subtypes of alveolar rhabdomyosarcoma (ARMS), embryonal rhabdomyosarcoma, pleomorphic rhabdomyosarcoma, and sclerosing/spindle cell rhabdomyosarcoma.[8] The most common RMS is the embryonal subtype, followed by the alveolar subtype.[8] These subtypes of RMS have different clinical manifestations. According to a small case study of adult RMS of the gynecological tract, the embryonal subtype was the most common (73%), followed by pleomorphic (13%) and alveolar (13%) subtypes.[7] Furthermore, among various primary sites of adult RMS of the gynecological tract, the vulva accounted for 13%, the cervix for 53%, the uterus for 20%, the fallopian tube for 7%, and the ovary for 7%.[7] Therefore, cases of ARMS in the vulva are extremely rare. We report here a case of vulvar RMS in a young woman who was admitted to and treated in our hospital.

Case report

A 20-year-old woman presented with a painless mass in the vulva, which had been present for 1 month, when she was admitted to the Gynecology Department in our hospital 2 years previously. Initially, the mass showed no movement with a change in body position and no enlargement under abdominal pressure. The volume of the mass gradually increased from the size of a bean to the size of a pigeon egg. An ultrasonic examination showed the presence of a well demarcated subcutaneous solid mass of 3.3×1.5 cm on the inner side of the right vulva.

Resection of the vulvar mass was performed on the day after admission to hospital. During resection, a yellow, hard, and poorly demarcated mass of 3.0×1.5 cm was found. A histological examination showed a small round cell malignant tumor of the vulva. An immunohistochemical examination of the mass showed a positive reaction for vimentin, B-cell CLL/lymphoma-2, desmin, S-100, Ki-67, and myogenin, and a negative reaction for creatinine kinase (CK), P63, CD99, MyoD1, HMB45, Melan A, chromograninA, synaptophsin, CD56/neural cell adhesion molecule, estrogen receptor, progesterone, myeloperoxidase, octamer-transcriptionfactor 3/4, alpha-fetoprotein, caldesmon, CD34, CD117, CK7, CK19, and CK5/6. Fluorescence *in situ* hybridization analysis showed gene translocation of FOXO1A (FKHR). The results of a full blood count, biochemical tests, and positron emission tomography-computed tomography (PET-CT) after surgery were normal and no regional lymph node involvement was observed. These examination findings confirmed the diagnosis of stage I ARMS on the basis of the Intergroup Rhabdomyosarcoma Study Staging System.[9] Multimodal treatment of surgery plus chemotherapy and or radiotherapy is currently standard care for RMS.

Adjuvant chemotherapy was administered 1 month after surgery. Six cycles of vindesine 5 mg on day 1 + tetrahydropyranyladriamycin 80 mg on day 1 + cyclophosphamide 1 g on day 1 for 3 weeks were administered. Bone marrow depression of degree IV developed during chemotherapy. Symptom treatment therapy, including elevation of leukocytes, was provided. Four months after surgery, whole-body PET-CT and magnetic resonance imaging (MRI) showed local recurrence in the right vulva, and abnormal signals in the iliac bone, pubic bone, thigh bone, and thoracic vertebra.

An additional two cycles of chemotherapy were administered 1 month after the last chemotherapy session as follows: ifosfamide 4 g on days 1 and 2, 3 g on days 3 and 4 + etoposide 100 mg on days 1 to 4, for 3 weeks. After this chemotherapy, the patient developed soreness and distending pain of the loins with a numeric rating scale score of 1. The patient then complained of weakness of the lower limbs, and numbness and a decreased pain sense developed below the xiphoid to both lower limbs. Twenty days after these two cycles of chemotherapy, the patient began to fall without landing on her head and was unable to walk. Emission CT showed an abnormal (increased) radiation signal in the eighth, ninth and eleventh thoracic vertebra, left sacroiliac joint, right pubic bone, and left thigh bone. PET/MRI showed bone metastasis in T3, T8, T10, L1, bilateral iliac bones, the right acetabulum, and the left thigh bone, and invasion in the T8 horizontal spinal canal. The diagnosis of thoracic vertebral metastasis with incomplete paralysis of both lower extremities post-incision of RMS in the vulva was made.

