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Completely inverted uterus secondary to uterine rhabdomyosarcoma mistaken for a cervical tumor and removed vaginally: case report and literature review

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Case report

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Abstract

Background Uterine rhabdomyosarcoma(RMS) is an extremely rare, underrecognized malignant tumor. It usually affects young women and has a dismal prognosis.

Case presentation A 19-year-old nulliparous girl presented to our institution with venous sinus thrombosis who subsequently developed complete uterine inversion, which was mistaken for a cervical tumor and removed vaginally. She experienced uncontrollable occurrence of multiple tumors and died within 6 months.

Conclusion Our case illustrates the typical presentation and aggressive behavior of uterine RMS. Abnormal uterine bleeding(AUB) in young women should be a sign to screen for uterine neoplasms. Anatomy should be fully evaluated before proceeding toward surgical intervention to ensure the correct procedure is done.

Background

Rhabdomyosarcoma is extremely rare in the uterine corpus and principally affects young women[1]. It is still an underrecognized aggressive neoplasm[2]. As of now, there is no established optimal treatment for these rare tumors in the literature. Adult patients with uterine RMS are felt to have a dismal prognosis[3]. In an effort to provide more understanding and therapeutic options for this rare malignancy, we report a young adult with uterine inversion and venous sinus thrombosis secondary to RMS of the corpus uteri. A search of English literature found 32 cases of inversion due to sarcoma reported with only 6 cases of RMS, including our case, from 1887 to 2020.

Case Presentation

A 19-year-old nulliparous girl presented to the emergency room of our institution under sedation due to unconsciousness and convulsions. She complained of headache, nausea and vomiting 5 days ago. Two days later, these symptoms worsened, and delayed response and convulsions appeared. She was admitted to a local hospital and was considered to have cerebral thrombus. Conservative thrombolysis and symptomatic treatment were given, which were ineffective. She had a history of abnormal uterine bleeding for one year and a history of copious, pink, thick, foul smelling vaginal discharge for half a year. A computerized tomography (CT) scan of the head demonstrated venous sinus thrombosis(Fig. 1.a). Emergency cerebrovascular angiography by femoral artery and femoral vein intubation was performed. The patient received thrombolytic therapy via femoral intravenous urokinase on the same day she presented to our institution. The treatment lasted for 7 days. Subsequently, her general condition improved. On the 19th day of hospitalization, a partial prolapse of the vagina appeared as a mass with massive vaginal bleeding. Her hemoglobin dropped from 10.8 to 6.3 in 3 hours. Gynecologist was asked to consult the patient. On gynecologic examination, the mass was approximately 17 × 15 × 10 cm, and the tissue showed with local congestion, infection and necrosis(Fig. 2). The mass originated from the upper

vagina, and the cervix was not visible or reachable. A rectal examination revealed no tumor effect. The mass was considered to be of cervical tumor. After a brief discussion of all therapeutic options, in view of her general condition was poor,emergency transvaginal resection of the mass was performed for hemostasis. The mass wass removed completely from the pedicle. Postoperative pathology suggested rhabdomyosarcoma of the embryonal type(Fig. 3). The tumor pedicle was negative. Immunohistochemical results showed the following staining results:CD10(+), CD117(-), CD34(-), CD68(+), pan-CK(-), desmin(+), DOG1(-), Ki-67(+), LAC(-), lysozyme(-), MyoD1(+), myogenin(+), S-100(-), SAM(-), and vimentin(+). The patient was misdiagnosed with rhabdomyosarcoma of the cervix. On the 15th day after the mass resection, laparoscopy and hysterectomy were planned. Intraoperative exploration showed that there was no uterus in the pelvic cavity. The bilateral adnexa near the uterus adhered to the scar on the pelvic floor at the top of the vagina. The visible parts of the bilateral fallopian tubes and ovaries were grossly normal. There was no palpable pelvic or paraaortic lymphadenopathy. According to the previous pathology, we believed that the mass that was removed vaginally was a completely inverted uterus. Finally, we performed laparoscopic resection of the bilateral fallopian tubes and residual cervical tissue. Postoperative pathology was negative for tumors. We recommended chemotherapy with radiation for her. In view of her general condition, she asked for adjunctive treatment to be postponed. The patient began her first cycle of chemotherapy 43 days after her first surgery. She was treated with chemotherapy comprising VAC. Seventy-two days after first surgery, she developed recurrence of a 5 cm mass in the pelvis (Fig. 1.b).Treatment failed to control the disease. During her fourth cycle of chemotherapy, the mass(pelvic MRI) rapidly increased to 16 cm in size(Fig. 1.c), and a chest CT scan revealed multiple metastatic nodules in both lungs(Fig. 1.d). During this time, she bled vaginally, which frequently contained shed tumor cells, and received multiple blood transfusions. The tumor occupied the pelvic cavity and caused urethral obstruction. She was later given palliative treatments with an overall survival time of less than 6 months.

