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Contents

Thrice Monthly Volume 11 Number 31 November 6, 2023

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Study

Clinical Trials Study

Observational Study

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 31 November 6, 2023

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 31 November 6, 2023

Contents

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CASE REPORT

Malignant peripheral nerve sheath tumor with hemophilic syndrome and bone marrow fibrosis: A rare case report

Hui Li, Li Wang, Ying-Hong Wu, Gang Chen, Hong-Xia Li, Li-Fen Fan, Min Gu, Cai-Hong Jiang

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Abstract

BACKGROUND

Malignant schwannoma is a rare tumor in the peripheral nervous system, accounting for approximately 5% to 10% of systemic soft tissue sarcomas. Especially, malignant schwannoma occurring in the broad ligament of the uterus with hemophilic syndrome and bone marrow fibrosis is extremely rare in clinical practice. Here, we report the first case of an patient diagnosed with malignant peripheral nerve sheath tumor (MPNST) of the broad ligament of the uterus with hemophilic syndrome and bone marrow fibrosis, and share our reference clinical diagnosis and treatment experience.

CASE SUMMARY

A patient was diagnosed with MPNST of the uterus harboring hemophilic syndrome and bone marrow fibrosis. She received combination, and repeated imaging revealed further encountered rare complications (hemophilia syndrome and bone marrow fibrosis) after two cycles of chemotherapy. Thereafter, combined treatment with pazopanib, gemcitabine, and dacarbazine was initiated. Unfortunately, the patient succumbed to death at hospital after two weeks.

CONCLUSION

This report firstly provided reference clinical practice for a patient with MPNST of the uterus harboring hemophilic syndrome and bone marrow fibrosis. Our case raises a reminder about the tolerance and safety of combination therapy, especially in young women.

Key Words: Malignant peripheral nerve sheath tumor; Hemophilic syndrome; Bone marrow fibrosis; Case report

Core Tip: We reported an extremely rare case of malignant neurilemmoma of the broad ligament of the uterus. The patient was easily misdiagnosed at the beginning of diagnosis, and in the subsequent treatment process, the patient combined with rare hemophilic syndrome and bone marrow fibrosis, resulting in a very poor prognosis.

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INTRODUCTION

As a schwann cell derived schwannoma, peripheral schwannoma is often derived from neurofibroma or neurofibroma malignancy[1]. However, schwannoma malignancy is rare and makes it difficult to distinguish its primary or malignant origin in clinical practice[2-4]. In addition, nerve sheath tumors originating from Schwann cells in the neuroectoderm or the neurointima of the mesoderm are more common in the limbs, head and neck, and retroperitoneum[5-8].

Peripheral malignant schwannoma located in the pelvic abdomen is extremely rare in clinical practice and difficult to differentiate from other retroperitoneal cystic solid tumors, such as liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma[9,10]. In addition, malignant nerve sheath tumors located in the pelvic cavity need to be differentiated from tumors of male or female reproductive cells and pelvic wall lymph node metastasis[11,12]. Up to now, due to the extremely low incidence rate of pelvic malignant neurilemmoma reported in recent decades at home and abroad, and the lack of specificity of the disease and clinical treatment guidelines that can be referred to, it is difficult to avoid misdiagnosis, and the prognosis of patients is extremely unsatisfactory[12-15].

In view of this, we reported an extremely rare case of malignant neurilemmoma of the broad ligament of the uterus. The patient was easily misdiagnosed at the beginning of diagnosis, and in the subsequent treatment process, the patient combined with rare hemophilic syndrome and bone marrow fibrosis, resulting in a very poor prognosis. We propose the following situations based on the CARE report checklist.

CASE PRESENTATION

Chief complaints

A twenty-six year-old unmarried woman was admitted to our hospital due to intermittent pain and discomfort in the lower abdomen. Prior to this, she had undergone laparoscopic exploration combined with retroperitoneal mass resection at other hospitals.

