Clinical Case Report

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Retroperitoneal extramedullary plasmacytoma

A case report and review of the literature

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Abstract

Rationale: The incidence of extramedullary plasmacytoma (EMP) accounts for 3% to 4% of all cases of generalized plasmacytoma. The most common pathogenic sites are the head and the neck. It is noteworthy that the pathogenic site in this case is extraperitoneal, which is uncommon in clinical practice. In this case report, we aim to discuss the clinical features and diagnosis as well as the treatment methods of EMP.

Patient concerns: A 30-year-old female was admitted to our hospital due to a palpable right upper abdominal mass without symptoms of abdominal pain, diarrhea, constipation, fever, or oliguria.

Diagnosis and interventions: Enhanced CT scan showed a right retroperitoneal mass, which we considered to be isolated fibroma. Multiple myeloma (MM) was excluded through whole-body diffusion weighted imaging (DWI) and bone marrow biopsy. The patient underwent retroperitoneal tumor resection, and the postoperative pathology revealed plasmacytoma. Thereafter, she received only postoperative radiotherapy.

Outcomes: During the radiotherapy, the patient's condition and appetite were acceptable with I° gastrointestinal reaction. The CT examination of the chest and upper abdomen performed 4, 8, and 12 months after the radiotherapy still showed postoperative and postradiotherapy changes after retroperitoneal plasmacytoma resection without obvious abnormal signs. No recurrence and metastasis were detected after a one-year follow-up.

Lessons: Retroperitoneal extramedullary plasmacytoma (EMP) is a rare condition that is frequently a diagnostic challenge, mainly due to its unusual location and nonspecific symptoms, especially in the early stages. The diagnosis of EMP is made through a combination of imaging and pathological examination. Presently, the combinations of radiotherapy and surgery or radiotherapy are the primary treatments, usually leading to an acceptable local control rate. The application of chemotherapy, however, should be carefully considered.

Abbreviations: DT = total dose, DWI = diffusion weighted imaging, EMP = extramedullary plasmacytoma, HB = hemoglobin, MM = multiple myeloma, PLT = platelets, WBC = white blood cells.

Keywords: extramedullary plasmacytoma, retroperitoneal space, therapeutics

1. Introduction

Extramedullary plasmacytoma (EMP) refers to plasmacytoma which primarily originates from soft tissues. Except for the bone marrow hematopoietic tissue, this rare type of malignant monoclonal plasma cell disease is not accompanied by multiple or isolated bone marrow. Plasmacytoma evolves from the pathological plasmablast, which is formed in the process of the first and second stages of the development of immature B cells into plasmablasts. The plasma cells are located predominantly in the bone marrow, but in rare cases, they can migrate to soft tissues with the help of adhesion molecules .[1] This mechanism is a likely explanation for the low incidence of EMP, which accounts for 3% to 4% of all cases of generalized plasmacytoma .[2] The most common pathogenic sites are the head and the neck, followed by the stomach, the intestines, and the skin .[3] It is noteworthy that the pathogenic site of this case is extraperitoneal, which is uncommon in clinical practice. A literature search, performed by a professional librarian using PubMed, showed that studies on only 6 similar cases with such neoplasms have been reported to date. To the best of our knowledge, the present study describes the third case of retroperitoneal EMP in China (Table 1).

2. Case report

Ethical approval was not applicable in this case since standard care was performed. Written informed consent for publication of the case details was obtained from the patient and their relatives.

The patient, a 30-year-old female, was admitted to the Shanxi Tumor Hospital on December 31, 2016 due to an inadvertently palpable "right upper abdominal mass." Upon admission to the hospital, the patient was in a good condition and had normal

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Written informed consent was obtained from the patient and their relatives for publication of this report.

The authors have no conflicts of interest to disclose.

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Table 1

Characteristics of patients with retroperitoneal extramedullary plasmacytoma.