Discussion And Conclusion

Primary RMS of the uterus is exceedingly rare[1]. and the first case to arise in a postmenopausal woman was documented by Anderson and Ödmansson in 1869. As of now, there have been fewer than 80 reported cases in the English literature. The signs and symptoms of uterine RMS typically include abnormal uterine bleeding(AUB), pelvic pressure/pain, and/or a uterine mass, although some women are asymptomatic[4] .Some studies have reported bleeding accompanied by a foul smelling vaginal discharge as part of the clinical presentation of uterine RMS[5].Our patient was not admitted to the hospital until central nervous system symptoms appeared after venous sinus thrombosis developed. She had almost all of the typical symptoms mentioned above. Unfortunately, all these typical symptoms were ignored. This was partly because she was obese, sexually inexperienced and had irregular periods.

The most common symptom of uterine RMS is AUB which is a common condition, especially in adolescents. A variety of things can cause AUB. Malignant tumors of the uterus comprise a rare cause of AUB. Hence, the presence of AUB in adolescents should be carefully investigated for the possibility of malignant tumors of the uterus so as to avoid delays in diagnosis. In particular, patients with persistent

AUB should undergo imaging, pelvic examination and hysteroscopy with biopsy, if indicated. Pelvic ultrasonography is the first line imaging modality for AUB. When ultasonography suspected uterine sarcomas, the chest/abdomen/pelvis by CT or combination MRI/CT should be performed. Following appropriate imaging assessment, the standard approach to diagnosis consists of multiple core needle biopsies or hysteroscopy with biopsy. Confirmation of the type of mesenchymal malignancy by expert pathology review is critical. Our patient did not undergo the process of evaluation and diagnosis of uterine sarcoma mentioned above. During thrombolytic therapy, she developed complete uterine inversion, which was mistaken for a cervical tumor and removed. Finally, postoperative pathology confirmed embryonal RMS of uterus. RMS can be subcategorized histologically and FOXO1 fusion gene status. Histologically, uterine RMSs have been classified into one of the following four types: embryonal, alveolar, spindled and pleomorphic. Embryonal RMS represents the majority of cases and usually affects women of reproductive age. Disease classification of RMS subtypes has been further refined by the identification of fusion-positive RMS and fusion negative RMS. FOXO1(encoding forkhead box protein O1) fusion genes are associated with poor prognosis. In addition to histology and molecular analysis for FOXO1 rearrangement, there are two staging systems to stratify patients with RMS into risk-based therapy groups: the clinical group (CG) and the tumor, node, metastasis (TNM) system. The TNM and CG staging systems complement each other.