History of present illness

The postoperative pathological report showed spindle cell sarcoma of the right broad ligament. In order to receive further treatment, we conducted pathological consultations on the patient's tumor lesion. The final consultation opinion showed that the right broad ligament and retroperitoneal malignant tumor were considered as malignant peripheral nerve sheath tumors (Figure 1). At the same time, we also conducted imaging examinations for the patient. Among them, abdominal computed tomography (CT) showed multiple lumpy low-density shadows in the pelvic cavity near the sacral anterior and bilateral iliac vessels, with unclear boundaries and a maximum volume of about 4.3 cm × 3.6 cm × 5.1 cm. Moreover, the lower end of the right ureter was affected, resulting in dilation and hydronephrosis of the ureter and pelvis. Based on the patient's medical history, tumor metastasis was considered. Chest CT showed multiple lesions in both lung lobes, combined with medical history so that we cannot rule out the possibility of tumor metastasis. The results of pelvic magnetic resonance (MRI) examination indicated that after surgery for malignant pelvic neurilemmoma, multiple lesions near the sacral anterior and bilateral iliac vessels are present in the pelvic cavity, and tumor metastasis is considered based on her medical history (Figure 2).

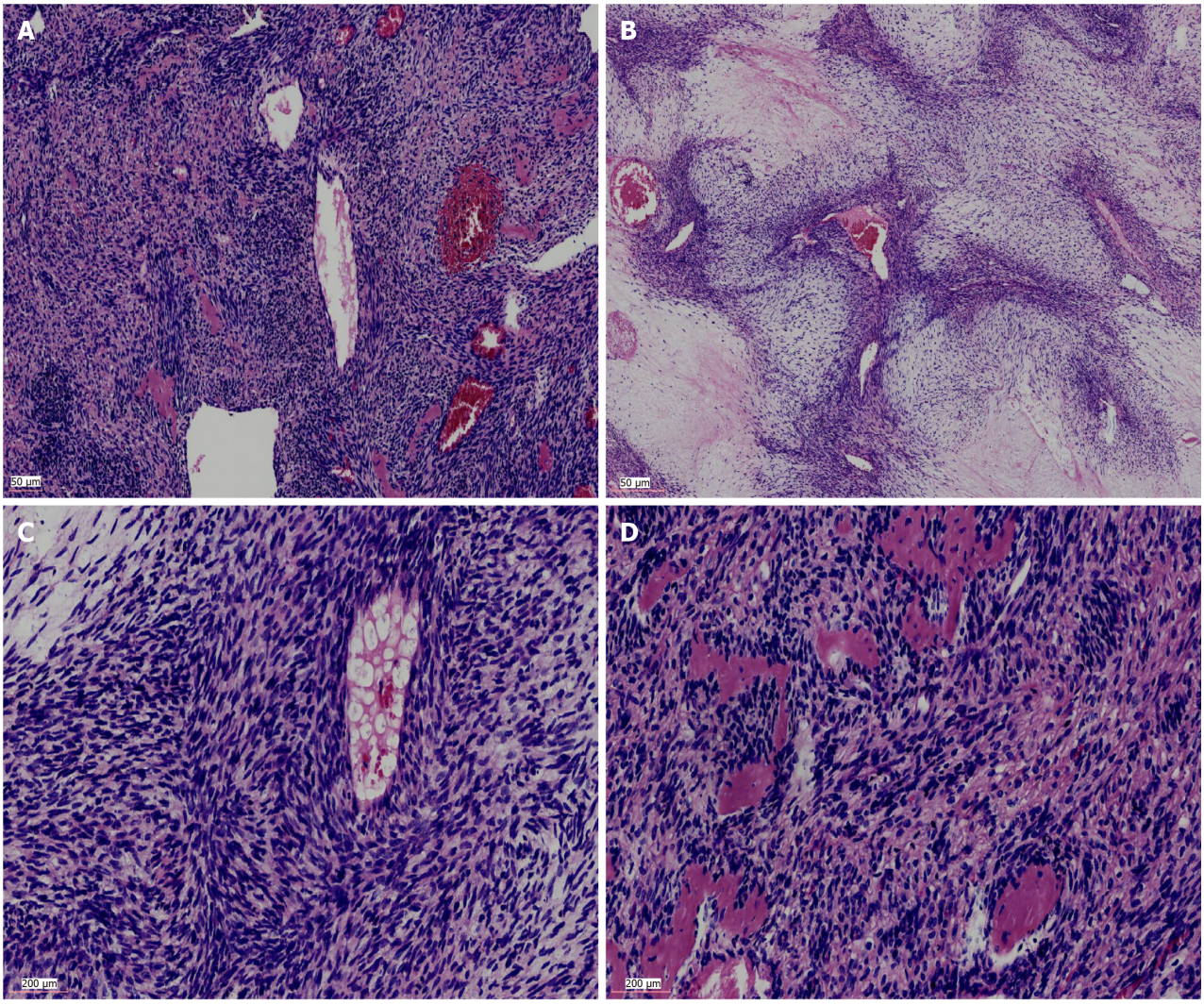

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Figure 1 Pathological results of hematoxylin eosin staining. A and B: The tumor lesion is composed of spindle cells arranged in a woven pattern and showing infiltrative growth; C and D: Local cells exhibit epithelial like interstitial mucus changes.

History of past illness

In view of this, we have implemented individualized treatment for the patient's condition, with the specific plan as follows: Doxorubicin liposomes+ifosfamide+arotinib, with a cycle of twenty-one days, and chemotherapy for two cycles. Before the patient received chemotherapy, the blood test results showed no significant abnormalities and no contraindications for chemotherapy. Due to severe bone marrow suppression (grade IV) after chemotherapy, the patient insisted on discontinuing the medication for over a month. Therefore, we consulted with external hospitals to modify the patient's chemotherapy regimen, which is