Study	Year	Country	Age	Gender	Side	Tumor size, cm	Treatment	Follow-up, months
Tanaka et al[23]	1993	Japan	46	Male	Left	NP	C+IR+C	33
Chen et al[5]	1998	Taiwan China	28	Male	Right	10×12×20	R+C	12
Saito et al[22]	2003	Japan	69	Female	Left	NP	C+R	12
Sharmaet al[6]	2004	India	44	Male	NP	18×16×10	C+extensive resection	16
Oh et al[21]	2007	Korea	58	Male	Left	30	C+R	6
Hong et al[7]	2009	China	26	Male	Right	30×16×10	ER	NP

C=chemotherapy, ER=extensive resection, IR=incomplete resection, NP=no report, R=radiotherapy.

appetite, without symptoms of abdominal pain, diarrhea, constipation, fever, or oliguria.

Physical examination: the general situation was acceptable; the superficial lymph nodes were not enlarged. Abdominal distension was noted, and a palpable mass was detected in the area of the right upper abdomen. The mass was hard, had clear boundaries and low activity, and was not accompanied by tenderness.

2.1. Investigations

Routine blood tests revealed the following data: 3.66×10^9/L white blood cells (WBC) (normal range 3.5–9.5×10^9/L), 122 g/L hemoglobin (HB) (normal range 115–150 g/L), and 176×10^9/L blood platelets (PLT) (normal range 125–350×10^9/L). The results of the liver and kidney function tests, as well as those of the routine urine, stool, and hepatitis tests were normal. The upper abdominal contrast-enhanced CT, performed on January 06, 2017, showed a right retroperitoneal mass, which was considered to be isolated fibroma (Fig. 1A). The color ultrasound on January 9, 2017 revealed a solid retroperitoneal cystic mass located in the right upper abdomen, and the liver and the right kidney were locally extruded.

2.2. Intraoperative findings

The patient underwent retroperitoneal tumor resection on January 11, 2017. The mass with dimensions $16 \times 10 \times 10$ cm was located behind the peritoneum, in the lower edge of the liver, and squeezed the right kidney (Fig. 2A). This lobulated formation, which was slightly crispy, tightly adhered to the surrounding tissues and was well supplied with blood vessels. The mass was tightly attached to the right side of the abdominal wall and infringed the right side of the diaphragm. We carefully dissected the site of the adhesion of the tumor to the surrounding tissues and removed a part of the diaphragm, which was repaired.

2.3. Pathological examination

The postoperative pathology examination showed plasmacytoma, which was confirmed by the molecular pathology results (using monoclonal rearrangement) (Fig. 2B). Then, on January 16, 2017, a chest radiograph was performed, which showed no obvious active lesion in the bilateral lung, heart, and mediastinum tissues. Whole-body diffusion weighted imaging (DWI) was done on February 9, 2017, and the following result was obtained: "the abnormal signals of adjacent to the right abdominal wall on