Dehydration therapy, including methylprednisolone and mannitol, was provided. A ninth cycle of chemotherapy was then administered as follows: irinotecan 240 mg on day 1 + cisplatin 70 mg on days 1 and 2. Seven days after this cycle of chemotherapy, resection and reconstruction of the metastatic tumor in the thoracic spine was performed. Five days after surgery, 400 mg bisphosphate was provided. A fever then developed and antipyretic treatment was provided. Muscle strength of the lower limbs of the patient then partially recovered.

Ten days after the second surgery, a multidisciplinary team meeting decided on the following treatment regimen: irinotecan + cisplatin + apatinib (irinotecan 100 mg on days 1 and 8; cisplatin 40 mg on days 1 to 3 for 3 weeks; apatinib 250 mg daily). This chemotherapy was administered 28 days after thoracic spinal tumor resection. One week following chemotherapy, an MRI examination showed recurrence in the right vulva, multiple metastases in bilateral thigh bones and lumbar area, and more metastatic foci compared with the previous examination. The chemotherapy regimen was then changed to lenvatinib 8 mg daily + oral administration of the PD-1 antibody Keytruda 200 mg.

Less than 1 year after the first surgery, the patient died because of advanced malignant tumors with systemic metastasis, complete paraplegia, bone marrow suppression, coagulation dysfunction, multiple organ failure, and pulmonary infection.

Ethics approval was obtained from the First Affiliated Hospital of the Medical School of Zhejiang University. Verbal informed consent for the procedures was provided by the patient, but consent for publication was not required because none of the data can be used to identity the patient.

Discussion

Adult ARMS is extremely rare. The most common primary site for adult ARMS is deep tissue of the extremities,[1] while a gynecological origin is less common.[7] We report a case of adult ARMS in the vulva and discuss the relevant literature.

Because of clinical trials and intensive treatment strategies, the treatment outcome in children and adolescent patients with RMS has greatly improved in the last few decades.[10] In contrast, the prognosis of RMS among adults is still poor.[11] A previous series showed a 5-year overall survival rate of 27% in adult RMS versus 61% in child RMS.[12] Additionally, the 5-year survival rate post-surgery in adult patients with ARMS is 29% ± 10%.[13]

The poor prognosis of adult RMS can be attributed to many reasons. First, adult patients with RMS often have an advanced disease presentation. According to a previous study, more than 60% of adult patients with RMS had regional or distant metastasis at the initial diagnosis.[14] Moreover, adult RMS shows a significant incidence of metastatic recurrence,[6] less tolerance for treatment, and resultant lower therapeutic dosage.[6,15] Furthermore, in adult RMS, there are unfavorable histopathological subtypes or anatomical locations compared with child patients,[6,16] and importantly, no standard treatment strategy has been established yet.[15–18] Recent trials of RMS largely included children and adolescent patients. Multidisciplinary management, including chemotherapy and surgery with or without radiation, has become the standard treatment for this population. However, treatment for adult RMS has not been well established yet. In most cases of adult RMS, surgery is performed, and chemotherapy and radiotherapy are used as adjuncts following the pediatric treatment protocol, which largely relies on the physician's judgment.[19] Moreover, age, size of the tumor, invasiveness, metastasis, regional lymph node involvement, and pathological response after chemotherapy are factors that affect the prognosis of RMS.[11,13] However, the site of the primary tumor does not appear to be significantly associated with the prognosis.[11]

Our patient was 20 years old when she was diagnosed with ARMS in the right vulva. Although the tumor was graded as stage I ARMS, local recurrence repeatedly developed and the tumor rapidly metastasized to the bone within a few months. This poor outcome may be partly attributed to the patient's low sensitivity and intolerance to chemotherapy. Additionally, findings in our case indicated that adult ARMS was highly malignant, metastatic in the early stage, and progressed rapidly.