To date, uterine RMS is treated with a multidisciplinary approach including surgery, chemotherapy and radiotherapy to improve the cure rate and to prolong the survival time. There is no unified protocol regarding the treatment of uterine RMS associated with inversion, as non-puerperal uterine inversion is an uncommon complication of a malignant uterine mass. It is usually precipitated by tumours exerting traction force on the fundus of the uterus, turning the uterus partially or completely inside out. A review of the English literature revealed that only 6 cases of uterine inversion due to RMS have been reported from 1887 to date, including the present case. Interestingly, the 6 patients ranged in age from 15 to 22 years (mean 18.5 years). All 6 tumors were large, and the average tumor size was 8.8 cm. Regarding the surgical treatment in all cases, a hysterectomy was performed. More details are provided in Table 1. In the literature on uterine inversion, in cases of malignancy, the first surgical maneuver is to return the uterus to its normal anatomic position followed by abdominal hysterectomy.[6] However, this type of surgery described in the literature may not be appropriate for patients such as ours, as the inversed uterus completely prolapsed of the vagina, and thus it was too large to return to its normal anatomic position. Moreover, return the massive inverted uterus secondary to uterine RMS to its normal anatomic position through vagina, which is not a good idea. However, as the enlarged and inversed uterus was removed vaginally, greater difficulties were involved, than would have been encountered with transabdominal hysterectomy. Currently, the data regarding adjuvant therapy for uterine RMS are limited and are usually extrapolated from nonuterine sites. The Intergroup Rhabdomyosarcoma study group compared the various modes of therapy in RMS and concluded that chemotherapy comprising VAC is considered to be the gold-standard treatment option with or without radiotherapy for children and adolescents. While radiotherapy reduces the frequency of recurrence, its impact on 5-year survival has not been proven[7]. An analysis of 171 adult patients with RMS performed by Ferrari et al. revealed treatments similar to those

recommended in the pediatric literature produced similar outcomes in the adult population[8]. In adults, however, the same protocols showed much less response[8, 9]. The outcome of uterine RMS is very poor[10]. Our patient experienced rapid spread of neoplastic metastases to the lung and died within 6 months.

Table 1

Author,year	Age(yr)	Histology	presentation	Mass size(cm)	Treatment	Follow-up ststus(mo)
Case,2005	21	ARMS	Bleeding	10.2 × 8.2	NACT, TAH + BSO,CT	ANED(20)
Ojiwang,2006	16	ERMS	Bleeding	10.5 × 9.0	NACT,TAH, RT	
Sharma,2006	18	RMS	Bleeding vaginal mass	17 × 15	TAH + BSO,CT	Pelvic recurrence(12)
Da Silve,2008	15	ERMS	Bleeding vaginal mass	11 × 9.7	TAH,CT,RT	Vaginal recurrence(1.5) DOD(9)
Ambreen,2019	22	ERMS	Bleeding vaginal mass	10 × 8	TAH + BSO, CT,RT	Live metastasis(12) DOD(20)
Current Case	19	ERMS	Venous sinus thrombosis	18 × 16	VH + BSO,CT	Pelvic recurrence(2.4) DOD(6)

ARMS:alveolar RMS; ERMS:embryonal RMS; TAH, total abdominal hysterectomy; BSO: bilateral salpingo-oophorectomy; VH: vaginal hysterectomy; CT: chemotherapy; RT: radiotherapy; NACT: neoadjuvant chemotherapy; ANED indicates alive with no evidence of disease; DOD, dead of disease;.

Our case illustrates the typical presentation and aggressive behavior of uterine RMS. However, the typical symptoms of uterine RMS were ignored and the diagnosis was delayed. AUB in young women should be a sign to screen for uterine neoplasms. In addition, anatomy should be fully evaluated before proceeding toward surgical intervention to ensure the correct procedure is done.

Abbreviations

RMS:rhabdomyosarcoma; AUB:Abnormal uterine bleeding; FOXO1:encoding forkhead box protein O 1

Declarations

Ethics approval and consent to participate

No institutional review board approval was required.

Consent for publication

Informed consent for clinical use of clinical data was obtained from the parents of the patient.

Availability of supporting data and material

Please contact author for data requests.

Competing interests

There is no conflict of interest in this work.

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Authors' contributions

Hongfa Peng corrected clinical data and drafted the manuscript. Jingjing Jiang helped with editing the manuscript. All authors have read and approved the final manuscript.