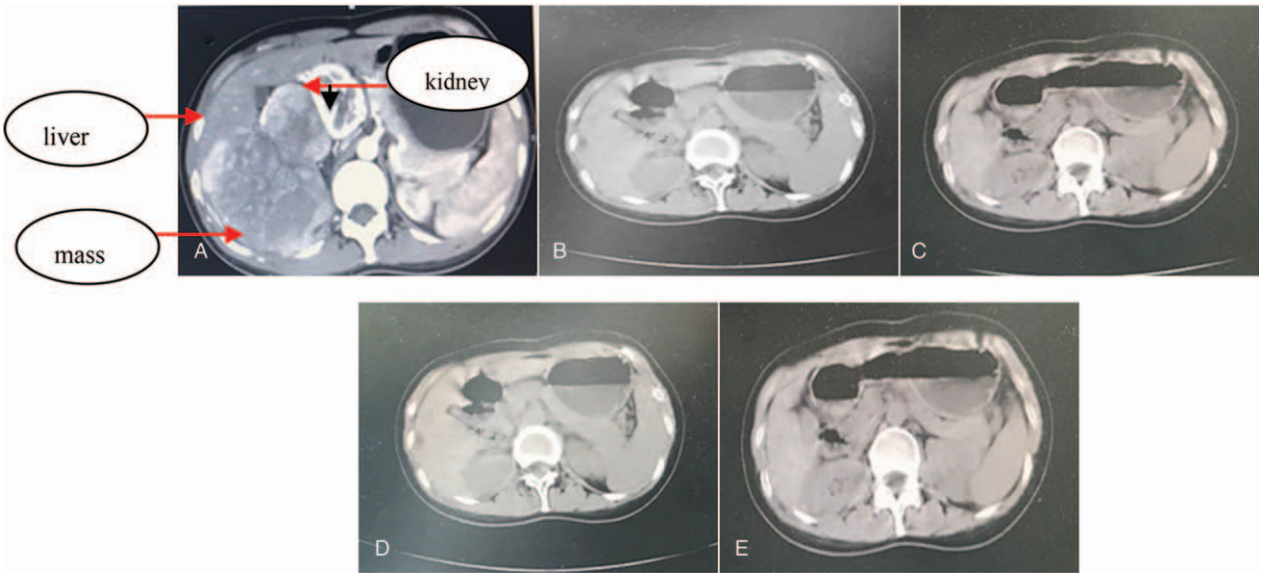

Figure 1. Abdominal enhanced CT scan revealed a retroperitoneal cystic solid mass (16 × 10 × 10 cm) located in the right upper abdomen, and the liver and right kidney were locally extruded. (A) Postoperative changes of retroperitoneal plasmacytoma without recurrence or metastasis after the operation; (B) postoperative and postradiotherapy changes of retroperitoneal plasmacytoma without recurrence or metastasis 4, 8, and 12 months after the radiotherapy, respectively (C, D, and E). CT=computed tomography.

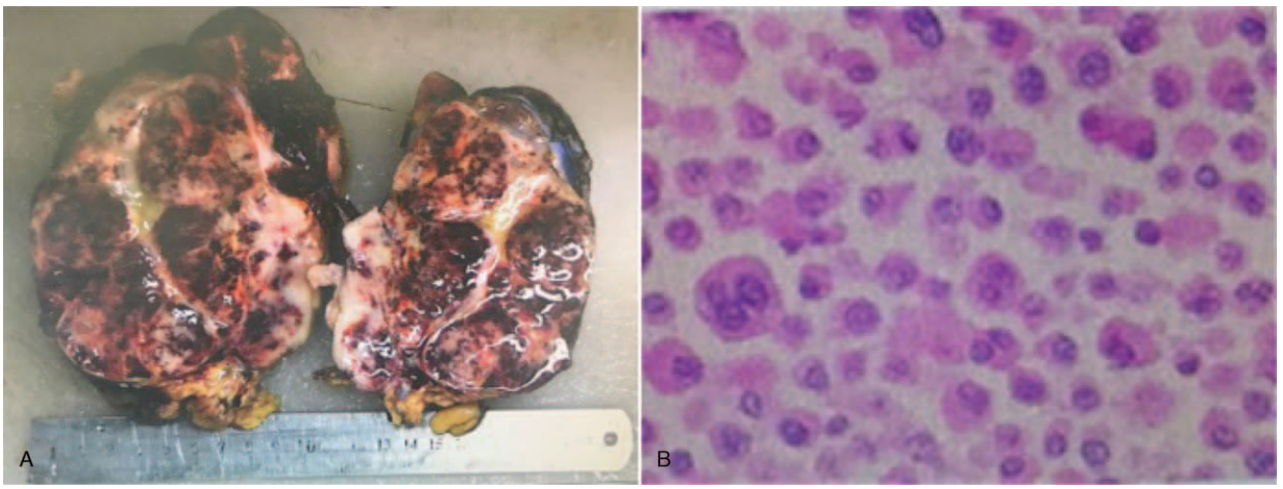

Figure 2. Postoperative gross tissue specimens. (A) Tumor cells with a homogenous amphophilic cytoplasm, round and asymmetric nuclei, coarsely stippled chromatin, some acidophilic nucleoli, and occasional binucleate (HE ×400) (B).