There have been seven published cases of adolescent or adult ARMS in the vulva.[20–24] Five patients with ARMS aged 15 to 24 years died after 4 to 22 months after surgery.[20–23] One patient aged 17 years was lost to follow-up after diagnosis.[24] Only one patient aged 15 years was alive 12 years after surgery by the time of writing this report.[20] Among the six cases with relatively complete information, the treatment was surgery, with chemotherapy plus radiation in four cases, and surgery plus chemotherapy for the remaining two cases. The only survivor aged 15 years had received surgery and chemotherapy plus radiation. She was staged as group 1 according to the Intergroup Rhabdomyosarcoma Study Clinical Staging Classification[25] (i.e., localized disease and complete resection). The early stage of the tumor may have been one reason for her better treatment outcome. Finding in these cases together with the current case support the previous conclusion that alveolar RMS affects older children and young adults, and frequently affects the extremities and perineal sites with a peak age at 20 to 25 years.[26] Moreover, these patients with ARMS consistently showed resistance to chemotherapy. Previous studies have shown that the efficacy of a chemotherapy regimen in adult RMS tends to be inferior to that in pediatric patients.[27,28] The overall response rate after chemotherapy in adult patients with RMS can reach 85%, which is lower than that in pediatric patients, but better than that in other adult sarcomas.[3] A study by Hawkins et al. suggested that chemotherapy may not benefit adult patients with RMS aged older than 21 years.[5] Additionally, the alveolar subtype is thought to be associated with a more aggressive clinical course and

poorer prognosis compared with the embryonal subtype among adult patients.[29] According to previous studies, the embryonal subtype had a longer progression-free survival and overall survival than the alveolar subtype, but no statistical significance was indicated.[13,28] However, a study by Esnaola et al. on 39 adult patients with RMS suggested that the response to chemotherapy was not associated with the histological subtype.[13] In our case, recurrence and metastasis occurred during chemotherapy at 4 months after surgery. Because systematic imaging assessment was not performed before surgery, we could not completely exclude the possibility of presurgery metastasis, especially subclinical metastasis, which is associated with worse efficacy of chemotherapy. That chemotherapy might not benefit patients, the alveolar subtype might be more malignant, and patients might have subclinical metastasis before surgery may be associated with the poor response of these adult patients with ARMS to chemotherapy following surgery.

Among the reported cases, including our case, ARMS in the vulva initially presented as a painless and mildly tender mass in two cases. However, ARMS in the vulva showed swelling, and was painful and hard in another two cases. At least four cases developed local recurrence (not all cases had relevant information). Three cases showed lung metastasis, two cases had bone metastasis, and one case had bone marrow metastasis (metastasis was not mentioned in three cases). Enzinger and Shiraki reported that, at autopsy, lymph node, lung, pancreas, and bone metastases were present in more than 50% of 110 cases of ARMS.[30] This high incidence of bone metastases is uncommon in other neoplasms of the vulva or sarcomas of the female genital tract.[31] The lungs and bone appear to be common sites of metastasis in cases of ARMS.

Conclusion

We report a case of a 20-year-old woman with ARMS of the vulva who presented with bone metastasis during treatment. This type of case is extremely rare. The prognosis of adult ARMS is poor because it tends to be metastatic at presentation and progresses rapidly. The lungs and bone appear to be common sites of metastasis in these types of cases.

List of abbreviations

ARMS–Alveolar rhabdomyosarcoma
CK–Creatinine kinase
CT–Computed tomography
MRI–Magnetic resonance imaging
PET–Positron emission tomography
RMS–Rhabdomyosarcoma.

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Authors' contributions

Weihua He provided the concept and design of the study, performed the literature search, performed data acquisition, and wrote the manuscript; Xinhui Zhou is the guarantor of integrity of the entire study; Ke Zhou participated in revising the manuscript; Rong Zhu participated in the literature search; Yue Jin edited and reviewed the manuscript.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Declaration of conflicting interest

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