Received: 19 March 2024 | Revised: 26 August 2024 | Accepted: 30 August 2024

DOI: 10.1002/ccr3.9437

CASE REPORT

Clinical Case Reports Open Access WILEY

A rare case of perianal alveolar rhabdomyosarcoma

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Key Clinical Message

Perianal alveolar rhabdomyosarcoma is a rare sarcoma that requires a high index of suspicion along with tissue biopsy for accurate diagnosis. Successful treatment, even in the setting of recurrence, requires a multidisciplinary approach.

KEYWORDS

anus neoplasms, case reports, sarcoma, treatment outcome

1 | INTRODUCTION

Rhabdomyosarcoma (RMS) is a highly malignant, soft tissue sarcoma that commonly occurs in children and adolescents. About 90% of cases occur in individuals under 25 years old, with most patients under 10 years old. Perianal RMS are extremely rare, accounting for only 2% of all RMS.[1] There are two main types of rhabdomyosarcoma—alveolar rhabdomyosarcoma (ARMS) and embryonic rhabdomyosarcoma (ERMS). On the one hand, ERMS, representing about 70% of the condition, affects infants and children under 10 years old. ERMS also tends to affect the neck and head regions. On the other hand, alveolar rhabdomyosarcoma (ARMS), frequently observed in adolescents, is a subtype of rhabdomyosarcoma and accounts for 20%–30% of all cases.[2] The most common primary sites affected are the extremities, trunk, and, rarely, the perianal region. ARMS typically presents as a painless swelling or with mass effect symptoms at the primary site in other cases. Approximately 25%–30% of patients have metastatic disease at the time of diagnosis with the most common sites of metastasis are bone marrow, lymph nodes, and bone.[3]

Diagnosis involves pathological assessment to describe the histological nature of the tumor. ARMS is characterized by neoplastic cells attached to a septum of fibrous connective tissue. The cells are polygonal with a round to oval hyperchromatic nucleus.[4] Immunohistochemistry and molecular studies are used to confirm the diagnosis and describe the tumor subtype.[5] The expression of translocations between chromosomes 2 and 13, t(2;13)(q35;q14), and 1 and 13, t(1;13)(p36;q14) occurs in 80% of ARMS cases.[6] This leads to the fusion of transcription factors PAX3 and FOXO1. The standard treatment for alveolar rhabdomyosarcoma is a combination of surgical resection, chemotherapy, and radiation therapy. The choice

Robert Rosenberg and Michal D. Honaker have equally contributed and share the last authorship.

of local treatment and control depends on multiple factors such as primary tumor site, size, age, nodal involvement, histology, and response to neoadjuvant chemotherapy.[7] Staging classification, as defined by the American Joint Commission on Cancer (AJCC), allows for the determination of overall prognosis of each patient.

This case study is important in understanding the diagnosis and the treatment plan for such a rare medical condition. Considering that PRMS is a rare condition in the economy, the case study provides the symptoms and signs that can be used for diagnostic purposes and improve the treatment plan of the condition. Although the incidence rate of this condition is rare, it mainly occurs in children, teenagers, and young adults. As the case explores the condition of a 21-year-old male, the information supports previous studies conducted highlighting the determination of the clinicians in treating the condition.

2 | CASE HISTORY/EXAMINATION

A 21-year-old male presented to the emergency department with a painless perianal induration that had been present for 2–3 months. It was associated with painful bowel movements for several days. The patient had been managed with Co-Amoxi 2 g once a day for 10 days without any improvement. Findings on examination were an 8 cm thick, elastic, nonfluctuating, and pressured swelling, with perianal redness extending from the right lateral perianal region right lateral to the perineum. Digital rectal examination was not possible due to pain.