the right renal level. Please combine with the clinical data (Fig. 3)." Bone marrow biopsy was made on February 15, 2017, showing no obvious abnormalities were observed in the immune solid electrophoresis, excluding multiple myeloma (MM). The results of the pathological consultation conducted by 2 senior pathologists from Beijing Friendship Hospital stated the following: "Retroperitoneal neoplasm and a thick fiber coat are observed in the analyzed tissues. Diffuse infiltration of a large number of plasmocyte-like cells is present under the envelope. The cytoplasm is abundant and eosinophilic. The nuclear size is abnormal, and the shape of the nucleus is round or irregular; nucleolus is not obvious. The pathological diagnosis is plasmacytoma."

2.4. Postoperative radiotherapy, outcomes, and follow-up

The patient was eventually diagnosed with "retroperitoneal EMP" and admitted to the Radiotherapy Department of our hospital on March 10, 2017. The results of the re-examination by routine blood, urine, and stool tests, as well as those of the liver and kidney functions, were normal. The upper abdominal CT showed postoperative changes of retroperitoneal plasmacytoma without recurrence or metastasis (Fig. 1B). The tumor bed was subjected to intensity-modulated radiation therapy with a dose of DT 39.6 Gy/22 times/32 days. During the radiotherapy, the patient's condition and appetite were acceptable with I° gastrointestinal reaction. No abdominal pain, diarrhea, fever, or other symptoms were present. No adverse reactions were detected, with the only exception of the decreased to 2.35×10^9/L leukocyte count (normal range $3.5–9.5 \times 10^9$/L). Nevertheless, the leukocyte count was restored to 5.85×10^9/L after taking the Diyushengbai tablet (a kind of drug that may promote blood cells), 2 tablets 3 times a day for 7 days. The patient was suggested clinic re-examination every 3 to 4 months after the radiotherapy. Re-examination in outpatient settings followed at 4, 8, and 12 months after the radiotherapy. The psychological status and appetite of the patient were good, without abdominal pain, diarrhea, constipation, and oliguria. The results of the routine blood tests and liver and kidney function examinations did not show abnormality. The CT examination of the chest and upper abdomen performed 4, 8, and 12 months after the radiotherapy still showed postoperative and postradiotherapy changes after retroperitoneal plasmacytoma resection without obvious abnormal signs (Fig. 1C–E). No abnormal shadows were seen in the lungs. The final follow-up was on March 13, 2018. The patient has remained alive and well until the time of preparation of this manuscript. The follow-up is still ongoing.

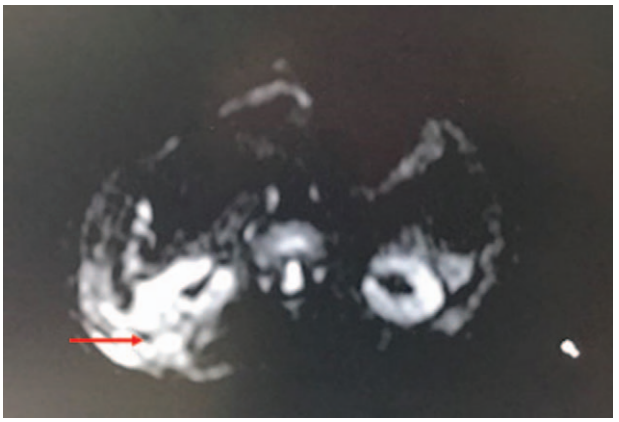

Figure 3. The whole-body DWI after the operation revealed abnormal signals in the upper part, adjacent to the right abdominal wall of the right renal level. DWI = diffusion weighted imaging.

