

Case Report

Malignant villous adenoma of the appendix invading the urinary bladder: a case report

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Abstract: Primary tumors of the appendix are rare, while malignant villous adenoma of the appendix invading the urinary bladder is extremely uncommon. We reported the present case of a 63-year-old male with malignant villous adenoma of the appendix invading the urinary bladder. The conventional cystoscope demonstrated a mass at the front right side wall of the urinary bladder, which misdiagnosed as bladder cancer initially. Computed tomography (CT) and ultrasound especially contrast-enhanced ultrasonography (CEUS) preoperatively revealed a malignant mass originating from the appendix, but not the bladder. At the intraoperative exploration and pathology, malignant villous adenoma of the appendix invading the urinary bladder was verified.

Keywords: Villous adenomas of the appendix, bladder tumor, malignant, ultrasonography, contrast media

Introduction

Primary tumors of the appendix are very rare, with the incidence rate of 0.9-1.4% of appendectomy specimens, and the most common type of which is malignancy including appendix carcinoid tumor, adenocarcinoma and malignant mucinous tumors [1]. Adenoma of the appendix is the benign tumor that may progress to invasive adenocarcinoma, which occurs more frequently in the colon and rectum [2]. However, villous adenoma malignant of the appendix invading the urinary bladder is extremely uncommon. Villous adenoma of the appendix is a pathological type of appendix adenoma, as an important precancerous lesion, which is exceedingly difficult to make a correct diagnosis before surgery. At present, only a few studies were published with the case report. In this study, we presented a case of malignant villous adenoma of the appendix invading the urinary bladder in a 63-year-old man. This report discussed the preoperative diagnosis and treatment of the tumor relating to the characteristics of the disease, in order to achieve a definite diagnosis preoperatively and select the most appropriate treatment modalities. This study was approved by the ethics

committee of the First Affiliated Hospital of Nanchang University, Nanchang, China. Written informed consent was obtained from the patient.

Case report

A 63-year-old male presented to the First Affiliated Hospital of Nanchang University (Nanchang, China) with painless hematuria and urinary frequency which had persisted for approximately four years, and then worsened for one month. He had no symptom of gastrointestinal tract. The physical examination showed no abnormalities. There was no history of the disease in his family and no other palpable risk factors. In addition, he had a lumbar fracture fixation surgery 2 years ago in our hospital. Laboratory tests after admission only showed microscopic hematuria. The level of tumor markers, including carbohydrate antigen 19-9 (CA19-9), carcinoembryonic antigen, α -fetoprotein (AFP) and prostate specific antigen (PSA), were normal particularly.

At the patient's local hospital, the bladder tumor was diagnosed by using the baseline ultrasound (only through the oral by the patient without the ultrasonic diagnosis report). In

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Figure 1. CT reveals the swelling appendix and a soft tissue density, protruding strongly into the bladder lumen at the level of the right anterior bladder wall.

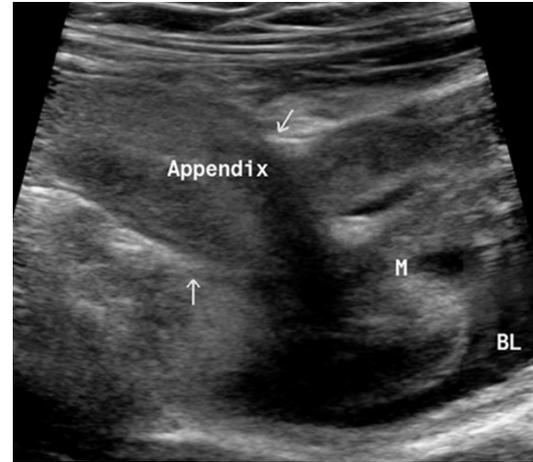


Figure 3. Baseline US revealed a hypoechoic mass in the front right side wall of the urinary bladder, closely connecting with the appendix.

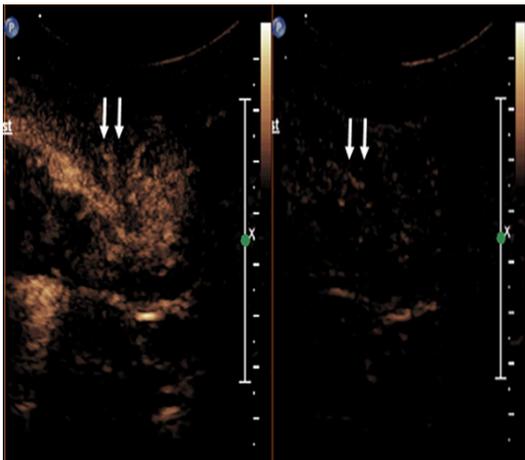


Figure 2. CEUS shows: Arterial late phase shows quickly inhomogeneous and strong enhancement of the tumor, and rapidly disappeared in the venous phase compared with the normal bladder wall.

