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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Jalaj Garg, FACC, MD, Academic Research, Assistant Professor, Division of Cardiology, Medical College of Wisconsin, Milwaukee, WI 53226, United States.
garg.jalaj@yahoo.com

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Primary mucosal-associated lymphoid tissue extranodal marginal zone lymphoma of the bladder from an imaging perspective: A case report

Zhen-Zhen Jiang, Yuan-Yuan Zheng, Chuan-Ling Hou, Xia-Tian Liu

ORCID number: Zhen-Zhen Jiang 0000-0002-1075-5306; Yuan-Yuan Zheng 0000-0001-8105-3590; Chuan-Ling Hou 0000-0002-9199-2492; Xia-Tian Liu 0000-0002-8282-5043.

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Zhen-Zhen Jiang, Yuan-Yuan Zheng, Xia-Tian Liu, Department of Ultrasound, Shaoxing People's Hospital (Shaoxing Hospital, Zhejiang University School of Medicine), Shaoxing 312000, Zhejiang Province, China

Chuan-Ling Hou, Department of Pathology, Shaoxing People's Hospital (Shaoxing Hospital, Zhejiang University School of Medicine), Shaoxing 312000, Zhejiang Province, China

Corresponding author: Xia-Tian Liu, MD, Chief Doctor, Department of Ultrasound, Shaoxing People's Hospital (Shaoxing Hospital, Zhejiang University School of Medicine), No. 568 Zhongxing North Road, Shaoxing 312000, Zhejiang Province, China. txt2015@126.com

Abstract

BACKGROUND

Mucosal-associated lymphoid tissue extranodal marginal zone (MALT) lymphoma is a low-grade tumor that rarely occurs in the urinary bladder. There is currently no consensus on the common imaging findings or most appropriate treatment in MALT lymphoma in the urinary bladder due to the limited number of reports.

CASE SUMMARY

A 48-year-old woman was admitted to the hospital with a 1-year history of macroscopic hematuria. Imaging showed a large homogeneous mass with an unclear boundary and an irregular morphology in the bladder. The mass had an abundant blood supply. For further diagnosis, transurethral cystoscopic biopsy and bone marrow biopsy was performed, and the patient was finally diagnosed with primary MALT lymphoma of the bladder. R-CHOP chemotherapy was carried out. After three cycles of chemotherapy, the mass disappeared and the bladder wall thickness was only 4 mm, which indicated excellent therapeutic response to the chemotherapy. To date, the patient remains asymptomatic and she visits our hospital regularly for the completion of the remaining chemotherapy cycles.

CONCLUSION

Primary MALT lymphoma of the bladder is rare, and there are certain characteristics in the ultrasonographic findings. Imaging findings play an important role in evaluating the therapeutic efficacy and are critical during long-term follow-up after therapy.

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Core Tip: Mucosal-associated lymphoid tissue extranodal marginal zone (MALT) lymphoma is a rare tumor that rarely occurs in the urinary bladder. There is no consensus on imaging findings or treatment due to the limited number of reports. We present herein, a rare case of primary bladder MALT lymphoma in a female patient from an imaging perspective. This case summarizes the imaging features of bladder MALT lymphoma and highlights the role of different imaging modalities in evaluating therapeutic efficacy and long-term follow-up after the therapy.

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INTRODUCTION

Mucosal-associated lymphoid tissue extranodal marginal zone (MALT) lymphoma is a rare tumor that mainly occurs in the gastrointestinal tract[1-3] and has rarely been reported to occur in the urinary bladder, with a low prevalence of 0.2% of the extranodal lymphomas[4]. To the best of our knowledge, there is no consensus on the common imaging findings or the best treatment due to the limited number of reports. Herein, we report the serial imaging findings and follow-up results of a patient with primary MALT lymphoma of the bladder. We also review the current literature to summarize the imaging findings to provide a detailed understanding of primary bladder MALT lymphoma.

CASE PRESENTATION

Chief complaints

A 48-year-old woman was admitted to the hospital with a 1-year history of macroscopic hematuria.

History of present illness

In the past year, the patient was found to have recurrent macroscopic hematuria. Her urine was intermittently bright red with blood clots. There were no accompanying symptoms, such as frequent urination, urgent urination, painful urination, fever, or weight loss.

History of past illness

The patient had no significant medical history.

Personal and family history

There were no special personal or family illness histories.

