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Cystitis Cystica as a Rare Cause of Obstructive Uropathy

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Cystitis cystica, previously thought to be premalignant condition or associated with malignancy, is actually a benign condition. It may present with lower urinary tract symptoms, abdominal pain or haematuria. The exact aetiology is unknown. Cystitis cystica may cause chronic bladder outflow obstruction resulting in hydronephrosis and hydroureter.
Case Presentation: A 53-year-old male was referred to emergency department with incidental finding of deranged renal profile. Physical examination was unremarkable. Ultrasound revealed gross hydronephrosis and hydroureter with bladder wall trabeculae suggestive of chronic bladder outlet obstruction. Cystoscopy revealed small tumour over the bladder neck. It was subsequently confirmed to be a case of cystitis cystica.
Conclusions: Cystitis cystica can only be confirmed by histopathology. Unless confirmed by histopathology examination, all suspicious tumours should be treated as malignancy until proven otherwise.

Keywords: Cystitis; cystic; bladder; obstruction; hydronephrosis; uropathy.

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1. INTRODUCTION

Cystitis cystica is a histopathological diagnosis, characterized by hyperplasia of the bladder submucosa. It is a benign, proliferative condition affecting the bladder. Previously, it was suggested that cystitis cystica to be a premalignant condition [1]. However, recent studies have refuted this suggestion. Smith et al followed up 103 patients with cystitis cystica et glandularis for up to 23 years and concluded that no evidence to suggest that cystitis cystica increases the risk of malignancy [1].

Cystitis cystica is seen more frequently in adult and uncommonly in children [2]. When cystitis cystica presents in children, it is predominantly affecting female. Milošević et al reported that out of 127 patients with confirmed cystitis cystica identified in 20 year period, only 2 were male [3]. The incidence of cystitis cystica is reported to be less than 1% [4].

Cystitis cystica may present with urinary tract infection, lower urinary tract symptoms or obstructive uropathy. Herein we present a case of cystitis cystica causing obstructive uropathy in a middle age man.

2. CASE PRESENTATION

A 53-year-old male presented to general practitioner clinic for health screening. It was noted that his serum urea was 38.7 mmol/L and creatinine level 1882 umol/L. One year prior to this his serum urea and creatinine was normal (urea 4 mmol/L, creatinine 108 umol/L). Otherwise, he denied any nausea, vomiting, or chest pain. No symptoms of lower urinary tract infection or abdominal pain reported previously too. He also denied prolong use of non-steroid anti-inflammatory drugs (NSAID), traditional medication or any sexual promiscuity. He had underlying hypertension, depression and psoriasis. His regular medications include tablet fluvoxamine 100 mg daily and tablet amlodipine 10 mg OD. He was subsequently referred to emergency department for acute renal injury.

Upon assessment in emergency department, patient was not tachypnoeic. His blood pressure was 146/98 mmHg, pulse rate 88 beat per minute, oxygen saturation of 100% under room air and temperature of 36.3°C. Abdomen was soft and non-tender. There was no renal angle tenderness. Other physical examinations were unremarkable.

His haemoglobin level was 8.6 g/dL and white blood cell was 7.5 x 10^9/L. All other blood results were within normal limit as shown in Table 1.

Urgent ultrasound kidney, ureter and bladder was performed. Moderate to gross bilateral hydronephrosis and hydroureter with tortuous bilateral ureters until bilateral vesicoureteric junction noted. However, no calculus seen. Circumferential urinary bladder wall thickening with trabeculation noted which may suggest chronic bladder outlet obstruction (Fig. 1). Prostate was homogenous and normal in size measuring 3.0 cm x 4.2 cm x 3.7 cm (Fig. 2).

Cystoscopy was subsequently performed and revealed multiple diverticuli with trabeculae of bladder wall. Small tumour approximately 0.5 cm visualized at bladder neck. Biopsy was taken and send for urgent histopathological examination.