3 | METHODS

Biopsy of the mass revealed soft tissue with infiltration of poorly differentiated small-cell appearing malignant cells (Figures 1 and 2). The tumor cells stained positive for proliferation marker Ki-67 with a proliferation rate of more than 80–90%. It stained negative for Lu5, CK5, p40, CD45, and synaptophysin. A sarcoma diagnosis was highly suspected with a differential diagnosis of Ewing-Sarcoma, rhabdomyosarcoma, and desmoplastic round cell tumor. Immunohistochemistry showed high-grade sarcoma with the expression of desmin and myogenin, corresponding to a rhabdomyosarcoma. A diagnosis of alveolar rhabdomyosarcoma was confirmed by the expression of the PAX3-FOXO1 fusion gene. Final TNM staging was cT2b, cN1, M0, G3, CWS subgroup H. MRI pelvis showed a tumor up to 6.5 cm in diameter, in the right ischioanal fossa with infiltration into the levator muscles and rectum. Metastases into the iliac and inguinal lymph nodes were also noted. However, there was no evidence of perianal abscess. Positron emission tomography/computed tomography (PET/CT) demonstrated a tumor in the right ischioanal fossa with infiltration of the levator muscle and rectum (Figure 3). PET demonstrated mild uptake, but increased from the surrounding tissues.

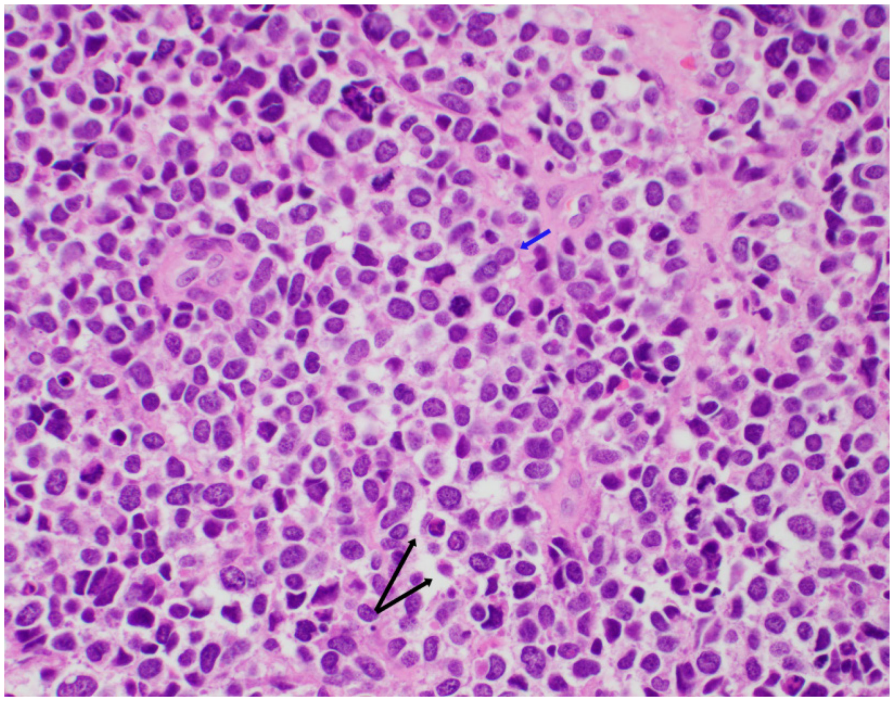

FIGURE 1 Representative H&E histologic stain. Black arrows point to representative pseudoalveolar architecture. Blue arrow points to representative small, round cell architecture.