Physical examination

The physical examination revealed no abnormalities. The patient had no percussion pain in the renal area bilaterally, and no tenderness in the ureteral and bladder areas.

Laboratory examinations

Tumor marker analysis revealed that the serum carbohydrate antigen 125 (CA125) level of the patient was elevated (67.44 U/mL), while other tumor markers were

negative. Routine blood tests revealed that the percentage of neutrophils was 77.6%, which was slightly elevated. Routine urinary tests revealed that the patient had a urinary tract infection (the urine white blood cell count was 2510.5/mL, and the urine bacteria count was 27736/mL), accompanied by hematuria and proteinuria (the urine red blood cell count was 37.9/mL, and the urine protein level was 1+). The thrombin profile revealed that the patient had coagulation function abnormalities (the prothrombin time was 17.4 s, the international standardized ratio was 1.45, the activated partial thromboplastin time was 49.4 s, the activated partial thromboplastin ratio was 1.5, and thrombin time was 21.3 s).

Imaging examinations

Ultrasound examination revealed a large hypoechoic mass in the bladder, and the size of the mass was 128 mm × 78 mm. Its boundary was not clear, and the shape was irregular. The mass had a homogeneous hypoecho with fine linear echogenic strands distributed inside. No signs of calcification or large patches of necrosis were encountered. Color Doppler flow imaging showed rich blood flow signals in the mass. An artery was detected within the mass, and it had a maximum flow velocity (V_{max}) of 22.9 cm/s and a resistance index of 0.57 (Figure 1). The right renal collection system was separated by 13 mm, and the right ureter was fully dilated. A contrast-enhanced computed tomography (CT) scan demonstrated that the bladder wall was thickened, and there were multiple low-density nodules in the bladder with unclear boundaries and irregular morphologies. A continuous enhancement of the nodules was observed. The ureteral and renal pelvis of the right kidney were dilated (Figure 2). The CT images indicated bladder carcinoma, and a biopsy was recommended.

FINAL DIAGNOSIS

For further diagnosis, a transurethral cystoscopic biopsy was performed. During the operation, multiple bulging bladder masses were found. Tumor tissue samples were collected, and histological findings revealed diffuse infiltration by atypical lymphoid cells. Immunohistochemical staining was positive for CD20, CD21, and CD79a and was negative for CD3, CD5, CD35, CD10, Bcl-6, CD45RO, Mum-1, and Cyclin D1, with a Ki-67 Labeling index of 10% (Figure 3). These data supported the diagnosis of MALT lymphoma. No primary or secondary lymphoma lesions were detected by imaging examinations. Additionally, a bone marrow biopsy revealed no signs of invasion of MALT lymphoma. The patient was diagnosed with primary MALT lymphoma of the bladder.

TREATMENT

Laboratory examinations indicated that the patient had a coagulation disorder and was unable to proceed with surgery. Based on the patient's condition and treatment guidelines, R-CHOP chemotherapy was carried out.

OUTCOME AND FOLLOW-UP

The patient had a favorable outcome. After two-cycles of chemotherapy, ultrasonography showed that the mass had disappeared with localized thickening (13 mm) of the bladder wall. After three-cycles of chemotherapy, the bladder wall thickness was only 4 mm, which indicated an excellent therapeutic response to chemotherapy (Figure 4). To date, the patient remains asymptomatic and she visits our hospital regularly for the completion of the remaining chemotherapy cycles. After finishing all the chemotherapy cycles, CT follow-up will be performed to verify the final therapeutic effect.

DISCUSSION

MALT lymphoma is a unique subtype of B-cell lymphoma predominantly involving extranodal sites, such as the stomach, orbit, conjunctiva, salivary glands, thyroid and

