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**Locally advanced cervical rhabdomyosarcoma in adults: A case report**

Xu LJ *et al.* Four-year follow-up of cervical rhabdomyosarcoma

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**Abstract**

BACKGROUND

Rhabdomyosarcoma is a soft tissue tumor of primitive mesenchymal cells origin, occurring predominantly in children and adolescents, but extremely rare in adults and the data regarding its treatment are sparse. Here, we would like to share our experience in the treatment of a locally advanced primary embryonal rhabdomyosarcoma of cervix in a 39-year-old female.

CASE SUMMARY

The patient was admitted with symptoms of intermenstrual bleeding and postcoital bleeding for six months. Physical examination revealed a friable, polyp-like mass (5 cm × 5 cm) in her cervix protruding into the vagina, while the uterus was mobile and normal-sized. Colposcopy-directed biopsy was performed, and a pathological diagnosis of embryonal rhabdomyosarcoma was made. Magnetic resonance imaging of the pelvis showed that the cervical volume was significantly increased, with a hypointense and hyperintense soft tissue mass on the right side, invading the cervical stroma; the mass was 5 cm × 5 cm with a clear boundary and confined to the cervix; there were no obvious findings indicating tumor invasion in the vaginal wall, parametrium, or pelvic wall; no enlarged lymph nodes were observed in the pelvic cavity. Based on our findings, the tumor was classified as stage IA according to the intergroup rhabdomyosarcoma studies criteria and IB3 stage according to The International Federation of Gynecology and Obstetrics 2018. The patient underwent two courses of neoadjuvant chemotherapy and a partial remission was achieved. Subsequently, she underwent laparoscopic radical hysterectomy, bilateral salpingo-oophrectomy and pelvic lymph node dissection and there were no risk factors revealed by postoperative pathological examination. Adjuvant chemotherapy was performed after surgery. The patient was disease-free until the last follow-up, 49 mo after completing the entire treatment.

CONCLUSION

Our experience suggests that neoadjuvant vincristine, dactinomycin, and cyclophosphamide chemotherapy followed by radical surgery and adjuvant chemotherapy might be reasonable therapeutic option for bulky cervical rhabdomyosarcoma in adults without fertility desire. Since large-scale studies on such rare conditions are rather impossible, further case reports and systematic reviews could help optimize the treatment of primary, bulky cervical rhabdomyosarcoma in adults.

**Key Words:** Rhabdomyosarcoma; Cervical rhabdomyosarcomas; Neoadjuvant chemotherapy; Adjuvant chemotherapy; Radical hysterectomy; Case report

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**Core Tip:** Because of the extreme rarity of adult primary cervical rhabdomyosarcomas, their treatment remains challenging. Accurate diagnosis is critical for a good prognosis since the treatment of cervical rhabdomyosarcoma differs from that of other cervical tumors, particularly in radicality of surgery and chemotherapy regimens. Our experience suggests that neoadjuvant vincristine, dactinomycin, and cyclophosphamide chemotherapy followed by radical surgery and adjuvant chemotherapy might be reasonable therapeutic option for bulky cervical rhabdomyosarcoma in adults without fertility desire. Since large-scale studies on such rare conditions are rather impossible, further case reports and systematic reviews could help optimize the treatment of primary, bulky cervical rhabdomyosarcoma in adults.

**INTRODUCTION**

Rhabdomyosarcoma is a soft tissue tumor of primitive mesenchymal cells origin, occurring predominantly in children and adolescents, but extremely rare in adults[1,2]. Approximately 30% of rhabdomyosarcomas originate in the genitourinary system, mostly in the vagina; less than 0.5% arise in the uterine cervix. Adult patients appear to have worse prognosis, that may be partially due to their rarity and the absence of standardized treatment protocols or guidelines[3,4]. We present a case of primary, locally advanced embryonal rhabdomyosarcoma of the cervix in a 39-year-old woman with a good prognosis, sharing our experience regarding treatment.

**CASE PRESENTATION**

***Chief complaints***

A 39-year-old woman was admitted with symptoms of intermenstrual bleeding and postcoital bleeding.

***History of present illness***

She had intermenstrual bleeding and postcoital bleeding for six months. No medical treatment was performed.

***History of past illness***

She reported a history of two normal vaginal deliveries (G2P2A0).