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Figures

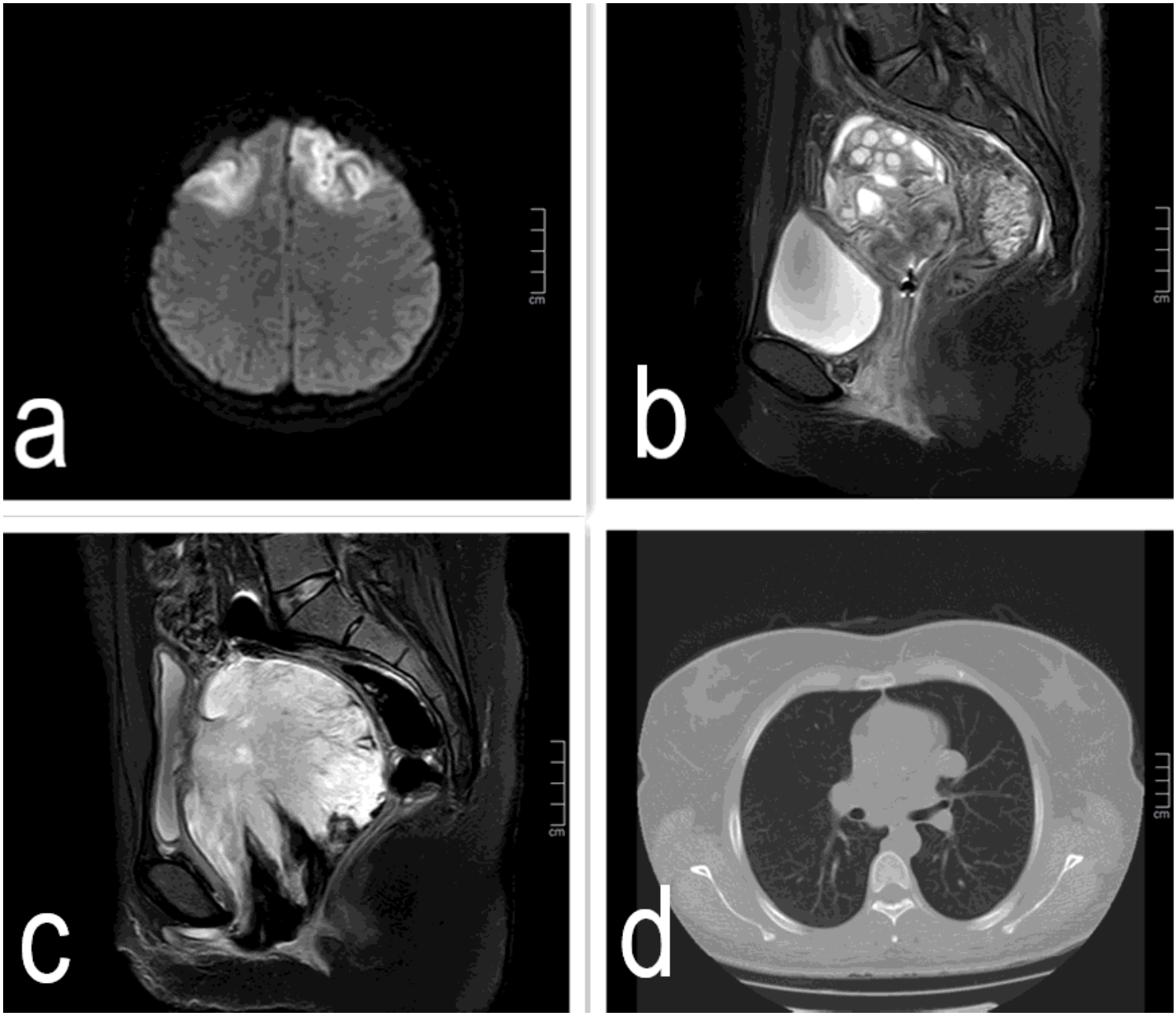

Figure 1

(a)The computerized tomography scan of the head demonstrated venous sinus thrombosis. (b,c)The Magnetic resonance of the pelvis demonstrated an enlarged nodular pelvic mass containing irregular intensities. (d)The computed tomography of the chest revealed multiple nodules in the lungs, which suggested pulmonary metastases.