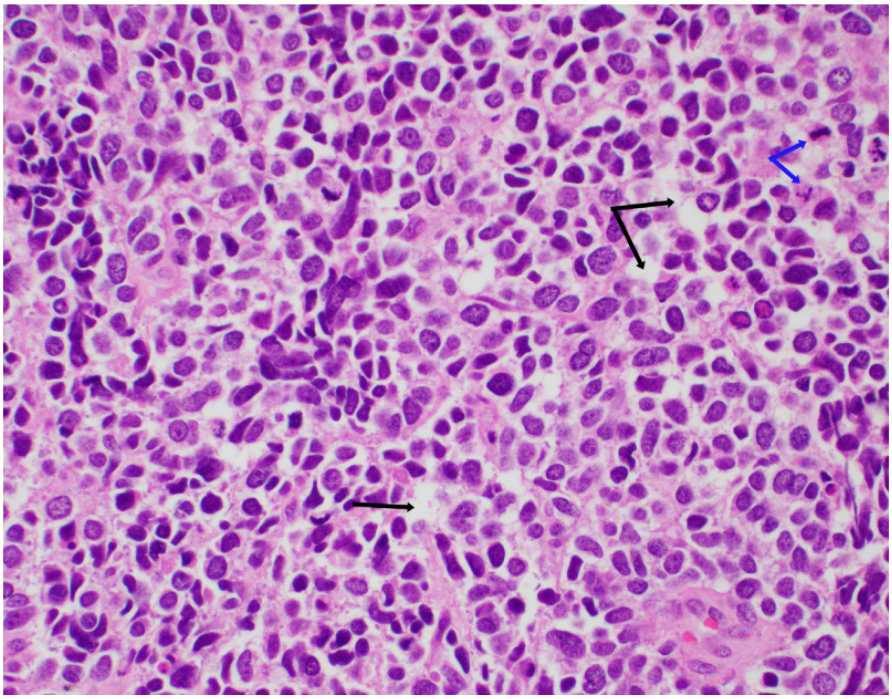

FIGURE 2 Representative H&E histologic stain. Black arrows point to representative pseudoalveolar architecture. Blue arrow represents mitotic figures.

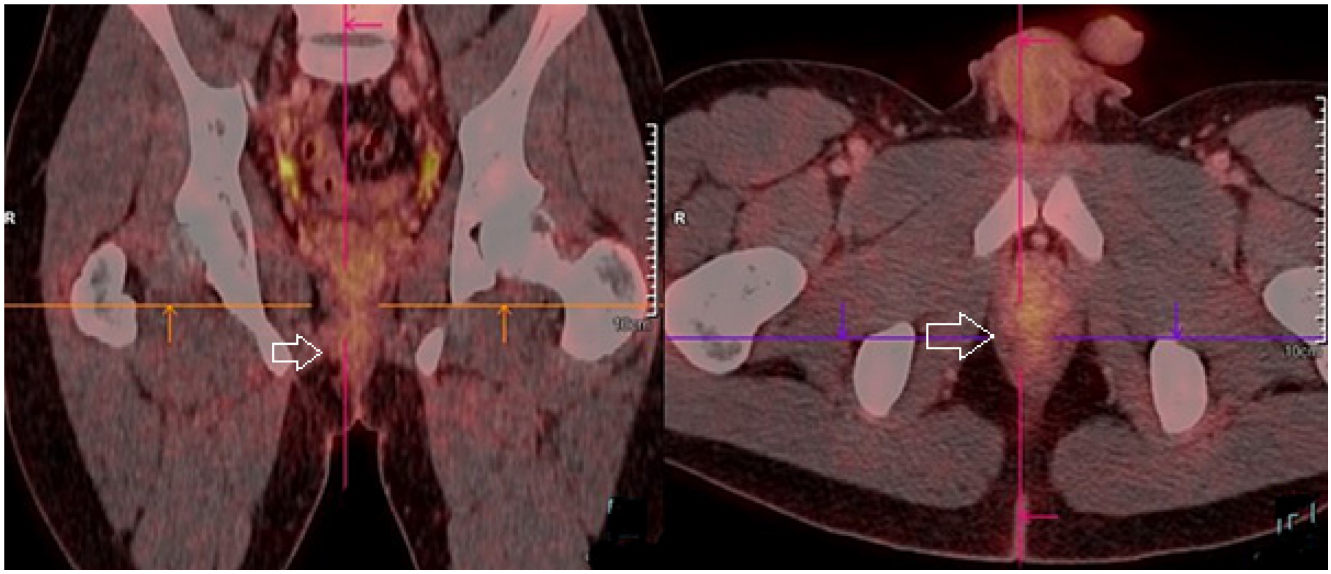

FIGURE 3 Pre-operative positron emission tomography/computer tomorgraphy. Arrows point to perianal mass and areas of mild, but increased hypermetabolic activity compared to background activity.

The patient was put on nine cycles of neoadjuvant radio-chemotherapy using VAIA III (vincristine, ifosfamide, doxirubicin). This was followed by a laparoscopic abdominoperineal resection with the formation of an end colostomy using the specific, measurable, achievable, realistic, and timely (SMART) technique. Resection of the pelvic lymph nodes and greater omentum were also performed. After surgery, the patient was maintained on cyclophosphamide and vinorelbine for 6 months.