***Physical examination***

Physical examination revealed a friable, polyp-like mass (5 cm × 5 cm) in her cervix protruding into the vagina, while the uterus was mobile and normal-sized.

***Laboratory examinations***

Colposcopy-directed biopsy was performed, and a pathological diagnosis of embryonal rhabdomyosarcoma was made (Figure 1). The tumor cells of embryonal rhabdomyosarcoma have various shapes, which basically reproduce the cells of various stages of the embryonic development of skeletal muscle. But spindle cell rhabdomyosarcoma is mainly composed of spindle cells, with inconspicuous or few rhabdomyoblasts. In addition, the embryonic type is more common in the genital tract, whereas spindle cell subtype is more common in the extremities.

***Imaging examinations***

Magnetic resonance imaging (MRI) of the pelvis showed that the cervical volume was significantly increased, with a hypointense and hyperintense soft tissue mass on the right side, invading the cervical stroma; the mass was 5 cm × 5 cm with a clear boundary and confined to the cervix; there were no obvious findings indicating tumor invasion in the vaginal wall, parametrium or pelvic wall; no enlarged lymph nodes were observed in the pelvic cavity (Figure 2A). Chest radiography revealed clear lung fields. There was no abnormality in the liquid-based cytology test or high-risk human papillomavirus (HPV) test of exfoliated cervical cells. The results of blood chemistry (routine blood tests and renal and liver function tests) and serum tumor markers, including squamous cell carcinoma antigen, cancer antigen (CA) 125, CA199, and carcinoembryonic antigen, were within normal limits.

**FINAL DIAGNOSIS**

Based on these findings, the tumor was classified as stage IA according to the intergroup rhabdomyosarcoma studies (IRS) criteria and IB3 stage according to The International Federation of Gynecology and Obstetrics 2018.

**TREATMENT**

Radical surgery was planned as the treatment strategy. Considering a tumor size greater than 4 cm, the patient underwent neoadjuvant chemotherapy with two cycles of vincristine, dactinomycin, and cyclophosphamide (VAC) every 3 wk before surgery. After neoadjuvant chemotherapy, the tumor size was reduced to 3 cm × 3 cm, as revealed by magnetic resonance imaging (Figure 2B). Subsequently, she underwent laparoscopic radical hysterectomy, bilateral salpingo-oophrectomy and pelvic lymph node dissection. The intraoperative blood loss volume was approximately 100 mL. There were no injuries to the major vessels or nerves, ureter, bladder, or intestinal tract. No postoperative urinary retention or other complications were observed.

Postoperative pathological examination revealed a polyp-like cervical mass measuring 3.5 cm × 2 cm involving the posterior cervical lip and confirmed the histotype of embryonal rhabdomyosarcoma of the cervix with partial cartilage differentiation (Figure 3). The vaginal wall, parametrium, endometrium, ovaries, and fallopian tubes were tumor-free, with no invasion of the pelvic lymph nodes and lymphovascular space. The surgical margins were tumor-free. Immunohistochemistry showed that the tumor was positive for WT1 (100%), myogenin (100%), MyoD1 (focal positive), and desmin (focal positive) (Figure 4).

Following the surgery, adjuvant chemotherapy with VAC was administered for four cycles at an interval of 3 wk. The patient experienced grade I diarrhea and hematological toxicity but no grade III/IV chemotherapy-associated side effects.

**OUTCOME AND FOLLOW-UP**

The patient was then followed up regularly, every 3 mo in the first two years, every 6 mo in the third year, and once a year after the fourth year. At each visit, history taking and clinical examination were carried out to detect treatment complications, and recurrent disease. The follow-up exam included physical exam, vaginal vault cytology, chest X-ray, abdominal and pelvic computed tomography scan. The patient was disease-free until the last follow-up, 49 mo after completing the entire treatment.

**DISCUSSION**

According to the 2020 World Health Organization classification, rhabdomyosarcomas are subdivided into four histological types: embryonal, alveolar, pleomorphic, and spindle cell/sclerosing rhabdomyosarcoma[5]. Embryonic type is the most frequent histology, which accounts for slightly more than half of all rhabdomyosarcomas. In adults, embryonal rhabdomyosarcoma of the cervix is rare and characterized by unique pathological findings[3]. There is no standard treatment for patients with rhabdomyosarcoma of the cervix. Clinically, the primary treatment options are surgery with or without adjuvant chemotherapy and radiotherapy[6]. We present a 39-year-old woman with cervical rhabdomyosarcoma who underwent neoadjuvant chemotherapy, followed by surgery and adjuvant chemotherapy. The patient was disease-free until the last follow-up, 49 mo after completing the entire treatment.