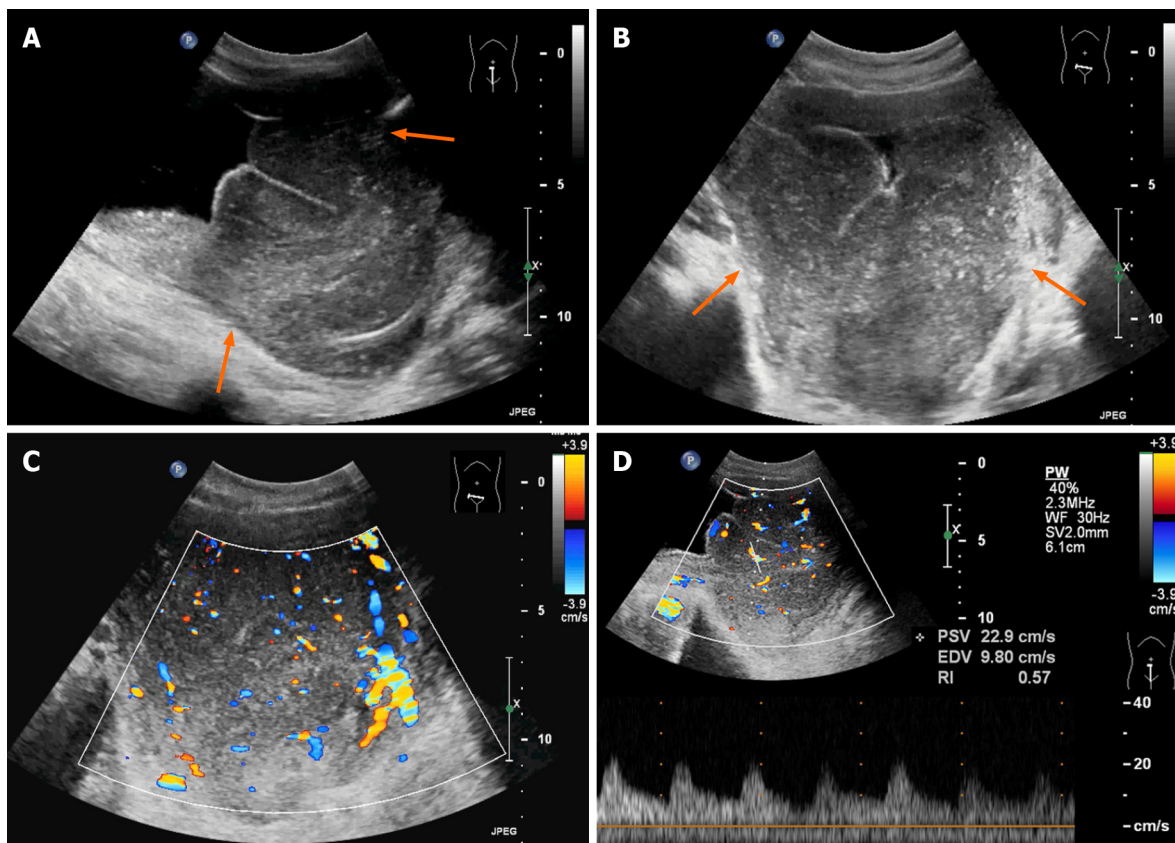


Figure 1 Ultrasonographic findings of the lesion. A and B: A large homogeneous hypoechoic mass was detected in the bladder (arrows), with an unclear boundary and irregular shape. There were fine linear echogenic strands distributed inside; C: Color Doppler flow imaging showed that there were rich blood flow signals in the mass; D: Spectral Doppler ultrasound imaging showed the artery spectrum detected within the mass ($V_{max} = 22.9$ cm/s, resistance index: 0.57).

lungs[2,5-7]. The bladder is rarely involved, accounting for only 0.2% of extranodal lymphomas[8]. The risk factors include chronic inflammation, urinary tract infections and autoimmune diseases[9,10]. As no naturally occurring lymphoid tissue exists in the bladder, the pathogenesis of primary bladder MALT lymphoma may be due to the accumulation of extranodal lymphoid tissue resulting from chronic inflammation, which is similar to the mechanism of gastric MALT lymphoma caused by *Helicobacter pylori* infection[1]. In our case, although the patient did not mention a history of chronic inflammation, her laboratory examinations indicated the existence of a urinary tract infection, which was compatible with the reported risk factors.

The clinical features of bladder MALT lymphoma are nonspecific. It more commonly affects female patients, the most common presenting symptom is hematuria, and less frequent symptoms include recurrent urinary tract infection, dysuria, and urinary retention[11]. Our patient was a 48-year-old woman with recurrent hematuria and evidence of a urinary tract infection; without the help of imaging and histological confirmation, it would have been difficult to make the correct diagnosis. However, a large mass in the bladder without any signs of peripheral metastatic infiltration should point toward the possibility of the diagnosis of lymphoma. Moreover, the presence of an elevated CA125 levels would increase the diagnostic confidence. As reported in the literature, CA125 is a glycoprotein expressed by epithelial ovarian tumors. Nevertheless, cytokines derived from malignant cells in patients with peritoneal involvement may also stimulate the secretion CA125 by mesothelial cells[12]. It has already been shown that the measurement of serum CA125 is useful for staging, monitoring, and estimating the prognosis in non-Hodgkin's lymphoma patients[12,13].