4 | CONCLUSION AND RESULTS

Six months later, he presented with a tumor recurrence around the distal abdominal aorta with extension to the left common iliac vein with mass effect on the inferior vena cava. He was started on salvage induction therapy using TECC protocol (topotecan, etoposide, carboplatin, cyclophosphamide) followed by radiotherapy. Surgical resection was done, which involved resection of the aortic bifurcation, partial resection of inferior vena cava,

and complete resection of the left common iliac vein. Reconstruction was conducted using self-made bovine pericardial tube graft and implantation of an infrarenal Y-prosthesis. The patient was subsequently maintained on oral chemotherapy using trophosphamide, idarubicin, and etoposide. Thirteen months after the second tumor resection, he presented with a new subcutaneous metastasis to the right scrotum. Thus, he underwent partial resection of the right scrotum achieving R0 resection. The current PET/CT showed no evidence of new lymphogenic or hematogenic metastases.

5 | DISCUSSION

Alveolar rhabdomyosarcoma constitutes up to 20%–30% of all rhabdomyosarcoma cases and has a poorer prognosis compared to other subtypes. This has been associated with its expression of PAX3-FOXO1 fusion genes that result from chromosomal translocations t(2;13)(q35;q14). The fusion of these genes leads to the expression of fusion proteins with a high rate of transcriptional activity. Tumors that express this gene are more aggressive, respond poorly to treatment, and express frequent recurrence.[8] Other prognostic factors for alveolar rhabdomyosarcoma depend on the primary tumor site, size being below or above 5 cm, age at diagnosis, and stage. From the case that has been presented, the primary findings showed the tumor site was 8 cm thick, supporting the notion of tumor size above 5 cm having worse prognosis and high risk for recurrence.

Rhabdomyosarcoma arising from the perianal region is rare and constitutes about 1% of all cases.[1] It carries a poor prognosis with a five-year survival rate of 20%–49%. It is commonly seen in patients above 10 years old and presents mainly with locally infiltrating tumors. This case builds on the current condition and contributes to the existing reports on symptoms and prognosis of the rare entity of perianal alveolar rhabdomyosarcoma (PRMS). This patient reported painful bowel movements for several days. This is in contrast from other rhabdomyosarcoma where patients usually experience difficulty in defecation or urination. Previous studies indicate that PRMS is characterized by perianal abscesses accompanied by pain in the abdomen. This vague complaint is often linked to misdiagnosis, thus, leading to delays in appropriate diagnosis. Attention should be placed on predisposing factors including HIV infection, Crohn's disease, diabetic ketoacidosis, and immune deficiency. Infiltration of lymph nodes is also frequently demonstrated with these tumors. All cases of alveolar rhabdomyosarcoma should, therefore, be evaluated for lymph node involvement.[9] PET scan has superior results in detecting nodes in this age group.[10]

Epidemiological characteristics tend to provide clues on the perianal abscesses associated with these tumors, which mainly affect infants below the age of 1 year.[11] However, this can be different based on the prevailing demographic characteristics for the PRMS. Empirical evidence suggests that when a woman, below the age of 20 years, presents with perianal tumor, differential diagnosis for malignant tumors should be considered. Understanding the challenges of appropriate diagnosis and in accompanying delays in correct assessment is critical for clinicians to understand the treatment plan for the condition. Previous studies indicate that there is a significant correlation between the average time intervals of the onset of the symptom to diagnosis.[12]

Preliminary examination of PRMS involves endorectal/endoanal ultrasound, which is radiation-free, accessible, and noninvasive. The advantage of ultrasound lies in distinguishing lacunar or cystic masses, which provides high sensitivity and specificity when diagnosing perianal abscesses.[13] Furthermore, endoanal ultrasound is also recommended in clarifying tumor involvement in the anal canal. It provides clues on the accuracy of diagnosis and the treatment to be given. In a study by Demoor-Goldschmidt et al., PRMS cases were reviewed to determine the effective strategy to be used in examination of the patient. The study confirmed that treatment of PRMS incidences was characterized by solid masses and intratumoral signals, which is consistent with previous studies conducted on PRMS. Previous studies have confirmed that using endoscopic ultrasound is recommended in the diagnosis of the condition due to minimal invasion and improved accuracy.