a combination therapy of pazopanib, gemcitabine, and dacarbazine, with a treatment period of three weeks. The patient experienced decreasing in platelet counts (grade III) in both the first two cycles of receiving the above protocol. After receiving targeted treatment, the patient's platelet indicators tended to improve, and chest and abdominal CT showed that the patient's condition was in a stable stage. However, during the interval after the third cycle, the patient suddenly experienced a decrease in platelet count (37×10^9/L), accompanied by severe cough and fever (Figure 3). In order to further evaluate whether the patient's condition has progressed or worsened, we conducted another chest CT examination of the patient, and the results showed that lung infection was not excluded, as was cancerous lymphangitis. So, we gave the patient antibiotic treatment for three days, and the condition continued to worsen, accompanied by severe chills and high fever.

Personal and family history

For this reason, we have increased the types of antibiotics used, including meropenem, moxifloxacin, vancomycin, caspofungin, cefoperazone sodium, sulbactam sodium, oseltamivir, and minocycline, but the patient's fever symptoms have not improved. So, blood culture continued, and the results showed that no microorganisms with suspected backgrounds such as fungi, bacteria, DNA/RNA viruses, parasites, mycoplasma tuberculosis complex, chlamydia, rickettsia, *etc.* were found. In addition, abdominal ultrasound indicates normal spleen size. For this reason, we performed platelet perfusion therapy on the patient, followed by two courses of platelet infusion. The results of bone marrow

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Figure 2 Presentation of imaging magnetic resonance imaging. A: T1WI displays low intensity mixed signals with unclear boundaries; B: T2WI shows slightly high signal intensity in the liposuction sequence, with focal high signal intensity visible internally.

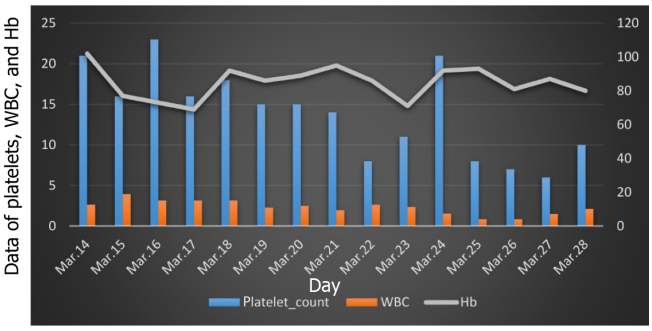

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Figure 3 Dynamic changes in blood count during chemotherapy for patients. WBC: White blood cell count; Hb: Hemoglobin.

puncture showed hypoplastic bone marrow. In addition, the patient's antinuclear antibodies and antiplatelet surface related antibodies were all negative.