To date, few studies have focused on the imaging findings of primary bladder MALT lymphoma because of its rarity. For the literature review, we summarized the imaging findings of reported cases of primary bladder MALT lymphoma in Table 1, including the present case. We found that most patients (9/13, 69.2%) presented with a solitary mass. The average size of the lesions that had been reported was 7.6 cm (3.4-12.8 cm). It has been reported that primary bladder lymphoma is more commonly seen in the lateral wall of the bladder, with only 10% of cases having a diffuse thickening of the bladder wall[14], which is consistent with our results (15% of cases had diffuse

Table 1 Imaging findings of the patients with primary bladder mucosal-associated lymphoid tissue extranodal marginal zone lymphoma ever reported (including the present case)

No.	Ref.	Solitary /multiple	Size (cm)	Location	Signs of ureteral obstruction	Imaging findings			Follow-up imaging methods
						US	CT	MRI	
1	Tasu <i>et al</i> [14]	Solitary	NA	Right lateral wall	No	Soft tissue mass	Soft tissue mass	No	NA
2	Tasu <i>et al</i> [14]	NA	NA	Entire wall	Yes	Circumferential thickening of the bladder wall	Circumferential thickening of the bladder wall	No	CT
3	Tasu <i>et al</i> [14]	Solitary	NA	Left wall	No	An isolated mass with local thickened bladder wall	An isolated mass with local thickened bladder wall	No	NA
4	Maninderpal <i>et al</i> [15]	Solitary	11.2	Trigone of the bladder	Yes	A hypoechoic soft tissue mass with local thickened bladder wall	A homogeneously enhancing mass with local thickened bladder wall	Homogeneously enhancing mass with hypointensity in T1WI, intermediate intense intensity in T2WI, and hyperintensity in STIR	CT
5	Szopiński <i>et al</i> [11]	Solitary	3.6	Posterior wall	No	Hypoechoic mass	No	No	US, CT
6	Morita <i>et al</i> [23]	Solitary	NA	NA	NA	No	Soft tissue mass with local thickened bladder wall	No	NA
7	Bacalja <i>et al</i> [24]	Solitary	8.5	Right posterolateral wall	No	Soft tissue mass	Expansive lesion of the bladder wall	No	CT, PET-CT
8	Matsuda <i>et al</i> [4]	Solitary	NA	Anterior to right side wall	Yes	No	Soft tissue mass with local thickened bladder wall	Soft tissue mass with local thickened bladder wall	US
9	Simpson <i>et al</i> [25]	Solitary	6.3	Anterior lateral	Yes	No	Soft tissue mass	No	PET-CT
10	Hsu <i>et al</i> [18]	NA	NA	Right wall	Yes	No	Eccentric thickened bladder wall	No	NA
11	Kadam <i>et al</i> [26]	Solitary	3.4	Posterior wall	NA	No	Soft tissue mass	No	NA
12	Xu <i>et al</i> [8]	Multiple	NA	NA	NA	Roughness in the inner bladder wall	Soft tissue mass	No	CT, PET-CT
13	Present case	Multiple	12.8	Posterior wall	Yes	A mass had a homogeneous hypoecho with fine linear echogenic strands distributed inside	Continuous enhancing mass with thickened wall	No	US

NA: Not available; US: Ultrasonography; CT: Computed tomography; MRI: Magnetic resonance imaging; T1WI: T1-weighted imaging; T2WI: T2-weighted imaging; STIR: Short tau inversion-recovery; PET-CT: Positron emission tomography/computed tomography.

thickened wall). Some of the patients (6/13, 46.2%) had signs of hydronephrosis, which may be due to an obstruction of the urethral orifices caused by large masses. In our case, the patient presented with a large sessile solitary mass with thickening of the bladder wall and right hydronephrosis, which was thought to occur because the mass originated from the lateral wall of the bladder and obstructed the right ureteral outlet, and the hydronephrosis was not likely secondary to tumor invasion.