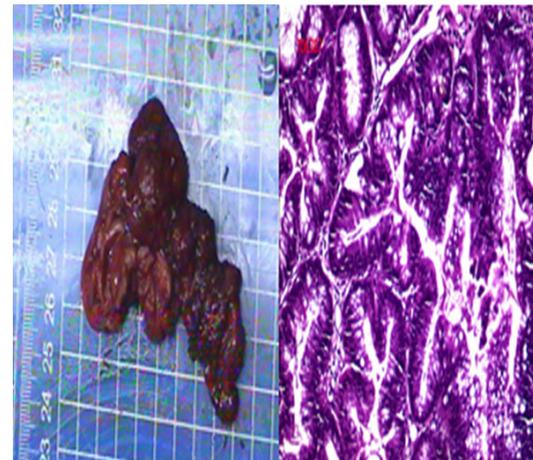


Figure 4. Specimens and low differentiated adenocarcinoma of the appendix. H&E, reduced from, $\times 100$.

order to achieve a definite diagnosis, the patient had undergone cystoscopy with transurethral biopsy in our hospital which showed the mass suspiciously originating from the bladder. However, the specimen was not diagnosed correctly because of the location of the biopsy tissue was superficial. Then the enhanced abdominal CT scan emerged the swelling appendix and a soft tissue density, measuring $3.0 \times 2.8 \times 2.1$ cm, protruding strongly into the bladder lumen at the level of the right anterior bladder wall (**Figure 1**). From the coronal multiplanes reconstruction imaging, the mass was subjected to contrast enhanced ultrasound (CEUS).

The bladder must be appropriately full before the ultrasound study. CEUS was performed by using the specific contrast software and ultrasound contrast agents (Sonovue, Bracco, Italy). A dose of 2.4 mL of Sonovue was injected through a 21 gauge peripheral intravenous cannula, followed by a 5 mL saline flush. The CEUS imaging (**Figures 2** and **3**) revealed a hypoechoic mass in the front right side wall of the urinary bladder, measuring $4.2 \times 2.7 \times 2.2$ cm, closely connecting with the appendix, but not extending to its submucosa. Arterial late phase showed quickly inhomogeneous and strong enhancement of the tumor, and rapidly disappeared in the venous phase compared with the

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normal bladder wall. Therefore, from the CEUS study, the mass might be defined as originating from the appendix and invading the bladder.

Minimally invasive surgery for the tumor resection was performed under general anesthesia. During the surgery, the tubular mass localizing between the ileocecal junction and the right anterior bladder wall and the appendix thickening were found, measuring well-defined 4.0 × 3.0 × 2.5 cm. The resected tumor appeared a red-gray gross appearance and consist of inconsistent soft tissue, while some parts are lumen-like. The resected specimen was then subjected to histopathology (**Figure 4**) and found villous adenomas of the appendix, malignant transformation, low differentiated adenocarcinoma formation (including mucinous adenocarcinoma component), invasion of the bladder wall, a broken end of the appendix and no tumor involvement. The patient received adjuvant chemotherapy with 5-fluorouracil after operation. The patient was discharged after the operation without any discomfort and told to receive a long-term follow-up every three months. The patient has no recurrence and the levels of tumor markers were normal so far.

Discussion

Primary carcinoma of the appendix was first described in 1882 by Berger A [3]. Tumors of the appendix are fantastically rare and usually misdiagnosed as appendicitis preoperatively, accounting for approximately 0.9-1.4% of appendectomy specimens. Malignant villous adenoma of the appendix invading the urinary bladder is extremely uncommon. Only some case studies have been reported. Histologically, malignant tumors of the appendix are classified into two types: Epithelial tumors and non-epithelial tumor. The most common is the mucinous adenocarcinoma of the epithelial tumors [4]. For lack of typical clinical symptoms or representative imaging features if no encroachment on the intestinal or urinary bladder occurs, correct diagnosis is usually more difficult preoperatively. Consequently, tumors of the appendix are generally misdiagnosed or even neglected. According to a study by KO YH *et al* [3], the surgery was performed in 60.0% of the patients with malignant tumor of the appendix who were found at initial presentation, and abdominal pain that accounted for 69.1% was the most common complaint at the