Cervical rhabdomyosarcoma differs from cervical squamous cell carcinomas and adenocarcinomas in several aspects. The former is often located in the upper part of the cervix or vagina. It grows rapidly outward to fill the entire vagina or even protract from the vaginal opening, preferentially invading the bladder, rectum, or other pelvic organs, and occurs predominantly in children and young adults. Patients commonly complain of irregular vaginal bleeding or a mass prolapse from the vagina. In contrast, cervical squamous cell carcinomas and adenocarcinomas are predominantly located in the cervix and grow more slowly than cervical rhabdomyosarcoma with a tendency to invade the parametrium. They usually occur in adult women with a sexual history, and irregular vaginal bleeding or contact bleeding is the most common primary symptom[7,8].

The diagnosis of cervical rhabdomyosarcoma largely relies on biopsy and subsequent pathological examination with immunohistochemistry. Cervical masses often have varied appearances, such as polypoid or grape-like, and are frequently misdiagnosed as cervical polyps[9]. Immunohistochemical staining for muscle markers, such as desmin and myogenin, has been considered helpful for the diagnosis and differential diagnosis of cervical rhabdomyosarcoma[10,11]. MyoD1 and myogenin are the most commonly used positive markers with high specificity and sensitivity for rhabdomyosarcoma[12,13]. WT1 and desmin help confirm a diagnosis of cervical botryoid rhabdomyosarcoma, particularly when they are positive in a large proportion of cells[11]. As in our case, the tumor cells are positive for all four markers, while these markers are often negative in cervical squamous cell carcinoma, adenocarcinoma, or polyp. In addition, limited data indicate that cervical rhabdomyosarcoma is generally HPV-negative[12], while most cervical squamous cell carcinomas and adenocarcinomas are HPV-positive, suggesting that HPV status could serve as a marker for differential diagnosis, and HPV-based cervical cancer screening and vaccination are unlikely to prevent cervical rhabdomyosarcoma[14,15].

Most patients with primary cervical rhabdomyosarcoma were diagnosed at an early stage and did well with surgery and adjuvant chemotherapy, although the number of cases and duration of follow-up were limited[16,17]. Surgical procedures include polypectomy, loop electrosurgical excision, cervical conization, cervical excision, hysterectomy, or radical hysterectomy, which are generally less radical than those for cervical squamous cell carcinomas and adenocarcinomas because of the young age and fertility needs of the patients and less frequent involvement of the parametrium. However, a systematic pelvic lymphadenectomy appears to be critical for cervical rhabdomyosarcoma because 13.3% of patients with cervical rhabdomyosarcoma who underwent pelvic lymphadenectomy had a nodal disease[9]. As adjuvant therapy, considering the age of the patient and the long-term irreversible complications of radiation therapy caused by fibrosis of adjacent organs and tissues that can seriously impair the quality of life, chemotherapy seems to be more suitable because of improved quality of life and good responsiveness. Adjuvant chemotherapy is generally essential for the treatment of rhabdomyosarcoma[18], and the commonly used chemotherapy regimens include vincristine plus dactinomycin (VA), VAC, and VA with ifosfamide (IVA)[19,20,21], which are different from platinum-based chemotherapy for cervical cancer. Furthermore, the IRS clinical group recommends adjuvant radiation therapy[22] to treat tumors at advanced stages, such as those with nodal involvement, distant metastases, or recurrent diseases[23].