The general imaging manifestations of MALT lymphoma are solitary or multiple solid homogeneous masses without cysts, necrosis or calcification[15,16]. The ultrasound features of MALT lymphoma could be described as interspersed linear echogenic strand patterns or segmental patterns, according to the thicknesses of the septa[17]. The pathological basis for the formation of linear echo may be the expansion

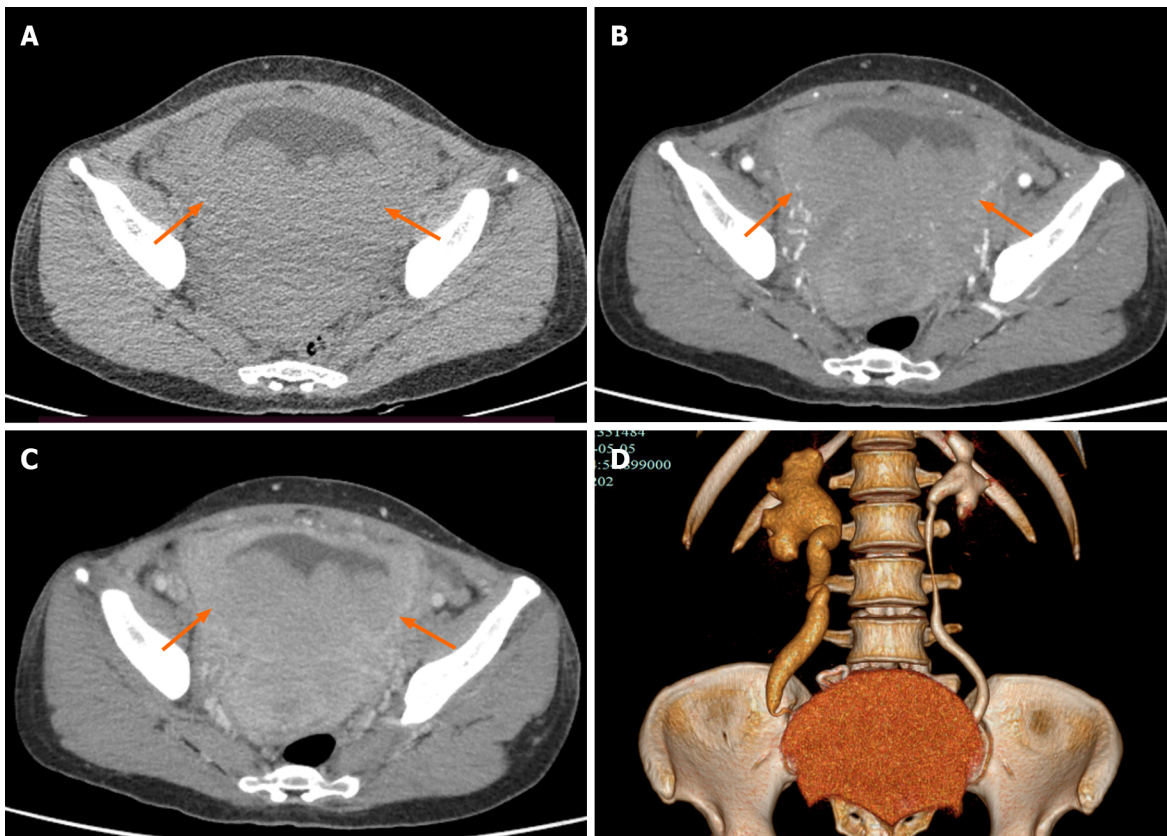


Figure 2 Computed tomography findings of the lesion. A: The bladder wall was thickened, and there were multiple low-density nodules in the bladder with unclear boundaries and irregular morphologies (arrow); B and C: Continuous enhancement of the mass was observed; D: The ureter and renal pelvis area of the right kidney was dilated.

of lymphoma cells bordered by fibrous bands. If the fibrous bands are wide, the ultrasonic findings show a segmental pattern[16]. In our present case, a homogeneous hypoecho mass with fine linear echogenic strands was found, and the ultrasound findings included a linear echogenic strand pattern. This may be consistent with the pathological basis of MALT lymphoma. As presented in Table 1, CT features in most cases contained homogeneously enhance solitary masses. Only one case described the magnetic resonance imaging features of primary bladder MALT lymphoma as a homogeneously enhancing mass with hypointensity in the T1-weighted phase, and intermediate intensity in the T2-weighted phase, and hyperintensity in the short tau inversion-recovery phase.