Physical examination

Continuing to review the patient's abdominal ultrasound report, it is indicated that the spleen is approximately 200 mm (length) and 63 mm (thickness), with an increase in spleen volume. Another bone marrow biopsy was performed, along with natural killer (NK) cell and CD25 testing.

Laboratory examinations

At this time, clinical suspicion was highly suspected of hemophilia syndrome. The bone marrow biopsy report for the patient again indicates that NK cell activity is reduced; SIL-2R/sCD25 soluble interleukin-2 receptor > 75000 U/mL, bone marrow biopsy showed that bone marrow fibrosis with bone marrow necrosis, tumor necrosis cannot be ruled out.

Imaging examinations

In addition, we found in the results of bone marrow puncture reports that bone marrow hyperplasia is active, the proportion of granulocytes is reduced, and toxic changes are visible in neutrophils, which meets the diagnostic criteria for hemophilia syndrome. In view of this, we gave the patient dexamethasone intravenous therapy, but the patient's condition did not improve and continued to worsen. She was declared dead at 5 am on March 28, 2022 (Figure 4).

FINAL DIAGNOSIS

Malignant peripheral nerve sheath tumor of the broad ligament of the uterus.

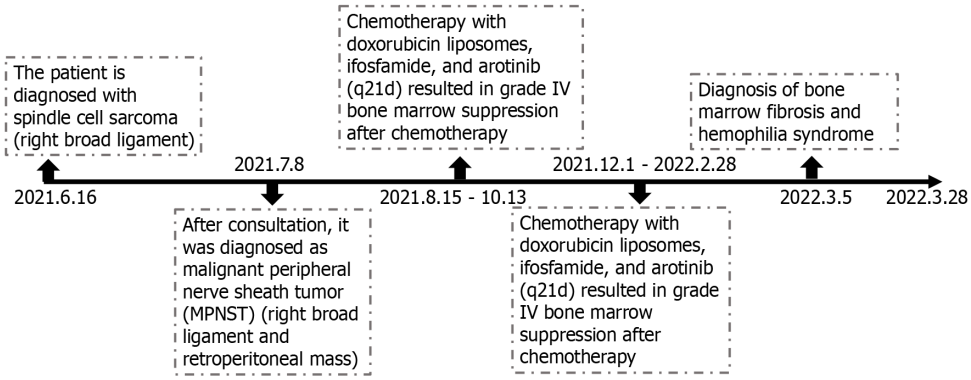

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Figure 4 Timeline from diagnosis of malignant peripheral nerve sheath tumor and treatment to death. This figure shows the progression schedule of patients who only use combination chemotherapy and change chemotherapy drugs. After the combination therapy, the patient died due to complications such as hemophilia syndrome and bone marrow fibrosis.

TREATMENT

Combined treatment with pazopanib, gemcitabine, and dacarbazine was initiated.

OUTCOME AND FOLLOW-UP

Unfortunately, the patient succumbed to death at hospital after two weeks.

DISCUSSION

Throughout previous studies, it has been shown that retroperitoneal schwannomas account for only 0.7% of retroperitoneal tumors, while pelvic retroperitoneal schwannomas are even rarer[16-18]. Because the most common cystic lesions in the female pelvic cavity are still cysts or tumors originating from the ovaries, including cystadenoma, cystadenocarcinoma, teratoma, *etc*., The malignant peripheral nerve sheath tumor (MPNST) are extremely prone to misdiagnosis as gynecological diseases[19,20]. Therefore, for gynecological examinations of adnexal masses closely adjacent to the pelvic wall, attention should be paid to distinguishing them from retroperitoneal tumors. In view of this, our inspiration is that for retroperitoneal tumors, CT and MRI are easy to detect, but when the tumor is large, it is difficult to determine the source of the tumor[11,21]. In addition, combined with conventional MRI scans, poor ovarian structure is the main reason for misdiagnosis. The qualitative analysis of pelvic masses depends on determining the source of the mass, and enhanced MRI scanning can improve the diagnostic rate. Fortunately, laparoscopic examination can further clarify the source of the tumor. In this case, after laparoscopic examination, the tumor was identified under laparoscopy and then converted to open surgery to remove the tumor[22]. Therefore, for female pelvic masses, the possibility of gynecological diseases should not be solely considered, especially those that are close to the pelvic wall. It is also important to be vigilant for retroperitoneal tumors. After enhanced scanning, the tumor significantly strengthens, which is different from ovarian tumors invading the pelvic wall, we should think of the possibility of schwannoma. If necessary, further diagnosis can be made under laparoscopy before surgical resection.

