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Case Report

Postmenopausal recurrent retrovaginal extramural gastrointestinal stromal tumor: a case report

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Summary

Mesenchymal tumors are divided into gastrointestinal stromal tumors (GIST) and extra-intestinal tumors (EGIST). They can occur in various parts of the abdominal cavity, including the greater omentum, rectovaginal septum, peritoneum, retroperitoneum and extremely rarely, in the vagina. Vaginal cancer is an uncommon gynecological tumor and recurrent posterior vaginal gastrointestinal stromal tumors are even rarer. Currently, surgical resection is the main treatment method for this disease. With the deepening molecular understanding of gastrointestinal stromal tumors, in particular the role of c-KIT mutations, targeted therapy with Imatinib has been used in the adjuvant setting, achieving good results. We report a recent case of postmenopausal recurrent retrovaginal gastrointestinal stromal tumor, treated at Linquan County Hospital.

Key words: Vagina; Gastrointestinal stromal tumor; Menopause; Imatinib.

Introduction

In the spectrum of gynecological and obstetric cancer, vaginal tumors account for about 1% of cases, with the vast majority of other tumors being leiomyomas. Mesenchymal gynecological tumors are extremely rare, and some scholars believe that such tumors originate from rectovaginal septum [1]. In contrast, mesenchymal tumors occur more frequently in the gastrointestinal tract, with gastrointestinal stromal tumors (GIST) being the most common. These tumors can arise outside the digestive tract, presenting with a similar tissue morphology and immunophenotype, but originating from the soft tissue of abdominal cavity or retroperitoneal cavity, with no involvement of the intestinal wall or visceral serosal surface [2]. Such tumors are collectively called "extra-gastrointestinal stromal tumors (EGIST)", and account for 5-7% of incidence. They can occur in various parts of the abdominal cavity including the greater omentum, rectovaginal septum, peritoneum, retroperitoneum and vagina [3-4]. The early stage of vaginal wall GIST has no obvious symptoms, and most patients do not seek medical treatment until the tumor volume increases and compression symptoms appear, therefore the early detection rate is low. We report case of recurrent posterior vaginal GIST, recently admitted and treated in the Linquan County Hospital, together with a relevant literature review.

Case Report

A 62 year old female patient, 3-0-0-3, 12 years postmenopause, was admitted for vaginal mass resection at Linquan County Hospital in 2014.The vaginal masses were found to have been admitted to the hospital for 4+ months. Post-operative pathological consultation in the first affiliated hospital of Anhui Medical University diagnosed a vaginal wall spindle cell tumor with mild atypia, consistent with GIST, and follow-up was recommended. The patients were not followed up or treated with proper medication. From October 2017, the patient showed symptoms of difficulty self-relieving, with urinary retention and constipation. Gynecological examination in Linquan County Hospital identified masses on the vaginal wall (details unknown). Ultrasonography showed that the size of the lower uterine segment was approximately 6.5 × 5.9 cm, with hypoechoic mass. Later, the patient was admitted to the first affiliated hospital of Bengbu Medical College. Gynecological examination showed that the diameter of the middle and lower vaginal mass had grown to 7-8 cm and, combined with the medical history, the recurrence of vaginal EGIST was considered. The patient was prescribed oral administration of Imatinib benzene sulfonate 400 mg QD and, within two weeks of commencing treatment, the above compression symptoms improved significantly. Ultrasound re-examination in Linquan County Hospital showed a solid mass of 4.4 × 4.5 cm on the left side of the pelvic cavity in December 2017, suggesting that oral Imatinib treatment was effective, and the patient continued with the 400 mg QD treatment until February 5, 2018. On February 12, 2018, she was re-admitted to hospital. Gynecological examination showed that vulva had delivered, the vagina was unobstructed, and a soft lesion with a diameter of about 4 cm, protruding into rectum, could be palpated. The cervix displayed slight atrophy and the uterine body was atrophied, but with no tenderness. Attached area: showed no obvious abnormal mass touching the double attachment, and no tenderness was found. Anal examination showed that rectal

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mucosa was smooth, and finger cuff stained with blood (-). Surgery was suggested, after admission to reaffirm stable vital signs, and heart and lung auscultation did not show any obvious abnormity. The abdomen was flat, there were neither gastrointestinal nor peristaltic waves, no rebound tenderness, with no abdominal pain or distention, no pyrexia and no anal prolapse. There was no family history of malignancy, no progressive emaciation, and diet and sleep patterns were normal. Please general surgery after admission consultation, it is suggested that improving the MRI, the MRI: uterine volume shrinking, see a vagina size is about $3.8 \times 3.2 \times 4.2$ cm is irregular wait slightly long T1 T2 signal, DWI for high signal can, border signal is uniform, with its backward oppression rectum and bladder filling, no obvious swelling in the pelvic lymph nodes and effusion signal, MRI diagnosis: a vagina suggested: the necessity of reinforcement. Inform the patient and her family of the possibility of consultation on the general surgical table during the operation, and improve the preoperative intestinal preparation. Surgical treatment included intraoperative exploration and a mass with some mobility, measuring $4 \times 4 \times 3$ cm in size, was identified on the posterior wall of the vagina. Longitudinal incision was performed along the surface of the mass, and the tumor was completely resected and sent for pathological assessment.The pathological report diagnosed a mesenchymal spindle cell tumor, with an immunohistology profile showing: CD117 (+), DOG-1 (+), CD34 (+), SMA (+), DES (-), GFAP (-), s-100 (-), CK (-), ki-67 (3% positivity). Combined with immunohistochemical results and medical history, this was entirely consistent with GIST. The patient was discharged, having been prescribed Imatinib mesylate therapy, along with regular follow-up.

