Perianal embryonal rhabdomyosarcoma: A case report

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Abstract. Perianal embryonal rhabdomyosarcoma (ERMS) is a rare disease with a poor prognosis. There are few reported cases of this disease, and specific clinical manifestations are lacking; therefore, making an early diagnosis before surgery is challenging. In November 2014, a 30-year-old man was admitted to Xiaoshan Affiliated Hospital of Wenzhou Medical University due to severe left perianal pain. Ultrasonography revealed a multilocular perianal abscess, and an emergency perianal abscess incision and drainage were performed. However, pathology combined with immunohistochemistry confirmed an ERMS. The patient did not receive postoperative radiotherapy or chemotherapy and died of multiple metastases and multiple organ failure 6 months later. Perianal ERMS is highly malignant and rare, and can easily be misdiagnosed as a perianal abscess. Clinicians must enhance their knowledge and improve preoperative diagnostic tests to prevent misdiagnoses.

Introduction

Rhabdomyosarcoma (RMS) is a malignant tumour that develops from mesenchymal cells and affects the head and neck, followed by the urogenital system, extremities, and rarely, the perianal area (1,2). Perianal RMS accounts for only 2% of RMS cases, is associated with high risks of mortality and low cure rates, and has a poor prognosis (3). RMS can be divided into four types based on histological and genetic characteristics: Embryonal RMS (ERMS), mainly composed of rhabdomyoblasts and small round cells; alveolar RMS, mainly composed of large round cells and rhabdomyoblasts; adult pleomorphic RMS, composed mainly of pleomorphic rhabdomyoblasts; and spindle cell/sclerosing RMS, composed mainly of spindle-shaped rhabdomyoblasts (4). ERMS is most common in children <10 years of age and rarely occurs in adults (5). Therefore, perianal ERMS in adults is extremely rare. Perianal EMRS in adults sometimes presents as perianal pain and an increased skin temperature, which can easily be misdiagnosed as a perianal abscess. The present report describes a case of perianal ERMS in an adult male that was misdiagnosed as a perianal abscess but later confirmed pathologically. This case is presented to improve our understanding of ERMS and reduce its future misdiagnosis.

Case report

Case presentation. A 30-year-old man was referred to the Emergency Department of Xiaoshan Affiliated Hospital of Wenzhou Medical University (Hangzhou, China) in November 2014, complaining of severe left perianal pain for 1 day, without chills, fever or other discomfort. Perianal examination showed that the skin temperature of the left perianal region was relatively high, and a mass was palpable at the anal edge at 5 o'clock in the lithotomy position, measuring ~4.0x3.0 cm in size, with pain, fluctuating sensation and no ulceration or pus. Perianal B-ultrasound showed a 3.6x2.2x4.2-cm hypoechoic dark area under the left perianal skin. The internal fluid was thick, and obvious blood flow signals could be seen, suggesting that it might be a left perianal subcutaneous multilocular abscess (Fig. 1). Based on the B-ultrasound results and the patient's symptoms, a perianal abscess was diagnosed, and perianal abscess incision and drainage were performed under general anaesthesia on the same day. During the operation, the mass was incised, and no obvious purulent liquid was found. The mass was tough in texture, and necrotic tissue and dark red jelly-like objects were seen. Three pieces of tissue were taken for pathological examination during the operation. The anti-infective drug ceftriaxone (2 g per day) was administered for five days after surgery; however, the patient's perianal pain was not significantly relieved.

Postoperative pathological microscopic observations revealed that the tumour was comprised of round cells that grew diffusely and infiltrated the adipose tissue (Fig. 2). The round cells were of medium size, with round or oval nuclei, a high nuclear-to-cytoplasmic ratio, frequent mitoses, obvious atypia, darkly stained chromatin, small nucleoli and regional tumour necrosis (Fig. 3). Immunohistochemical (IHC) staining and specific staining indicated the following results: Desmin(+) (Fig. 4), myoblast determination protein 1 (MyoD1)(+) (Fig. 5),