time of initial diagnosis. However, in the study, he presented with only urinary symptoms last for four years, such as hematuria and urinary frequency. This may be the main reason why the misdiagnosis of bladder cancer at first. What's more, in the present case, the mass was not correctly diagnosed by cystoscopy biopsy on account of the location of the biopsy tissue is superficial. It is likely that the tumor was no infringement the muscle layer and mucosa of bladder. Similarly, the study of Arisawa C *et al* indicated that aspiration cytology may be useful in the diagnosis of tumor in the patient [5].

With the rapid development of imaging technology, the conventional imaging techniques like CT and US are usually used to find the appendix mass as the most common way of diagnosis, but making it difficult to diagnosis and ant diastole precisely. On CT, swollen appendix, size and sites can be used as its main features. Balthazar *et al* [6] revealed that adenocarcinoma of the appendix is visualized as an irregular, low-density area with infiltration into adjacent organs on CT, which is obviously specific compared with other types of the appendix. In the present case, it was acknowledged that the lesion was visualized as an elongated mass and low-density area stating at the appendix with invading the bladder confirmed pathologically. On baseline US, it can display the location, size, internal echo of the tumor and so on, while it is not sensitive for the assessment of blood flow in the tumors. In the recent years, tumor angiogenesis has been widely accepted in oncology. Angiogenesis is the growth of new blood vessels from existing intravascular tumor growth and metastasis of tumor, which was an important factor for determining prognosis including many tumors [7]. Since its introduction to Japan in January 2007, the ultrasound contrast agent Sonovue has been used in detailed studies on liver tumors at the first time [8, 9]. As we known, unlike CT and Magnetic Resonance Imaging (MRI) contrast agents that diffuse into the extravascular space to enter the equilibrium phase, Sonovue is a blood pool agent, which may better display the flow distribution of the tumor [10]. However, there are only few reports about the diagnosis the appendix tumors by the CEUS. Despite of its characteristic imaging on CT, the patient could clearly be diagnosed, which was difficult

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to accurately discriminating categories or prognostic factors of the tumor compared with CEUS. It is worth mentioning that a large amount of radiation of CT is harmful to the human body. At CEUS, it is the most significantly matter that the mass need to have been distinguished from the bladder tumor. Compared with the appendix tumor, the CEUS findings of bladder carcinoma have two characteristics [11]: bladder cancer mostly occurred in the posterior wall; the CEUS shows a faster washout in bladder cancers than the tumor of appendix compared with the normal bladder wall. Consequently, there is great value in the diagnosis and differential diagnosis among them. Wakui N *et al* [12] also suggested that the utility of US combined with CT for diagnostic imaging of appendix tumor, with CEUS being particularly useful for the assessment of blood flow in the diagnosis of the mass. Moreover, CEUS always does not leave the blood vessels, non-toxic side effects and even become a real-time dynamic monitoring of perfusion of tumor microcirculation, which is obviously superior to the enhanced CT or MRI [13]. We have to point out that CEUS combined with CT is more advantageous to the diagnosis of the disease. Contrast enhanced ultrasound has a high diagnostic accuracy for the disease, but more diagnostic tests are still needed to provide evidence of evidence-based medicine.

The report suggested that all patients should be treated with appendectomy, segmental bladder resection or cystectomy [14]. In addition, radiation and chemotherapy are necessarily performed [15, 16]. In the present case, although there was no lymph node metastasis, tumor radical cystectomy was performed. The patient received adjuvant chemotherapy with 5-fluorouracil after operation without radiation therapy. The patient had no recurrence and the levels of tumor markers were normal so far. However, the effecting of the adjuvant therapy needs more studies to validate in the further.

In conclusion, at the present case, malignant villous adenoma of the appendix invading the urinary bladder after the tumor resection and adjuvant therapy had a great prognosis, while it is exceedingly different than other tumors invading the bladder. Above all, we suggested that a diagnosis of malignant villous adenoma of the appendix invading the urinary bladder must be considered by CT and US, especially

CEUS combined with transurethral biopsies preoperatively, which may be effective to the treatment modalities and prognosis of the patients.

Disclosure of conflict of interest

None.

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