Microscopically, the tissue showed fragment of bladder mucosa with focal hyperplastic urothelial lining without any dysplasia or papillary architecture. Invaginations of few well-defined clusters of urothelium forming a centrally dilated lumina were noted in the connective stroma (Fig. 3). No intestinal metaplasia was seen. No granuloma or evidence of malignancy detected. It was confirmed as cystitis cystica.

Patient subsequently underwent one episode of haemodialysis. He was well throughout admission and denied any difficulty urinating or episode of urinary retention. He was followed up regularly by medical team to assess his renal function. Renal replacement therapy could be initiated depending on his renal function. Long term antibiotic was given.

3. DISCUSSION

Exact aetiology of the cystitis cystica is unknown. Chronic inflammatory condition is thought to be the precursor. It is usually associated with recurrent urinary tract infection, chronic bladder outlet obstruction and prolonged catheterization [5]. It was proposed that infection was the underlying aetiology. This was mainly based on the fact that cystitis cystica mostly reported in patients with recurrent urinary tract infection. This hypothesis was strengthened with the apparent clinical improvement following eradication of bacteriuria in these patients [3].

Cystitis cystica developed when the proliferation of bladder urothelium invades the lamina propria. These invaginated cluster of transitional cells of bladder urothelium are termed as Brunn's nest. Over time, Brunn's nest may become cystically dilated and become what we known as cystitis cystica [5]. As mentioned previously, all these changes occurred microscopically and could only be diagnosed by histopathological examination.

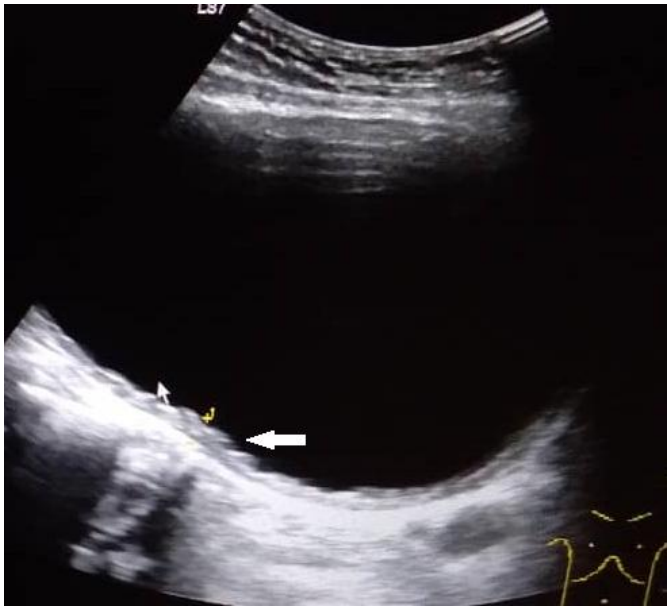

Fig. 1. Ultrasound showed urinary bladder wall thickening with trabeculation. Maximum thickness of bladder wall measuring 0.6 cm

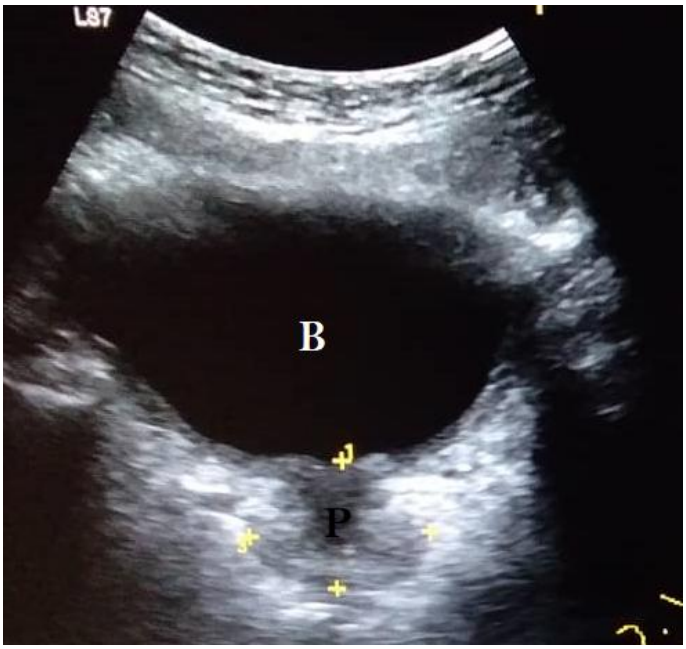

Fig. 2. Ultrasound showed homogenous prostate measuring 3.0 cm x 4.2 cm x 3.7 cm (B= Bladder & P= Prostate)