Previous studies have shown that chemotherapy is ineffective in improving the prognosis of MPNST, and some scholars have used chemotherapy drugs such as doxorubicin combined with cyclophosphamide to have good effects on individual cases[23-25]. In addition, there is controversy over the efficacy of radiotherapy for MPNST. Some scholars believe that radiotherapy has no significant effect on improving prognosis, while others believe that postoperative radiotherapy, brachytherapy, and intraoperative radioactive particle implantation have significant effects on controlling local recurrence and improving prognosis[25-27]. Considering the low resection rate of MPNST surgery and the uncertain effectiveness of adjuvant treatments such as radiotherapy and chemotherapy. In our case, we used a combination therapy of pazopanib, gemcitabine, and dacarbazine for three weeks to control the tumor in a stable phase without progression. However, the increased complications caused by postoperative adjuvant therapy cannot be ignored, especially in the case of hemophilia syndrome and bone marrow fibrosis, which is particularly challenging in MPNST treatment. Although the specific mechanism is not yet clear, we infer three possible explanations for the patient's death. First, the hemophilic syndrome may be related to the dysfunction of T and NK cell regulation, leading to excessive activation of macrophages and lymphocytes, leading to a significant increase in cytokines in the blood and the occurrence of systemic inflammatory response syndrome. The results of the patient's two bone marrow punctures indicate a lack of specificity in the early stages of the disease. Therefore, in the event of fever, rash, decreased blood cells in the second or third line, liver injury, or neurological manifestations that render anti-infection treatment ineffective, hemophilic syndrome should not be ruled

out, and multiple bone marrow punctures should be performed to assist in the diagnosis. Looking back at the patient's medical history, except for high sensitivity constitution, hypertension, and myocardial ischemia, there is no other previous medical history. During the hospitalization diagnosis and treatment process, the possibility of viral, bacterial infection, autoimmune, or malignant tumor diseases has been ruled out. However, the patient complained of cough on the first visit, and the history of upper respiratory tract infection cannot be ruled out. High sensitivity constitution can highly suspect certain defects of the patient's immune regulatory function, but the cause cannot be determined and there is no evidence of primary disease, This makes treatment difficult and only symptomatic, but it is important to be vigilant that if the cause cannot be removed, the condition is prone to recurrence and the prognosis is extremely poor. Second, the secondary bone marrow fibrosis refers to the proliferation of bone marrow fibrous tissue and abnormal hematopoietic function on the basis of a clear primary disease, which can be seen in various malignant diseases in clinical practice, such as chronic myeloproliferative diseases, acute and chronic leukemia, multiple myeloma, and metastatic cancer. We can speculate that the patient already has metastatic tumor lesions, which is extremely prone to secondary bone marrow fibrosis during subsequent treatment. Given this, the treatment options for MPNST patients with combined hemophilic syndrome and bone marrow fibrosis are limited, and the survival is very poor.

CONCLUSION

To our knowledge, this is the first report of a MPNST of the broad ligament of the uterus with hemophilic syndrome and bone marrow fibrosis. The patient experienced progression during combined treatment. The combination of pazopanib, gemcitabine, and dacarbazine could provide a potential treatment for these patients. However, the tolerance and safety of combination therapy deserved our attention.

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FOOTNOTES

Co-first authors: Hui Li and Li Wang.

Author contributions: Jiang CH made substantial contributions to conception and design. Li H, Wang L, Wu YH and Chen G took part in drafting the article or revising it critically for important intellectual content; Li HX, Fan LF, and Gu M were responsible for organizing, collecting, and verifying clinical case data for this article; All authors agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work; Li H is the supervising physician of the patient in this article, and Wang L is the pathological diagnostic physician of the patient; during the hospitalization and follow-up period of the patient, the two of them jointly traced the changes in the patient's condition and diagnosis and treatment; They jointly collected, organized, and wrote the preliminary data of the case report, so they are considered as the co-first authors.

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