There are few reports on the treatment of bulky cervical rhabdomyosarcoma in adults. Baiocchi *et al*[24] presented a 47-year-old woman with a 10 cm rhabdomyosarcoma of the cervix in Group IA based on the IRS Group criteria. The patient underwent an upfront radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. The pathology demonstrated a “grape-like” or “cauliflower-like” tumor based on the endocervix with more than 50% depth infiltration and uterine isthmus extension. Fifty lymph nodes were analyzed, and no metastases were observed. As the patient had localized disease, which was confined to the site of origin and was completely excised, she received 12 courses of adjuvant VAC chemotherapy over one year. However, detailed follow-up information was not available. Yuan *et al*[25] reported nine cases of stage I embryonal rhabdomyosarcoma of the female genital tract, one of which was a 36-year-old woman with a 5.7 cm rhabdomyosarcoma lesion of the cervix. She was treated with neoadjuvant chemotherapy, surgery, and adjuvant chemotherapy and was free of disease during a 9 mo follow-up period. In our study, the patient was 39 years old, with a bulky, cervix-confined tumor and no fertility needs. We performed two courses of VAC neoadjuvant chemotherapy to reduce the tumor size, increase the operability, and optimize the surgical outcome, and a radical surgery including hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection was performed laparoscopically. Pathology revealed that the tumor had invaded the inner 1/3 of the cervical muscle wall, and no clear intravascular tumor plugs were found around the tumor. The resection margins were negative; 64 lymph nodes were analyzed, and no metastases were found. After surgery, the patient received adjuvant chemotherapy. The patient was disease-free 49 mo after treatment completion, which indicated a high probability of cure. Our case, with a long follow-up period, provides valuable data on the oncologic outcome of bulky cervical rhabdomyosarcoma in adults after adequate treatment.

**CONCLUSION**

Because of the extreme rarity of adult primary cervical rhabdomyosarcomas, their treatment remains challenging. Accurate diagnosis is critical for a good prognosis since the treatment of cervical rhabdomyosarcoma differs from that of other cervical tumors, particularly in radicality of surgery and chemotherapy regimens. Our experience suggests that neoadjuvant VAC chemotherapy followed by radical surgery and adjuvant chemotherapy might be reasonable therapeutic option for bulky cervical rhabdomyosarcoma in adults without fertility desire. Since large-scale studies on such rare conditions are rather impossible, further case reports and systematic reviews could help optimize the treatment of primary, bulky cervical rhabdomyosarcoma in adults.