Primary bladder MALT lymphoma needs to be differentiated from bladder carcinoma, glandular cystitis, and metastatic lymphoma of the bladder. Comparisons of the imaging findings of these diseases are summarized in Table 2. Briefly, the ultrasound manifestations of bladder carcinoma are hypoecho masses with narrow base and rough boundaries. Glandular cystitis is characterized by a diffuse thickening or nodular eminence of the bladder wall with mild enhancement. The lesion does not invade the muscle layer and is hypovascular. Most patients with bladder metastatic lymphoma had a history of primary tumors and extensive abdominal lymphadenopathy.

The most effective therapeutic approach for primary bladder MALT lymphoma remains controversial. A complete resection of the tumor may not be required, as radiotherapy and chemotherapy can be useful and effective[18]. In this case, R-CHOP chemotherapy was used and resulted in remission after taking into consideration the patient's condition and the therapeutic efficacy of systemic chemotherapy.

In the follow-up of MALT lymphoma, imaging modalities, such as contrast-enhanced CT, are effective in detecting the lesion[19]. The value of positron emission tomography/CT for the staging and response assessment of MALT lymphoma with multiple site involvement has also been reported[20]. However, the optimal follow-up imaging modalities have not been determined due to the limited case number. In our experience, the therapeutic response or the presence of a relapse after the remission of a primary bladder MALT lymphoma could be evaluated by tracking the changes in the

Table 2 Comparison of image findings among the present case, previously reported cases, typical bladder carcinoma and typical glandular cystitis

	US	CT	MRI
Present case	Hypoecho mass with sharp boundaries	Solitary mass with continuously enhancement and thickened bladder wall	No
Common findings of cases reported	Hypoecho mass	Solitary mass with homogeneously enhancement	Homogeneously enhancing mass with hypointensity in T1WI, intermediate intense intensity in T2WI, hyperintensity in STIR
Common findings of bladder carcinoma	Hypoechoic masses with rough boundaries	Irregular solid mass with significantly heterogeneous enhancement	Early significantly enhancing mass with iso to hyperintensity in T1WI, intermediate intensity in T2WI, hyperintensity in DWI, and decreased ADC value
Common findings of glandular cystitis	Diffuse thickening or nodular eminence of the bladder wall	Thickened bladder wall with mild enhancement	Mild enhancing thickened bladder wall with intermediate intensity on T1W, hyperintense on T2W, and slightly hyperintense on DWI

NA: Not available; US: Ultrasound imaging; CT: Computed tomography; MRI: Magnetic resonance imaging; T1WI: T1-weighted imaging; T2WI: T2-weighted imaging; DWI: Diffusion-weighted imaging; ADC: Average diffusion coefficient.