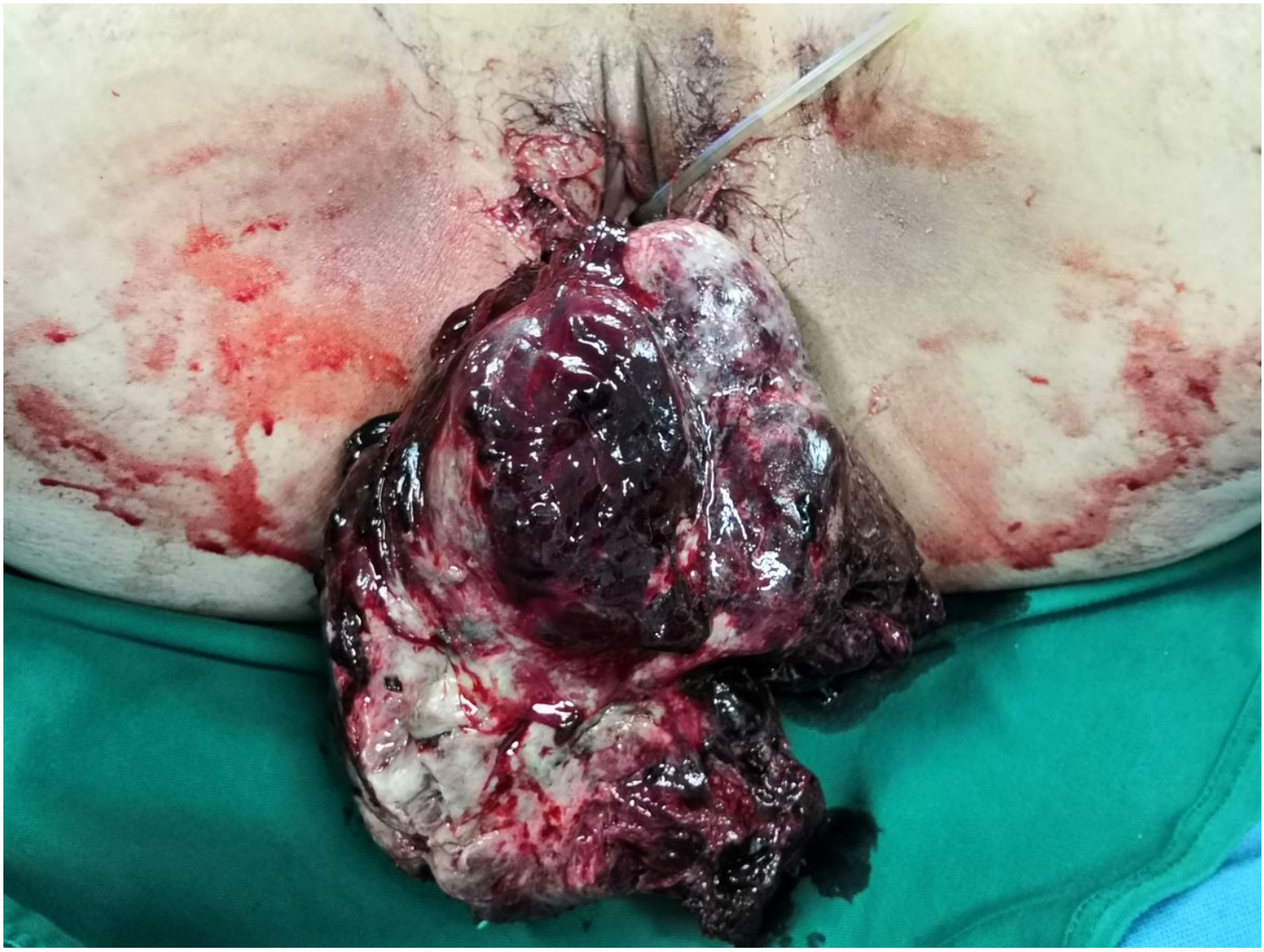

Figure 2

The complete uterine inversion secondary to uterine RMS.