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**Footnotes**

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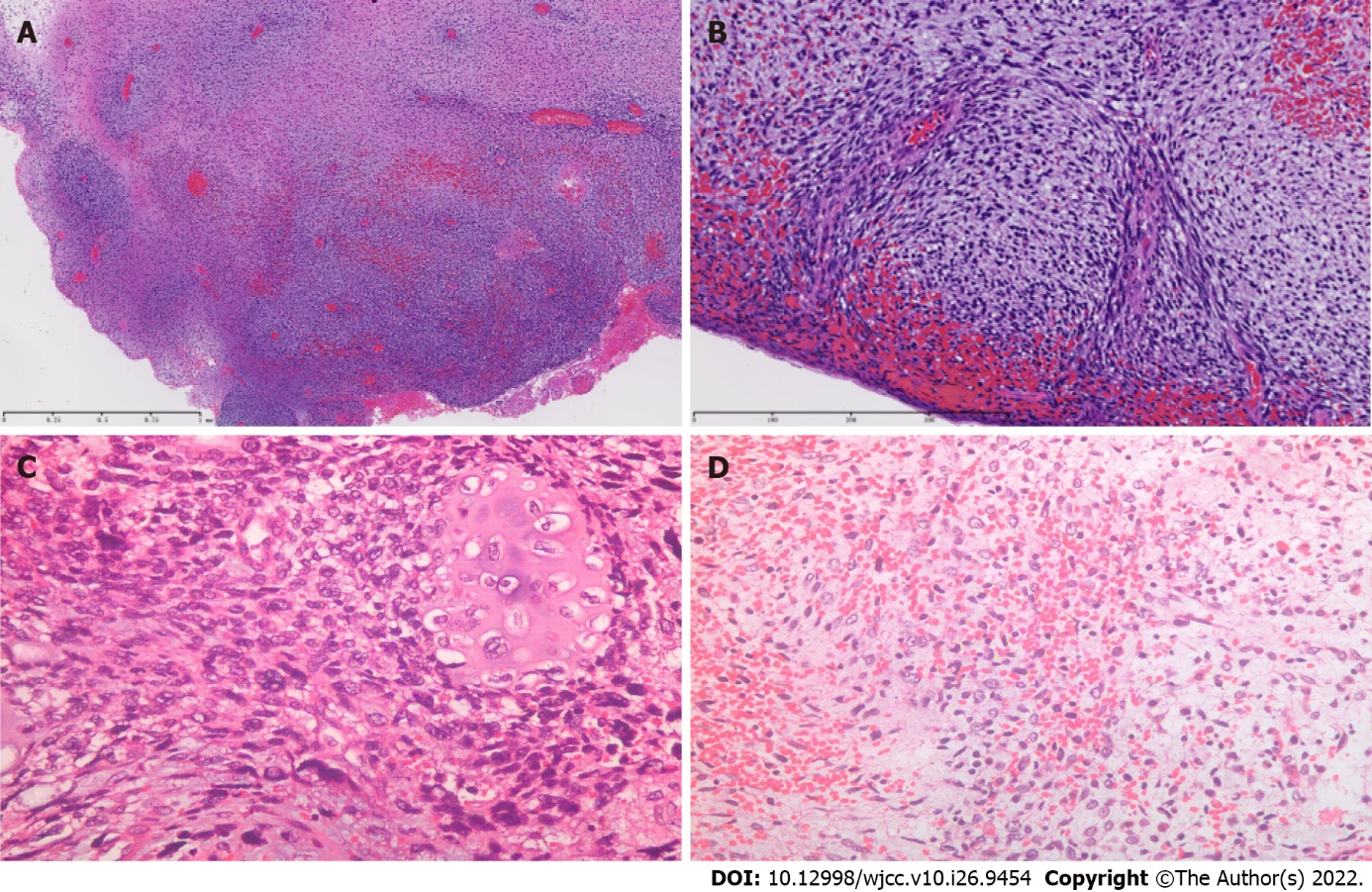
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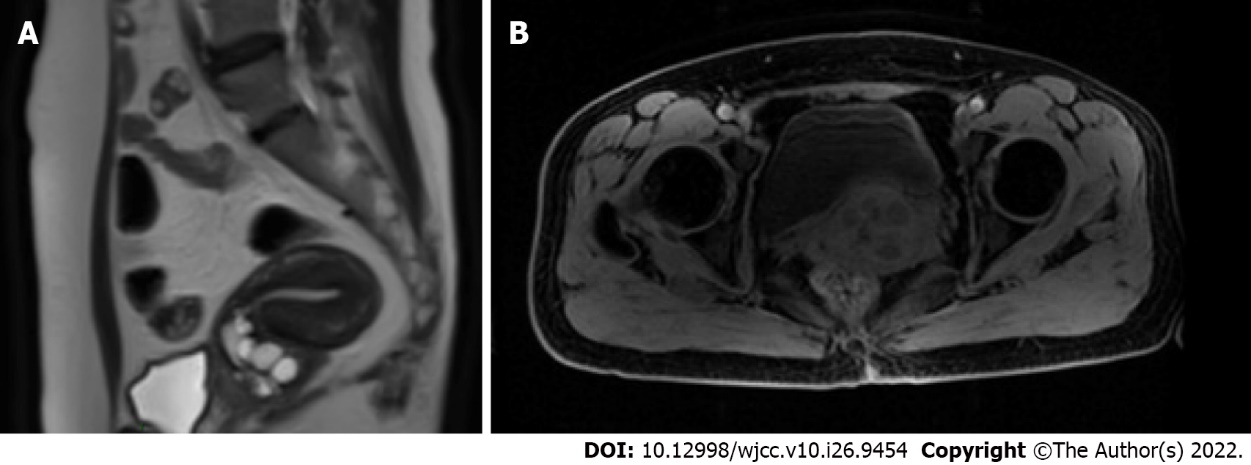
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**Figure Legends**