In most cases, the sonographic features characterizing PRMS are nonspecific and variable and pose limitations in assessing distant metastases and deep-tissue lymph nodes.[14] As such, evaluating the patient's possibility for conducting MRI or CT scan in further evaluating the condition is critical. PRMS in the pelvic organs requires MRI as it provides information on the degree of soft tissue invasion.

Pain is a vague symptom and tend to mislead the physician and result in delays in diagnosis. The clinician can easily perform surgical intervention aligned to the location of pain, which can damage the tumor's integrity and make radical complex surgery difficult.[15] This scenario will lead to an unfavorable prognosis of the condition. When PRMS is diagnosed immediately and there is exclusion of distant metastases, surgical treatment can be undertaken. With the assessment of the different possibilities in which treatment is undertaken, it is easier to ascertain the challenges and issues impacting the treatment of the condition.

Improved survival has been demonstrated with combined surgical excision, chemotherapy, and radiotherapy.[16]

Chemotherapy is a standard treatment for all cases of rhabdomyosarcoma. The success of surgical resection is dependent on the primary site. Complete resection is not advised if the risk of functional morbidity is high.[17] Primary surgical resection aims to completely remove the tumor with a margin of normal tissue. Delayed surgery or secondary resection is indicated if a good tumor response has been achieved after neoadjuvant chemotherapy plus preoperative radiation therapy. In such cases, surgery can be considered if it results in the tumor's complete resection (R0).[18] Radiotherapy can be used alone or in combination with surgery to control the local disease. Patients should be classified into risk groups before discussing the mode of treatment. There are four risk groups based on the combination of tumor stage, age at diagnosis, histological subtype, tumor resectability, and metastasis.[19] Our patient was in the high-risk group. The failure-free survival (FFS) for this group is generally between 20% and 30% despite aggressive chemotherapy, radiotherapy, and surgical resection.[20]

Consideration of the measures that should be undertaken in improving the overall conditions of the patients should be provided to the patient in order to obtain informed treatment decision making. Surgical resection has been shown to be the appropriate treatment for PRMS when surgically feasible. Other treatments modalities include systemic chemotherapy and radiation therapy which is considered effective in the treatment of the condition.

In conclusion, perianal alveolar rhabdomyosarcoma is rare and often misdiagnosed secondary to vague complaints by the patient. At presentation, most patients have nodal disease. Management involves a combination of surgical resection, chemotherapy, and radiotherapy. Stage classification should be completed before establishing a management plan. In this case, a high-risk tumor was managed by multimodal therapy including radical surgery in combination with chemotherapy and radiotherapy. The case provided the effective treatment plans that should be considered and were found to be aligned with previous studies providing evidence-based approaches to the treatment of this extremely rare condition. Even though the tumor recurred on two occasions, in both cases, complete surgical resection was able to be undertaken. However, the prognosis for a high-risk tumor is still poor despite the currently available management options.

AUTHOR CONTRIBUTIONS

Anas Taha: Conceptualization; investigation; writing – original draft; writing – review and editing. **Amjad Maeky:** Investigation; writing – original draft; writing – review and editing. **Larissa Wentzler:** Conceptualization; investigation; writing – original draft; writing – review and editing. **Stephanie Taha-Mehlitz:** Conceptualization; investigation; writing – original draft; writing – review and editing. **Robert Rosenberg:** Investigation; writing – original draft; writing – review and editing. **Michael D. Honaker:** Investigation; writing – original draft; writing – review and editing.

FUNDING INFORMATION

No funding was received for the submitted work.

CONFLICT OF INTEREST STATEMENT

The authors have nothing to disclose or conflicts of interests to report.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

ETHICS STATEMENT

The authors affirm that this manuscript adheres to the principles of medical ethics. All research involving human subjects was conducted with appropriate ethical approval, and informed consent was obtained from all participants. Any potential conflicts of interest have been disclosed.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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How to cite this article: Taha A, Maeky A, Wentzler L, Taha-Mehlitz S, Rosenberg R, Honaker MD. A rare case of perianal alveolar rhabdomyosarcoma. *Clin Case Rep*. 2024;12:e9437. doi:10.1002/ccr3.9437