Discussion

EGIST is a unique type of tumor, very similar to GIST in histological morphology, but with a different origin. There are two opinions about the origin of EGIST; that it either originates from gastrointestinal Cajal cells, or from a more primitive mesenchymal stem cell, which can differentiate into various mesenchymal tissues [5]. Both GIST and EGIST are difficult to distinguish from leiomyoma and neurogenic tumor by conventional HE morphology, especially spindle cell type stromal tumor. Currently, most clinicians rely on immunohistochemical diagnosis, with CD117 (+) or CD34 (+) as the diagnostic requirement, with CD117 being more sensitive and specific than CD34. CD34 is expressed on bone marrow hematopoietic precursor cells, endothelial cells and myofibroblasts. CD117, also known as c-KIT, is a receptor tyrosine kinase expressed on bone marrow hematopoietic stem cells. As a biomarker for GIST, it has the advantage of being expressed by 95% of stromal tumors, is highly specific, is not affected by histological image, and is not affected by location or stage. These factors result in a better specificity for stromal tumor diagnosis than CD34. CD117 positive tumors may respond well to Imatinib mesylate [1]. The immunohistochemical results in this case showed positivity for both CD117 and CD34, and the accessory markers also confirmed the diagnostic criteria of GIST.

At present, most clinicians believe that stromal tumors cannot be simply classified as benign or malignant. According to the consensus of Chinese experts on the diagnosis and treatment of GISTs (2011 edition): Tumor volume, mitotic number and anatomical site are important indices for the prognosis of benign and malignant tumors. Extremely low risk is generally classified as a tumor diameter of < 2 cm and mitotic phase $<$ 5/50HPF. A tumor diameter of 2-5 cm, and mitotic phase $<$ 5/50 HPF is low risk. Moderate risk corresponds to a tumor with a diameter < 5 cm, mitotic phase $<$ 5/50HPF or mitotic phase $<$ 5/50HPF, and a tumor diameter of 5-10 cm. High risk classification is when the tumor diameter is > 5 cm and the mitotic phase is $>$ 5/50 HPF, or the tumor diameter is > 10 cm with any rate of mitosis, or the tumor is of any size but the mitotic phase is > 10 /50 HPF [6].

Vaginal wall gastrointestinal stromal tumors are rare, and recurrent vaginal wall GISTs are even rarer. The present patient was classified with a moderate-risk tumor based on tumor size and mitotic phase of 3%.

Vaginal wall stromal tumors are clinically characterized by local compression symptoms, such as frequent urination, constipation, or simply the presence of a local mass. Currently, surgical resection is the main treatment modality. Surgery should be decided on the size and location of the tumor. With potential malignancy in mind, the scope of surgery should be slightly expanded and a margin of normal tissue should be removed. EGIST lymph node metastasis is extremely rare, so lymph node dissection is not recommended. Postoperative adjuvant therapy should be given and close follow-up conducted [7]. EGIST can also be treated by radiotherapy, but it is easy to cause a variety of complications, such as radioactive cystitis and proctitis, rectal or bladder vaginal fistula or vaginal radionecrosis. Therefore, caution should be taken with radiotherapy and chemotherapy for this type of tumor [8].

Imatinib mesylate, an ATP-competitive tyrosine kinase inhibitor targeting both BCR-ABL and CD117, is an exciting prospect for EGIST targeted therapy, inhibiting cell proliferation and inducing apoptosis. CD117 positive tumors are highly responsive to imatinib, and EGIST is characteristically CD117 positive. There have been cases where Imatinib mesylate has been used successfully in the treatment of GISTs, arousing wide attention [7]. Adjuvant chemotherapy is recommended for adult patients following complete resection of stromal tumors, and large clinical studies have demonstrated the safety and effectiveness of Imatinib in the adjuvant setting. Unfortunately, some patients develop drug resistance, or cannot tolerate the side effects of the drug, such as edema, diarrhea and musculoskeletal pain, and metastatic advanced patients rarely achieve complete relief. However, the standard median survival time of patients with recurrent metastatic stromal tumors, which was

only 15 months prior to Imatinib therapy, has progressed to five years since the introduction of this targeted therapy [9]. It has also been shown that neoadjuvant therapy in CD117+ GIST can significantly reduce the tumor size improve surgical outcome [10]. For EGIST, the neoadjuvant Imatinib is also very effective, significantly reducing tumor volume and laying a foundation for successful GIST laparoscopic surgery [11]. In this case, the patient was admitted to the first affiliated hospital after presenting symptoms of compression. After treatment with Imatinib, the symptoms of compression were significantly improved after two weeks, and the tumor volume was reduced by nearly half after three months of taking the drug. However, because of its high cost, the patient stopped taking the drug, so we cannot exclude the possibility that the drug could have led to a complete cure. For patients with a standard income, the drug presents an extremely heavy economic burden, which leads to its failure as it cannot be widely used in clinical practice in China. In comparison, the cost of surgery is far lower than Imatinib therapy. Therefore, in pragmatic terms, surgery remains the first choice for the treatment of this disease, but short-term postoperative Imatinib therapy is necessary to optimize operative success and prevent tumor recurrence.

In conclusion, clinical cases of posterior vaginal wall GIST are rare, and there is no clear diagnosis and treatment standard for this disease at present, demanding long-term follow-up studies of more patients. Currently, surgical treatment is the preferred method, but short-term Imatinib neo-adjuvant and adjuvant targeted therapy is recommended.

Author contributions

Guolin Liu is responsible for writing the article. Zhang is responsible for the imaging examination and the review of articles.

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Conflict of interest

There is no Conflict of Interest.

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