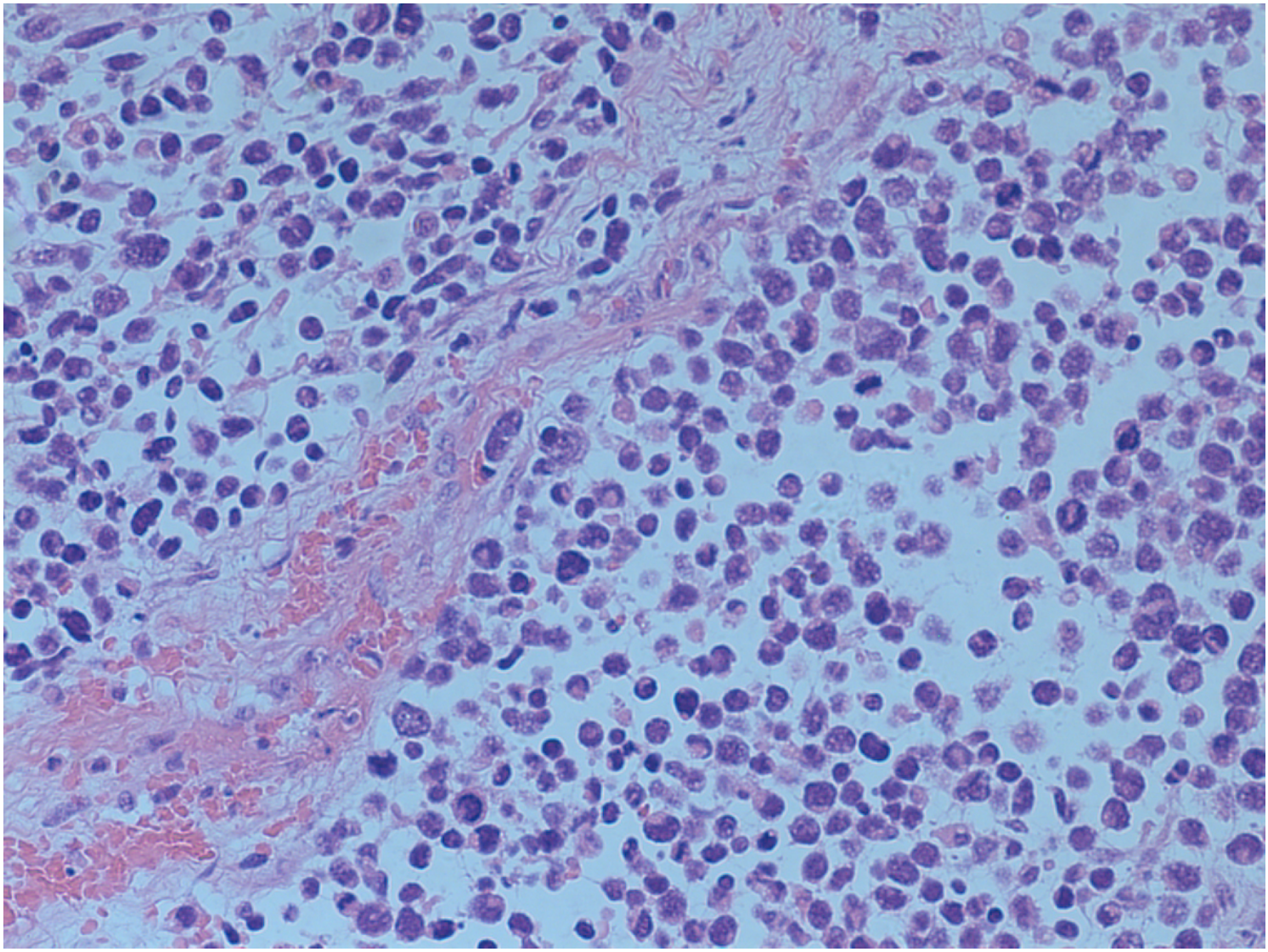

Figure 3

Histology demonstrated embryonal rhabdomyosarcoma: relatively uniform spindle cells with dark nuclei and inconspicuous nucleoli (HE stain, 20x).