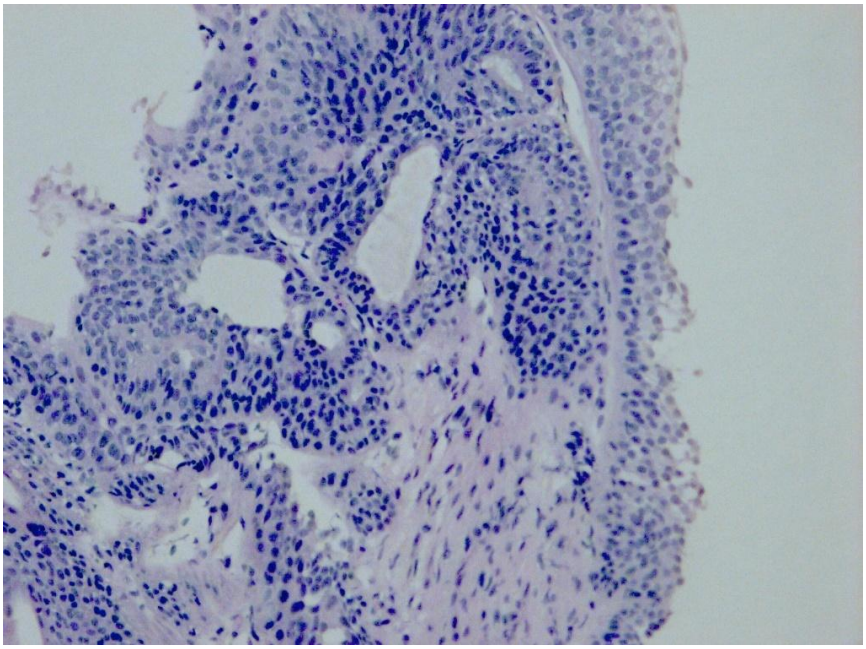

Fig. 3. Histopathogical examination showed focal hyperplastic urothelial lining with few well-defined clusters of urothelium forming centrally dilated lumen (at x 200 magnification)

Table 1. Blood result during admission

Blood Investigation	Result	Normal Value
Urea	38.7 mmol/L	2.76 mmol/L – 8.07 mmol/L
Creatinine	1882 umol/L	40 umol/L – 80 umol/L
Haemoglobin (Hb)	8.6 g/dL	11.5 g/dL – 18.0 g/dL
White Blood Cell (WBC)	7.5 x10^9/L	4.0 x 109/L – 11x109/L
Corrected Calcium	2.15 mmol/L	2.15 mmol/L – 2.55 mmol/L
Phosphate	2.1 mmol/L	0.81 mmol/L – 1.45 mmol/L
Venous Blood Gas		
pH	7.27	7.35 – 7.45
HCO3	14.7 mmol/L	21.0 mmol/L – 28.0 mmol/L
Lactate	1.3 mmol/L	
Base excess	-11.2 mmol/L	

Cystitis cystica predominantly affects the trigone and the bladder neck [6]. Cystitis cystica may appear as luminescent or pearly cyst with intact urothelium from the cystoscopy examination [7]. In most cases, it may appear normal or erythematous, owing to the chronic inflammatory process. In rare case, it may appear as large bladder mass [8,9,10].

Cystitis cystica, if presents as tumour or pseudo-tumour, must be distinguished from infiltrating carcinoma of the bladder, endo-cervicosis and nephrogenic adenoma [4].