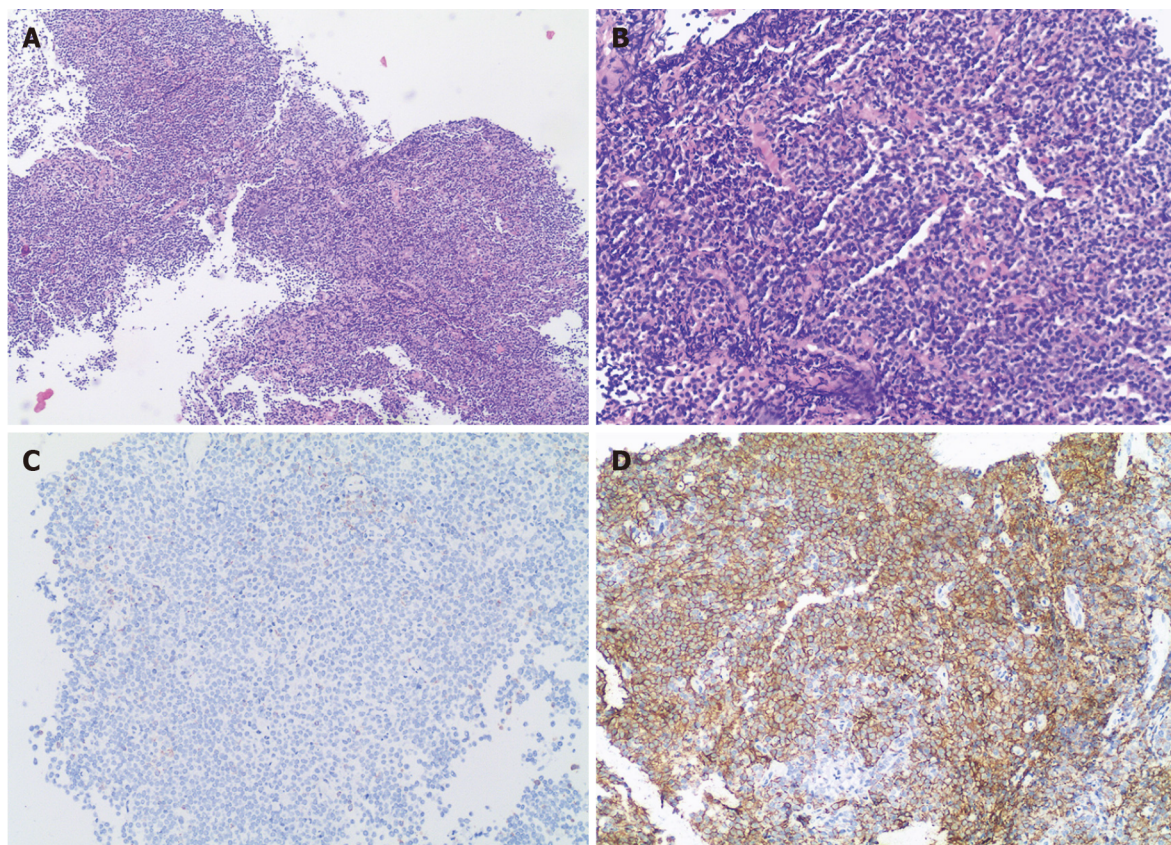


Figure 3 Histopathological findings of the mass tissues. There was diffuse infiltration of atypical lymphoid cells. A: Hematoxylin and eosin (HE) staining, magnification 40 ×; B: HE staining, magnification 100 ×; C: Immunohistochemical (IHC) staining, negative for CD3, magnification 100 ×; D: IHC staining, positive for CD20, magnification 100 ×.

bladder wall thickness by ultrasound. In the long-term follow-up of MALT lymphoma in hollow organs, such as the stomach and bladder, ultrasonography can be a valuable tool for the evaluation of wall infiltration by measuring the wall thickness[21,22].

CONCLUSION

Primary MALT lymphoma of the bladder is rare, and the imaging findings have certain characteristics. The diagnosis of MALT lymphoma should be considered if a

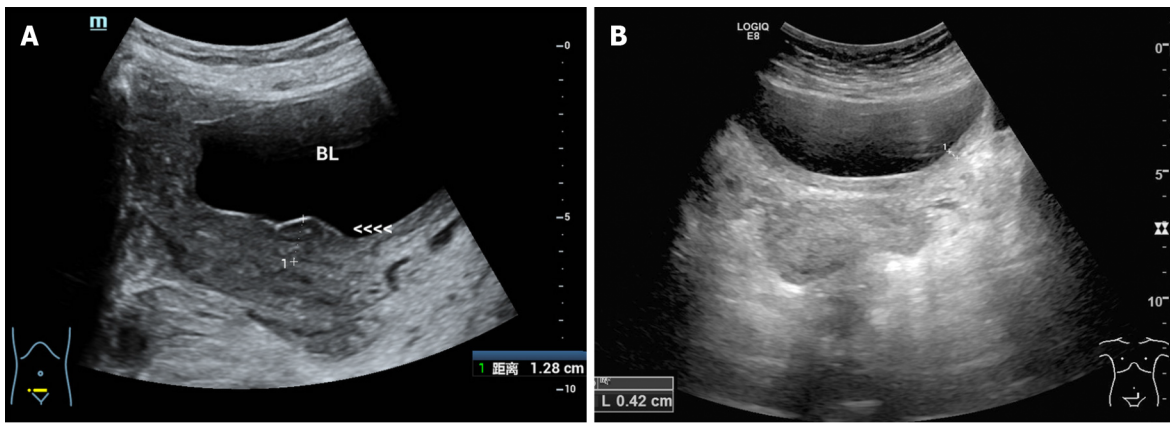


Figure 4 Ultrasonographic findings during the chemotherapy. A: After two cycles of chemotherapy, the mass had disappeared with localized thickening (13 mm) of the bladder wall; B: After three cycles of chemotherapy, bladder wall thickness was only 4 mm, which indicated excellent therapeutic response to the treatment.

large mass has no signs of extravesical spread. Primary bladder MALT lymphoma is a low-grade, localized indolent tumor with a good prognosis, so early diagnosis can reduce unnecessary surgeries. In addition, ultrasound can be used as an imaging method for evaluating the therapeutic efficacy and is critical for long-term follow-up after therapy.

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