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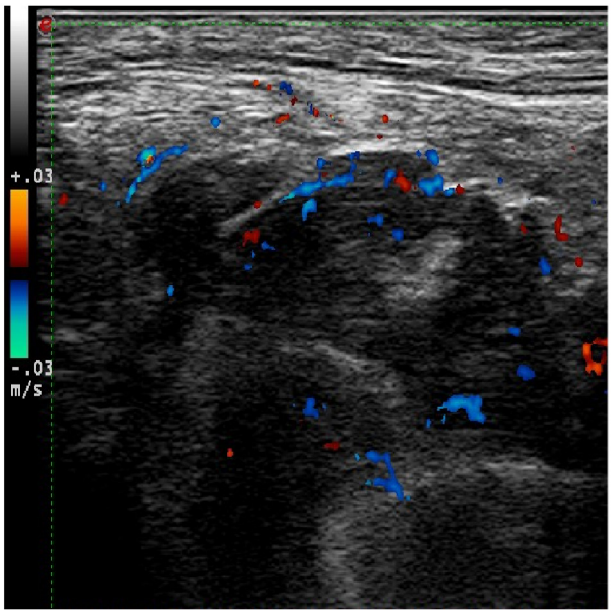

Figure 1. B-ultrasound showed a low-echo dark area under the left perianal skin, with thick internal fluid and obvious blood flow signals.

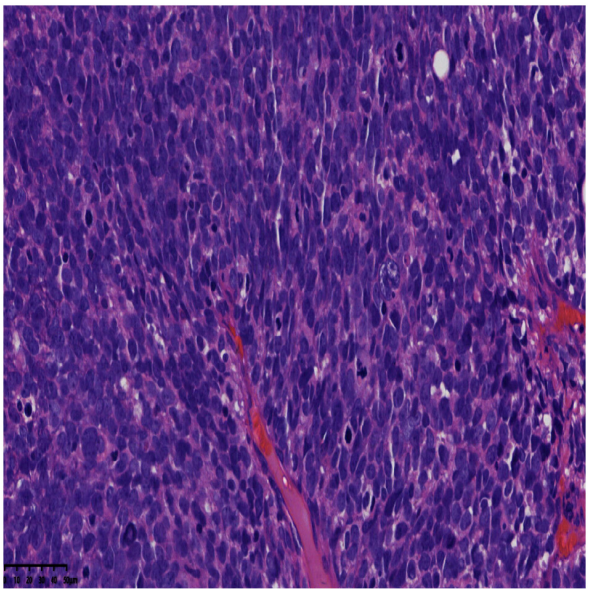

Figure 3. Pathological microscopic observations showing round cells with round or oval cell nuclei, a high nuclear-to-cytoplasmic ratio and frequent mitoses (hematoxylin and eosin; magnification, x400; scale bar, 50 μm).

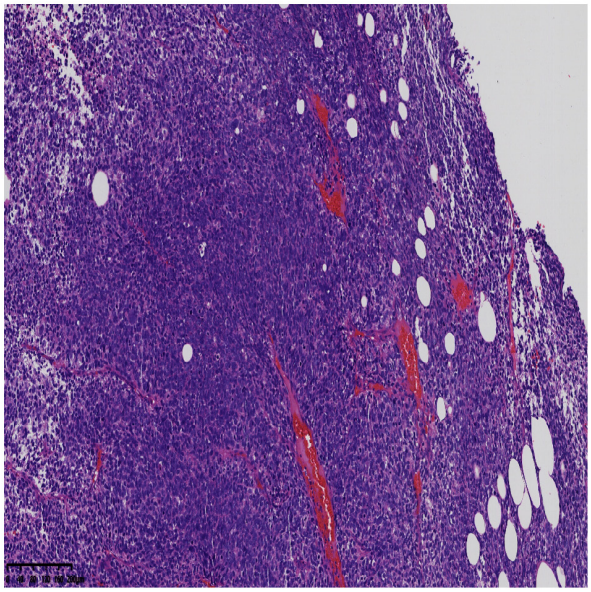

Figure 2. Pathological microscopic observations showing tumour tissue growing diffusely from round cells and infiltrating the adipose tissue (hematoxylin and eosin; magnification, x100; scale bar, 200 μm).