3. Discussion

EMP refers to plasmacytoma which primarily originates from soft tissues, except for bone marrow hematopoietic tissue, and is not accompanied by multiple or isolated bone marrow cells. EMP can occur in any part of the body, but more than 80% of the tumors are located in the head and the neck, whereas the other bodily parts are comparatively rarely affected .[4,5] The main clinical symptoms of EMP are pain and those are caused by the compression exerted by local masses on the affected organs. Nonetheless, there is no clinical specificity and systemic symptoms, such as those caused by multiple myeloma, including anemia, high serum calcium level, renal function damage, and bone destruction. In the present case, the lesion of the young

female patient was located behind the peritoneum, which is relatively rare in clinic. Her lesion was hard to detect because of its location. Importantly, her spirit and appetite were good, without symptoms of abdominal pain, diarrhea, constipation, fever, and oliguria on admission. The author speculates her nerve sensitivity was poor, because she did not experience discomfort in spite of the large size of her lesion, which even squeezed her right kidney and liver. This location of the tumor increased the difficulty of surgery and radiotherapy. In a previous case, Sharma et al[6] reported that radiotherapy was effective in achieving long-term local control but was associated with high morbidity, particularly when used for the treatment of large retroperitoneal tumors. The imaging features were also atypical, with multiple manifestations of isolated and localized soft tissue masses, with or without lymph node metastasis and local bone destruction. Similarly, Wei et al[7] considered the mass to be a common type of tumor, such as schwannoma or sarcoma, before operation and serum electrophoresis were performed. The patient in this case was diagnosed with fibroma by preoperative enhanced CT. Therefore, the disease diagnosis relies mainly on the application of a combination of imaging and pathological examination. Wax et al[8] reported the use of a fine needle puncture for EMP. In most cases, it was difficult to meet the needs of histological diagnosis and immunohistochemical staining. Thus, surgical resection and endoscopic forceps biopsy are necessary to obtain adequate tissues.[9]

It is widely believed that EMP may be insidious MM. Hence, it is suggested that after definite diagnosis by CT and pathologic examination in the relevant parts, a combination of DWI, bone scan, bone marrow biopsy, and other examinations should also be conducted to further eliminate the possibility of merging MM. As mentioned, the lesion of the young female patient in this case occurred in the extraperitoneal area, which is relatively rare in clinic. The diagnosis was confirmed by multiple examinations of pathological sections, whole-body DWI, and bone marrow biopsy, which excluded MM and clarified the clinical diagnosis.

