Case - Eosinophilic cystitis in a patient with COVID-19: From rash to bladder mass

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INTRODUCTION

KEY MESSAGES

- EC can mimic bladder tumors, needing cystoscopy and biopsy to rule out malignancy.
- Consider EC after COVID-19 infection if a patient has atypical urinary symptoms.
- Multidisciplinary care (urology, immunology, hematology) is vital for best diagnosis and treatment.

Eosinophilic cystitis **(**EC) is a rare inflammatory condition of the bladder, with its cause, underlying mechanisms, and treatment options still not well understood. The incidence of EC is unknown, and it can occur at any age, with no particular predilection for sex or ethnicity.(1) Commonly reported symptoms are dysuria, haematuria, and pain.(2) There are no specific imaging findings suggestive of EC; however, cystoscopy with bladder biopsy is the key procedure for the diagnosis. Cystoscopy typically reveals an inflamed, ulcerated, oedematous or necrotic mucosa. In some cases, a mass that mimics a true tumour may also be observed.(3) Histopathological diagnosis is defined by eosinophilic infiltration of the bladder wall, mucosal fibrosis, and muscle necrosis.(2)There is no established treatment consensus due to its rare occurrence, but effective treatments typically include antihistamines, corticosteroids and nonsteroidal anti-inflammatory drugs, though in some cases, surgical intervention may be necessary.(1) In this context, to the best of our knowledge, we present the first case of EC that developed following COVID-19 exposure.

Case report

A man in his twenties with a complex medical history, including global developmental delay, cerebral palsy, and epilepsy, presented to the emergency department passing blood clots in his diaper. This presentation occurred two weeks after he had tested positive for SARS-CoV-

2, for which he was treated with Remdesivir and Dexamethasone and had shown clinical improvement. He was voiding freely with no history of chronic catheterization. On examination, the patient was vitally stable with a soft and lax abdomen. Laboratory tests revealed a haemoglobin level of 142 g/L, white blood cell count of 7.8 x10^9/L, platelets of 228 x10^9/L , creatinine of 38 µmol/L, and a notable eosinophilia at 11.9%. Urine culture was negative and urine cytology revealed atypical urothelial cells. A contrast-enhanced computed tomography of the abdomen and pelvis (Figure 1) showed diffuse bladder wall thickening, which appeared mass-like, without associated hydronephrosis. Cystoscopy revealed a mass approximately 4 cm in size on the left lateral bladder wall. The patient subsequently underwent transurethral resection of the bladder tumor (TURBT). Histopathology confirmed pseudotumoral eosinophilic cystitis (Figure 2). During hospitalization, a multidisciplinary approach involving hematology and allergy specialists was implemented. Treatment with antihistamines and corticosteroids was initiated, resulting in the normalization of eosinophil counts. The patient was discharged home in stable condition. A telephone follow-up with the patient's mother at three months revealed resolution of the haematuria, and the patient remained asymptomatic. A follow-up cystoscopy performed one year later demonstrated complete resolution of the lesion with normal-appearing bladder mucosa. Relevant past history included an extensive urticarial rash and eosinophilia that occurred three years prior, 28 hours after receiving the COVID-19 mRNA vaccine. A skin biopsy at that time showed an inflammatory infiltrate with numerous eosinophils and focal vasculitis, which resolved with a short course of corticosteroids.

DISCUSSION

EC is a rare inflammatory condition of the bladder. While the exact cause remains unclear, previous reports have linked it to allergic reactions, bacterial infections, parasitic infestations, medications, and various other medical conditions.[4] Our patient exhibited a temporal association with COVID-19 exposure and subsequently developed hypereosinophilia and eosinophilic cystitis. However, it is essential to emphasize that this association remains a hypothesis, not a proven causal relationship. No current evidence definitively establishes SARS-CoV-2 as a direct trigger of EC. This distinction is important to avoid overinterpretation, especially considering the rarity and multifactorial nature of EC. Existing literature suggests that eosinophilic disorders may be unmasked or exacerbated by immune stimuli. Reports in the literature have associated EC with viral infections such as BK virus and Epstein-Barr virus, and opportunistic fungal infections like *Candida glabrata*. Table 1 summarizes these related cases. The clinical symptoms of EC are varied and often unusual, with common manifestations including frequent urination, urgency, dysuria, haematuria, and pelvic pain, among others.[2] The diagnostic significance of laboratory tests for EC is limited. Approximately 43% of patients with EC exhibit eosinophils constituting more than 5% of their total white blood cells.[5] Urine cultures are generally negative; however, in cases with concurrent bacterial infections, there may be an increase in urine white blood cell counts, and urine cultures could yield positive results. Similarly, the specificity of imaging studies is also limited, with the primary indicators being irregular bladder wall thickening and the presence

of focal masses.[6] Together, these findings highlight the challenges in accurately diagnosing EC. Pathological examination is the primary method for diagnosing EC. This analysis often demonstrates substantial infiltration of eosinophils in both the bladder mucosa and muscularis. Currently, there is no established standard therapeutic protocol for EC, leading to a range of reported medical regimens. These include antibiotics, antihistamines, corticosteroids (both oral and intravesical), and nonsteroidal anti-inflammatory drugs.[1] Although some researchers suggest that EC may be a self-limiting disease,[6] it is important to note that it can progress into a diffuse and aggressive form, which is resistant to medical treatment. Antibiotics can be appropriately utilized for patients presenting with bacterial infections. If a patient's condition continues to deteriorate despite conservative management, combined transurethral resection may offer a more effective solution. Furthermore, in instances where symptoms persist following both medical treatment and transurethral resection, more invasive options such as partial cystectomy, total cystectomy, or urinary diversion may need to be considered.[7] The variability in treatment approaches underscores the importance of individualized patient care and the need for further research to establish more definitive treatment guidelines for EC.