Histological examination will show a centrally dilated lumen with well-defined nests of urothelium. No Goblet or columnar cells present in cystitis cystica as opposed to cystitis glandularis [7].

Patient with cystitis cystica may present with lower urinary tracts symptoms, dysuria and haematuria with or without abdominal pain. Parker reported that frequency and painful micturition were the most common presenting complaint, followed by haematuria [11]. Agrawal et al. however, revealed that haematuria was the most common presenting symptoms, followed by frequency and dysuria [5]. These symptoms are non-specific. Patient with cystitis cystica may be asymptomatic.

Imaging may be of little value to diagnose cystitis cystica. Ultrasound of kidney, ureter and bladder may reveal underlying associated pathology such as prostatomegaly, bladder tumour or bladder stone which may cause chronic bladder outflow obstruction. Milošević et al attempted to evaluate urinary bladder wall thickness as diagnostic tool for cystitis cystica. In their study, they concluded that urinary bladder wall (UBW) thickness of less than 3.9 mm had a negative predictive value of 100% which meant that the probability of having cystitis cystica was zero if the UBW thickness was less than 3.9 mm. Meanwhile, those with UBW thickness of more than 3.9 mm has positive predictive value of 95.2% which meant they are more likely to have cystitis cystica [12]. However, ultrasound will only guide toward the diagnosis. It could not be used as diagnostic tools as cystitis cystica is a histological diagnosis. Increase in UBW thickness may prompt the clinician to proceed with cystoscopy and biopsy, if needed as in our case.

Blood investigation may be normal. Urine analysis may show haematuria or evidence of infection, but will not pinpoint toward the diagnosis of cystitis cystica.

Treatment of cystitis cystica is usually tailor to the underlying pathology. Most of the literatures focused on the treatment of cystitis glandularis which was the progression of cystitis cystica or may develop in association with cystitis cystica. Agrawal et al reported complete resolution in 23.43% patients solely treated with transurethral resection. Recurrence was high with transurethral resection alone [5]. Capozza et al. reported no recurrence at 12-30 month following transurethral resection and long-term antibiotic [13]. Milošević et al. from their study of 127 patients with cystitis cystica also recommended regular and long-lasting antibiotic for treatment of this condition [4]. Long-term antibiotic is therefore recommended, guided by the urine culture and sensitivity. However, to our knowledge, there is no consensus on the duration of antibiotic. Risk of antibiotic resistance needs to be put into consideration when deciding the duration of antibiotic.

Other modalities have also been reported. Mitre et al. has trial intravesical bacillus Calmette-Guerin (BCG) injection weekly for total of 8 doses in recurrence glandular cystitis. However, resolution was only achieved after 2 cycles of treatment and after 2 years following the first dose of intravesical BCG injection [14]. Yuksel et al. prescribed oral steroid for 6 months in recurrent cystitis glandularis after attempted transurethral resection, partial cystectomy and intavesical BCG injection [15]. Other treatments that have been tried include intavesical steroid application and YAG laser administration [16,17]. However, all these modalities are based on case reports. Further studies may be needed before any sound recommendation could be made.

Regular cystoscopy was previously recommended as it is strongly believed that cystitis cystica is a premalignant condition or is associated with malignancy. However, since it is now proven to be benign condition, regular cystoscopy is no longer recommended. Smith et al in his study concluded that regular cystoscopy is not recommended [1]. This was supported by Agrawal et al who reported no progression to malignancy in 64 patients with median follow-up of 5 years and 5 months [5].

4. CONCLUSION

Awareness of cystitis cystica is important. Despite its being a benign condition, it may mimic other sinister condition such as malignancy. Unless confirmed by histopathology examination, all suspicious tumours should be treated as malignancy until proven otherwise. In general, transurethral resection with long term antibiotic are the gold standard treatment for cystitis cystica. However, further research and study need to be done to establish the optimal duration of antibiotic to prevent antibiotic resistance.

CONSENT

All authors declare that written informed consent was obtained from the patient's guardian for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTEREST

Authors have declared that no competing interests exist.

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