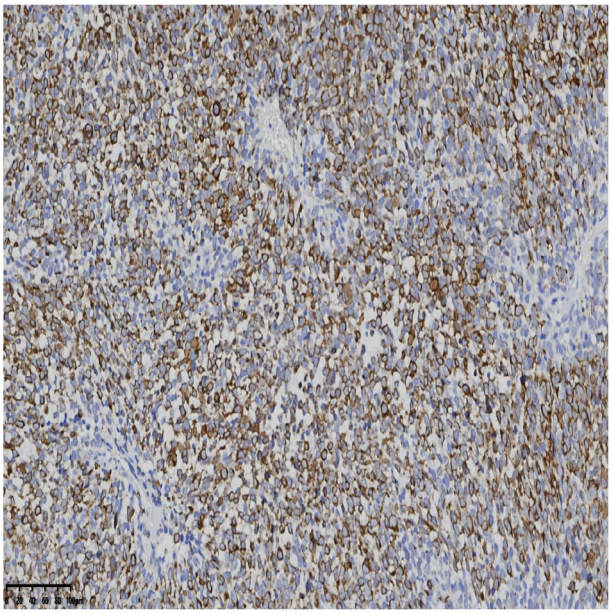

Figure 4. Immunohistochemistry staining of the tumour showing a positive result for desmin (magnification, x200; scale bar, 100 μm).

Ki-67(+; 75%), Melan-A(-), S-100(-), human melanoma black 45 (HMB45) (-), leukocyte common antigen(-), prostate-specific antigen(-), chromogranin A(-), synaptophysin(-), CDX-2(-), creatine kinase (CK)(-) and epithelial membrane antigen(-). The pathological diagnosis was of a perianal ERMS. We recommended that the patient undergoes postoperative radiotherapy and chemotherapy, but the patient did not accept it and requested to be discharged from the hospital 10 days after the surgery. The patient then visited a higher-level hospital for radiotherapy. However, during the follow-up period, the patient died of multiple metastases and multiorgan failure at 6 months post-surgery.

Staining methods

Postoperative pathology. The tissue was fixed with 4% neutral formalin (24 h at 25˚C) and embedded in paraffin, and 4-μm serial sections were prepared and subjected to staining with H&E (Beijing Jinqiao Zhongshan Biological Co. Ltd.; OriGene Technologies, Inc.) for 8 h at 25˚C. Observation was performed using a Leica DM2000 light microscope (Leica Microsystems GmbH).

IHC staining. The undyed tissue sections (4 μm) were placed in an oven at 60˚C for 120 min and then dewaxed in xylene (500 ml) three times at 25˚C for 10 min each. The sections were rehydrated by washing in an ethanol