CONCLUSIONS

This case links EC to COVID-19 exposure in a patient with a complex history. EC's exact cause is unclear, but this suggests SARS-CoV-2 may trigger eosinophilic responses. Clinicians should consider eosinophilic disorders in patients with unusual urinary symptoms post COVID -19 exposure. Further research is needed to guide EC diagnosis and management related to COVID-19, ensuring timely and appropriate care.

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FIGURES AND TABLES

Figure 1. Contrast-enhanced computed tomography (CT) scan (axial section) showing a diffuse bladder wall thickening, most pronounced in the left wall, where it appears mass-like and measures up to 3.7 cm in thickness (indicated by the arrow), with areas of mild extension beyond the bladder wall, measuring at least 0.9 cm.

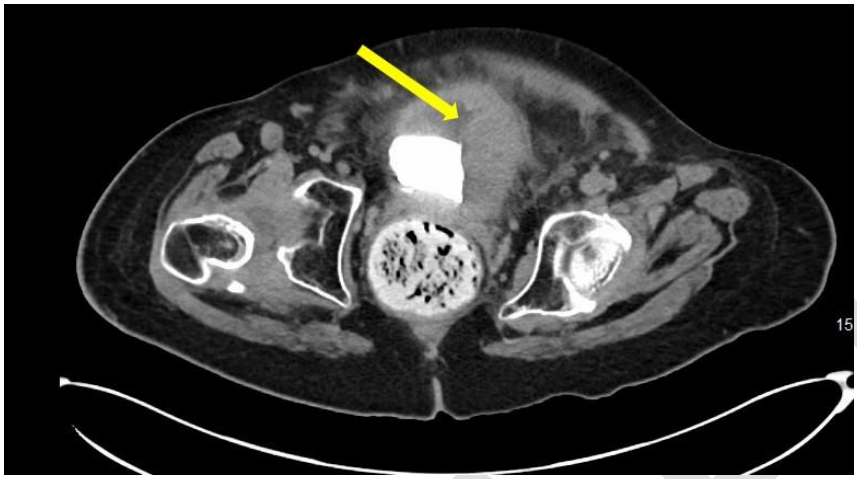

Figure 2. Histopathologic images of the bladder biopsy showing features of pseudotumoral eosinophilic cystitis (H&E stain) at multiple magnifications: (A) The lamina propria is congested, hemorrhagic and expended with heavy inflammation as well as urothelial proliferation located at the superficial lamina propria. H&E 40x). (B) Urothelial thickening with reactive changes and Von Brunn s nests. Heavy eosinophilic inflammatory infiltrates involving the epithelium with eosinophil micro abscesses. The lamina propria is congested and expended with heavy eosinophil predominant inflammation. (H&E 100x). (C) Heavy Eosinophilic inflammatory cellular infiltrates identified deep within the muscularis propria detrusor muscle fascicles. H&E (200x).

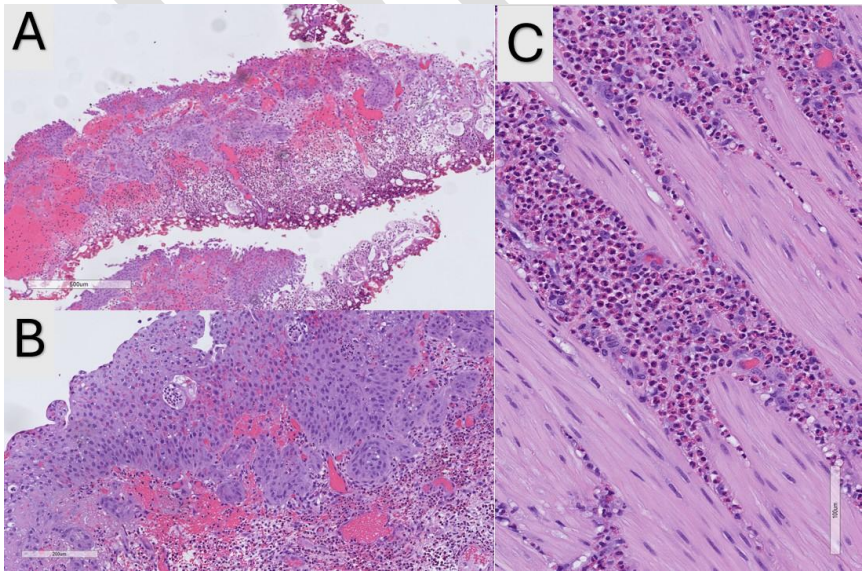

Table 1. Eosinophilic cystitis cases and associated conditions/triggers					
Clinical manifestations and functional outcomes in children with eosinophilic cystitis	Thompson et al. (2005)[8]	5–18 years (mean 10.8), 3M/1F	Viral infections (EBV, URTI), allergic disease background	Dysuria, frequency, haematuria; 2 cases with bladder masses mimicking malignancy	3 resolved with conservative care (antihistamines/NSAIDs); 1 required partial cystectomy
Eosinophilic cystitis caused by Candida glabrata: A case report	Duong & Goodman (2019)[9]	61/M	Candida glabrata infection	Urinary frequency, urgency, nocturia, prior gross hematuria; bladder wall thickening and ulceration	2-week oral fluconazole → symptom resolution; bladder biopsy confirmed complete resolution of EC

EBV: Epstein-Barr virus; NSAIDs: non-steroidal anti-inflammatory drugs; URTI: upper respiratory tract infection; UTIs: urinary tract infections.