Because of the low incidence of EMP, there is no uniform standard for its treatment. After a review of related publications, some scholars [10] advocated surgical treatment or simple radiotherapy, or surgery plus radiotherapy. They recommended that patients with affected local lymph nodes need to undergo radiotherapy for the affected lymph nodes at the same time. There were also case reports of chemotherapy alone or chemotherapy plus radiotherapy. It is generally believed that EMP is a low-grade malignant tumor with high radiosensitivity, and it is mainly treated through local radiotherapy. Most reports indicate that the local control rate after radiotherapy is from 79.0% to 100%, and the total 10-year survival rate in is within the range 50.0% to 100.0% .[11–13] Nasr Ben Ammar et al[14] conducted a 10-year follow-up to five EMP patients and found that radiotherapy was exceedingly effective as a treatment. Generally, in the therapy of EMP, the priority of radiotherapy has been basically agreed. The study of Wang et al[15] including 28 EMP patients revealed that preventive regional lymph node irradiation should not be recommended except for EMP which originates in the Waldeyer's ring. Concerning the choice of radiotherapy dose, most authors believe that 40 to 50 Gy can achieve good local control rates without severe radiation injury .[10,11,13,16] Mendenhall et al[16] reviewed the specialized literature available and found that a local control rate of 94% was reported at radiotherapy doses higher than 40 Gy but 69% at those under 40 Gy. Thus, the authors suggested that the radiotherapy dose should be higher than 40 Gy. Surgery and radiotherapy are local treatments, but in some cases, the choice of surgery is also needed for effective clinical treatment. For example, most scholars suggest that for lesions which are circumscribed and have a sufficiently large cut edge or a wide scope and a big tumor load, radiotherapy is difficult to achieve by a radical cure dose, and operation or added postoperative radiotherapy are reasonable choices for treatment.[17] Because the patient in this case was a young woman, and the tumor was located in the retroperitonea with a diameter > 10 cm, no affected regional lymph node was found during the surgery. As the radiation resistance of the tumor-adjacent organs was poor, the patient preferred surgical treatment that would reduce the tumor load while obtaining a clear pathological result. After the surgery, the preoperative tumor location was referred to, and the tumor bed was subjected only to intensity-modulated radiation therapy, balancing tumor dose and normal organ protection. The radiotherapy was conducted using total dose (DT) 39.6 Gy/22 times/32 days. D'Aguillo et al[18] suggested that aggressive radiotherapy was the most common treatment modality for EMP, and a combination of surgery and radiotherapy led to better survival outcomes. Zhang et al[19] reported a case of a patient with tracheal EMP treated with surgery, followed by adjuvant radiotherapy, which achieved better local control too. We consider that the EMP should follow the principle of individualized treatment, taking into account the location and the size of the lesions. Other factors to be considered are whether it is initial treatment or recurrence and the radiation tolerance features of the surrounding normal organs. Using this complex approach, all advantages of radiotherapy and surgery will be achieved, providing patients with the treatment of the largest local control rate possible. On the choice of radiation dose, Mendenhall et al[16] and Mayr et al[20] suggested that higher doses (DT60–70 Gy)may be used if there is extensive involvement or a poor response during the course of irradiation.

The chemotherapy of EMP is still lacking medical-based evidence obtained after examinations of large samples. Sharma et al[6] reported a case of retro-peritoneal EMP, where chemotherapy was ineffective. In clinical practice, EMP and MM are two diseases with completely different biological behaviors. For example, Oh et al[21] reported a case of advanced retro-peritoneal EMP, whose follow-up CT showed progression of lesions just after implementation of radiotherapy and 3 cycles of chemotherapy. Moreover, multiple metastases were progressing to the right kidney, liver, spine, and peritoneum after six months of treatment. The author suggests that chemotherapy has the potential to treat distant metastasis but with little effect. Meanwhile, we should not subject 85% or more of the patients to chemotherapy with uncertain curative effects and many side effects because of the possibility that only 15% of EMP cases can convert to MM and metastasize. Saito et al[22] reported that the application of a combination of chemotherapy and radiation therapy resulted in a marked reduction in the development of advanced retro-peritoneal EMP. Tanaka et al[23] reported a case of EMP in the retroperitoneal space, which involved the left kidney, spleen, pancreas, and stomach, which was treated surgically combined with chemotherapy. The patient died of the disease 33 months after the initiation of the treatment. After reviewing relevant literature on similar cases, we suggest that chemotherapy can be used as an attempt and, to some extent, as a partial treatment for lesions with multiple recurrences, metastasis, high degree of malignancy, and after ineffective surgery, and radiotherapy treatment.

In conclusion, the present study describes the atypical clinical symptoms and imaging features of EMP. The disease diagnosis relies mainly on the application of a combination of imaging and pathological examination. Importantly, we conclude that EMP should follow the principle of individualized treatment, in which radiotherapy, surgery, or their combination is chosen specifically in each individual case. The use of chemotherapy should be carefully reconsidered. Given the limited experience in the treatment of EMP, further comprehensive studies are required to determine more precisely the appropriate regimen in each specific case.

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Author contributions

Conceptualization: Jing Wang, Jie Li.
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Formal analysis: Jing Wang, Jie Li, Fuli Zhang, Ping Zhang.
Project administration: Jie Li.
Writing – original draft: Jing Wang.
Writing – review & editing: Jie Li, Fuli Zhang, Ping Zhang.

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