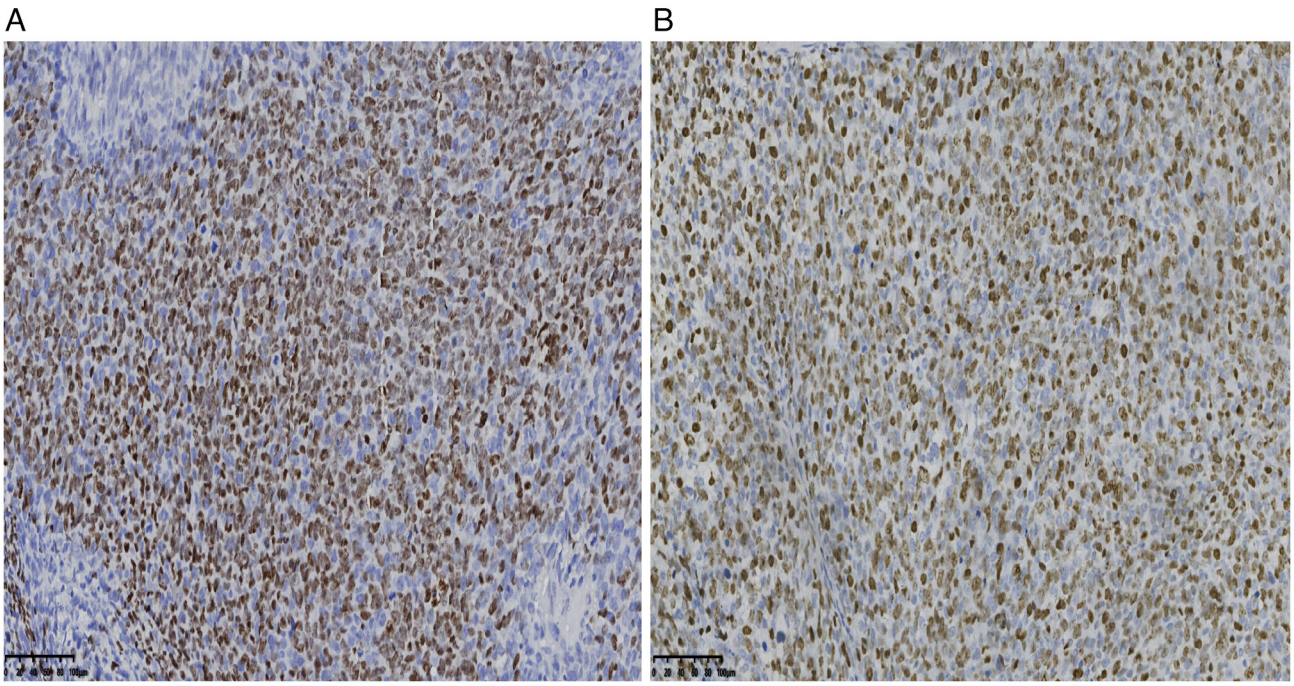

Figure 5. Immunohistochemistry staining of the tumour showing a positive result for (A) myoblast determination protein 1 and (B) Ki-67 (magnification, x200; scale bar, 100 μm).

gradient series (100 and 95% for 3 min, and 85 and 75% for 1 min) and then rinsed with distilled water. The sections were placed at 100˚C in EDTA (pH 9.0±0.2) buffer (1:50; cat. no. ZLI9069; Beijing Zhongshan Jinqiao Biological Co. Ltd.; OriGene Technologies, Inc.) and the repair solution was used for antigen retrieval for 20 min (hot repair at 100˚C in EDTA 1:50, 2,500 ml liquid for 20 min). Subsequently, sections were washed with distilled water, treated with 3% H_2O_2 (blocking reagent) solution at 25˚C for 10 min to inhibit endogenous peroxidase activity and washed with PBS. Tissue sections were then incubated at room temperature for 40 min with primary antibodies. Following primary incubation, sections were washed three times with PBS for 5 min each time and incubated with sheep anti-rat/rabbit IgG polymer labeled with HRP (ready-to-use type; cat. no. PV-8000D; Origene Technologies, Inc.) at 25˚C for 15 min. Sections were washed three times with PBS for 5 min each time. Tissues were incubated with 3,3'-diaminobenzidine color development solution (1:50 dilution; cat. no. PV-8000D; Beijing Zhongshan Jinqiao Biological Co. Ltd.) at 25˚C for 5-10 min, and then washed with distilled water. Hematoxylin was applied at 25˚C for 1 min and samples were washed in tap water and then blued in PBS. Afterwards, the slide was washed with 75, 85, 95 and 100% ethanol (500 ml each) for 1 min each to remove excess water and facilitate observation under the microscope. Finally, tissue sections were placed in xylene (500 ml) three times for 1 min each and a drop of neutral gum was added to seal. IHC sections were observed under a light microscope (Leica DM2000; Leica Microsystems GmbH) without software analysis. IHC was performed using an EnVision IHC kit (polymer method; cat. no. KIT-0014; Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.; Origene Technologies, Inc.) using primary antibodies obtained from Beijing Zhongshan Jinqiao Biological Co., Ltd. and Fuzhou Maixin Biotechnology development Co., Ltd. to target the following proteins (pre-diluted working solutions unless otherwise indicated): Desmin (working solution; cat. no. 20092713), MyoD1 (working solution; cat. no. 20121719), Ki-67 (1:200 dilution; cat. no. 21030436), Melan-A (working solution; cat. no. 19122684), S-100 (working solution; cat. no. 2012240585C8), HMB45 (working solution; cat. no. 21065615), leukocyte common antigen (working solution; cat. no. 201140037a), prostate-specific antigen (working solution; cat. no. 2012160146f), chromogranin A (working solution; cat. no. 20090705), synaptophysin (working solution; cat. no. 2101060742a), CDX-2 (working solution; cat. no. 2105190631CEPR2764Y), CK (1:200 dilution; cat. no. 21061509) and epithelial membrane antigen (EMA; 1:100 dilution; cat. no. 21020730).