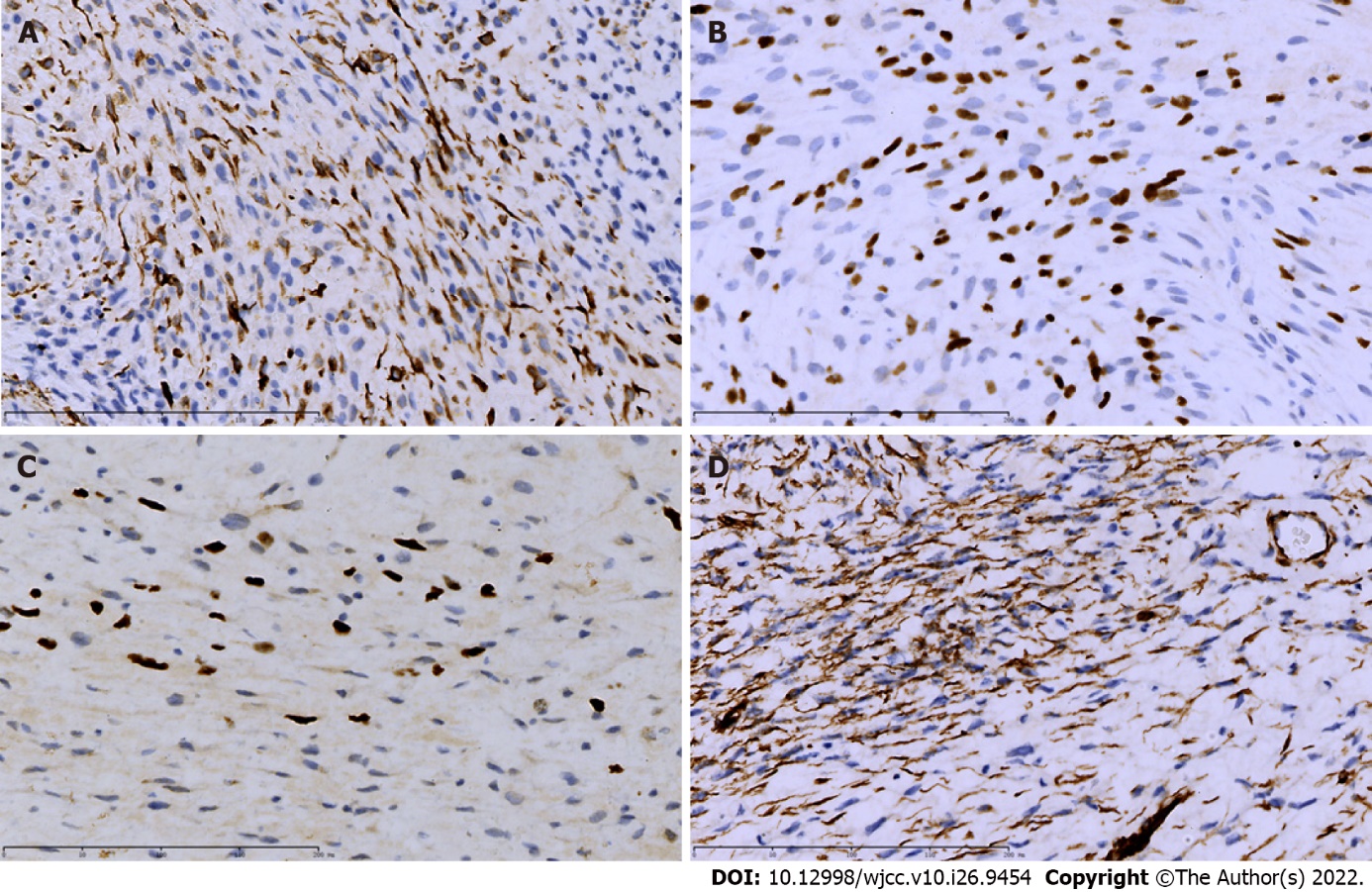
**Figure 1 Pathologic examination of cervical embryonal rhabdomyosarcoma.** A: Lower power view of the tumor cells; B: Higher power view of the tumor cells; C: Cartilage component (200 ×); D: Primitive stellate cells (200 ×).



**Figure 2 Magnetic resonance imaging of the pelvis before and after neoadjuvant chemotherapy.** A: The initial cervical mass size was about 5 cm; B: After neoadjuvant chemotherapy, the tumor size was reduced to 3 cm.



**Figure 3 Gross appearance of the resected cervical tumor. The neoplasm infiltrates the cervical walls and grows in a polypoid fashion in the posterior cervical lip.**



**Figure 4 Immunohistochemistry showed in the tumor cells cytoplasmic positivity for Desmin, MyoD1, Myogenin, and WT-1.** A: Desmin; B: MyoD1; C: Myogenin; D: WT1.



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