Case Report

A case of follicular cystitis treated successfully with diethylcarbamazine

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Abstract
Follicular cystitis is a non-specific inflammatory condition of the bladder where the aetiology is unknown. The extent of the disease can be mild or proliferative and bulky. Antibiotics, steroids, therapies used for interstitial cystitis, palliative cystectomy and radiotherapy have been reported as successful treatment options. We report a case of follicular cystitis that responded to a course of oral diethyl carbamazine.

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1. Introduction
Follicular cystitis is a rare inflammatory disease of the bladder that is more common in women. The condition was first described in 1856 by Cruveilhier [1]. The clinical features are non-specific and variable. Dysuria and frequency are the common features. The cystoscopy reveals white, gray or pink nodules on a background of erythematous mucosa [2]. Histopathologically it is characterized by formation of lymphoid follicles in the lamina propria of the bladder wall. Inflammation and bacterial infection are among the proposed aetiological agents, though exact cause is not yet established [2]. Various treatment modalities are available including antibiotics, anti-inflammatory drugs as well as surgical resection with varying success rates. Although symptoms are mild and non-specific in some, it could be disabling and non-responsive to pharmacological agents in a minority. Such resistant cases have been treated with radiotherapy and even cystectomy to relieve disabling symptoms [3].
2. Case report

A 46-year-old man sought medical advice for severe dysuria persisting for 3 months. He had an episode of visible haematuria in the past. He was a clerk by profession with no exposure to chemicals or smoking. His physical examination was unremarkable. His initial mid stream specimen of urine yielded a growth of coliforms. The subsequent urine cultures were continuously negative, but the patient continued to have persistent pyuria. His urinary tract ultrasonography and computed tomography (CT) urogram were normal. Mantoux test, urine for acid-fast bacilli and urine culture for *Mycobacterium tuberculosis* were negative. Serum indirect fluorescent antibody test (IFAT) for filariasis was negative. The cystoscopy showed yellowish nodules in a background of inflammatory changes. There was no tumour. Cystoscopic biopsy was performed.

Macroscopically, the biopsied specimen consisted of several fragments of tan-coloured soft tissue, largest measuring 4 mm×3 mm×3 mm and smallest measuring 3 mm×2 mm×1 mm. Microscopically the bladder mucosa was lined by non-dysplastic urothelium. The submucosa showed florid chronic inflammation with extensive lymphoid follicle formation (Fig. 1). Some lymphoid follicles contained germinal centres. The background showed moderate-to-severe chronic inflammation with oedema. There was no evidence of granuloma formation or caseous necrosis. There was no dysplasia or malignancy. The condition was diagnosed as follicular cystitis.

Despite several courses of antibiotics (ciprofloxacin 500 mg twice a day for 7 days), amitriptyline, potassium citrate and tolterodine, patient continued to have symptoms interfering with his day-to-day activities. A course of nitrofurantoin 50 mg once a day in the night for 3 months did not relieve his symptoms. Hence he was treated with oral diethylcarbamazine (DEC) 100 mg three times a day for 3 weeks. Six weeks later his symptoms were minimal and urinalysis was normal. Two years later patient remains asymptomatic with no pyuria.

3. Discussion

Follicular cystitis, though more common in women, can occur in men. The clinical presentation is variable, and the clinical features are non-specific. The common symptoms are frequency and dysuria, the latter being the presenting complaint in our patient. In view of the non-specific nature of symptoms, it is not surprising that these patients are often treated for bacterial cystitis prior to the diagnosis of follicular cystitis. Our patient initially had a positive urine culture and pyuria throughout the clinical course. In most instances, urinary tract ultrasonography is normal but may show a pseudo-tumour rarely.

The cystoscopy is helpful to identify the white, gray or pink nodules on an erythematous mucosa. These changes are most commonly seen in the area of the trigone. The cystoscopic appearance may resemble that seen in tuberculosis, though the degree of inflammatory changes visible is much less in follicular cystitis. The cystoscopic bladder biopsy provides the necessary information to arrive at a diagnosis and more so to exclude more sinister causes like bladder malignancy and tuberculosis. It shows well developed lymphoid follicles with germinal centres involving the mucosa and submucosa of the bladder wall [2]. There are numerous plasma cells and lymphocytes scattered within the mucosa and submucosa of the bladder wall. Absence of granulomatous inflammation with or without caseous necrosis excludes tuberculosis.

The differential diagnoses on the microscopy include malignancies such as follicular lymphoma and other non-Hodgkin lymphomas, granulomatous processes and cystitis with sporadic lymphocytes. These can be excluded by immunohistochemistry [2]. Aetiological factors include inflammation, bacterial infections, bladder outlet obstruction, repeated urinary tract infections particularly *Salmonella* associated cystitis, intravesical Bacillus Calmette-Guérin (BCG) treatment and intravesical chemotherapy.

Most patients have been treated with several courses of antibiotics by the time biopsy and histological diagnosis is made. Thereafter, various therapeutic agents have been attempted like prednisone, vitamin A, pentosan polysulfate sodium, dimethyl sulfoxide, amitriptyline and duloxetine [4]. Those who develop bulky infiltrative disease simulating a tumour have been treated with transurethral resection of the mass lesion, palliative cystectomy and radiotherapy. This patient was having less bulky disease and was treated empirically with DEC since filarial infestation and chyluria is common in the patient’s residing area [5]. His symptoms subsided with treatment though it could be incidental. Filarial cystitis is a well-known entity in endemic areas where patients may have features of persistent cystitis or even tumour like mass lesions. Hence the clinical presentation may mimic follicular cystitis. In filarial cystitis bladder mucosa shows a normal urothelium with mild degree of inflammation comprising of lymphocytes and eosinophils and microfilariae of *Wuchereria bancrofti* can be seen in the bladder wall rarely [6,7].

![Figure 1](image-url)  
**Figure 1** Histopathological examination of bladder biopsy. (A) Multiple lymphoid follicle within the lamina propria (H&E, 40×); (B) Lymphoid follicle with germinal centers (H&E, 100×); (C) Inflammation in the lamina propria (H&E, 400×).
our patient, microfilariae were not seen in the biopsy specimen and serum IFAT for filariasis was negative though there was a good response to DEC. Several recent studies have investigated the efficacy of DEC in inflammatory conditions like lung injury and acute hepatitis [8,9]. Accordingly DEC has strong anti-inflammatory effects which may have lead to improvement of the chronic cystitis of our patient.

4. Conclusion

In cases of follicular cystitis not responding to usual forms of treatment, it may be worth trying a course of DEC before embarking on more invasive and aggressive forms of therapy.

Author contributions

Study design: Maduwe Gedara Sagara Ruwan Kumara, Anurudda Abeygunasekara.
Data acquisition and analysis: Prasnga Thiranagama.
Drafting manuscript: Maduwe Gedara Sagara Ruwan Kumara.
Critical revision of manuscript: Anurudda Abeygunasekara, Cherine Sosai.

Conflicts of interest

The authors declare no conflict of interest.

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