Discussion

ERMS originates from myogenic precursor cells and is more common in children and adolescents (6). The disease occurs in various locations, with recent reports focusing on the head and neck, urogenital tract, trunk and extremities (7,8). ERMS arising in the perianal region is rare (9). Perianal ERMS often presents as extensive diffuse lesions around the anus, with unclear edges, normal or grey skin colour, no obvious tenderness or fluctuation, and a hard, fixed texture (2). When complicated by an infection, there may be symptoms such as redness, swelling, heat and pain that need to be differentiated from the indications of a perianal abscess. Clinically, there have been a number of cases of misdiagnosis as a perianal abscess (10,11). The present case was initially misdiagnosed as a perianal abscess; however, it was later pathologically confirmed as an ERMS.

The clinical manifestations of ERMS are diverse, characterised by the poor differentiation of tumour cells, rapid tumour growth, strong invasiveness, high rate of metastasis and mortality, and can only be diagnosed pathologically (12). The morphological appearance under ERMS microscopy is mainly similar to the muscles during the 7-10-week embryonic development, but it can also resemble the morphology of muscle cells at various stages of development. The tumour cells are round or oval with a very small amount of eosinophilic cytoplasm, deeply stained nuclei and well-differentiated smooth muscle blasts, with large round or bizarre nuclei (13). Immunohistochemical labelling is an essential method for diagnosing ERMS. Most ERMS tumours are positive for desmin, Myogenin and MyoD1. Among these, desmin and MyoD1 are sensitive markers for identifying RMS and require nuclear staining to be considered positive (13,14).

Perianal RMS treatment includes surgery, radiotherapy and chemotherapy. A combined abdominoperineal radical resection can be performed for localised perianal tumours. In larger cases, radiotherapy can be administered, and surgery is performed after the tumour shrinks (15). In addition, when there are no suitable treatment options, multi-target inhibitors and supportive care may be good alternatives for patients with EMRS (5,16). These tumours are now routinely tested for molecular characterization, particularly TP53 mutation status. However, since perianal ERMS is a rare disease, the hospital had little experience of such cases in the present study and not much was known about the molecular characteristics at that time. The patient received brief treatment in the Xiaoshan Affiliated Hospital of Wenzhou Medical University and was discharged to a higher-level hospital for treatment after the pathological results were obtained. Therefore, no molecular characterization tests were performed on the tumour. The patient did not receive any treatment and was discharged to another hospital for consultation. During the follow-up period, the patient died of multiple metastases and multi-organ failure at 6 months after the operation.

In summary, the present study reports a case of perianal ERMS in an adult that was initially misdiagnosed as a perianal abscess. The rarity of perianal ERMS in adults poses a challenge with regard to its aetiology and diagnosis; therefore, a detailed evaluation is required before surgery. The prognosis of perianal ERMS in adults is poor and requires active postoperative treatment and close follow-up. In addition, the analysis of clinical signs and immunohistochemistry deepens our understanding of perianal ERMS and provides a diagnostic reference for clinicians encountering these conditions in the future.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YJ and JL performed case data collection, drafting of the manuscript and conception of the study. BH and GL obtained medical images and analyzed patient data. JL and YJ confirm the authenticity of all the raw data. YJ revised the manuscript and interpreted the data. In addition, all authors agreed on the journal to which the article has been submitted and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The patient provided written informed consent for the case study to be published.

Competing interests

The authors declare that they have no competing interests.

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