Urological Complications of Hirschsprung-Related Crohn's Disease: A Case Report

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ABSTRACT

Hirschsprung disease (HSCR) is a rare congenital intestinal disease characterized by the absence of ganglion cells in the myenteric and submucosal plexuses of the intestine. Individuals with HSCR demonstrate a higher risk for inflammatory bowel disease (IBD), with Chron's disease (CD) commonly observed. Renal and urinary involvement is reported by between 4 and 23% of IBD patients, which manifests as urinary calculi, fistulas, and ureteral obstruction, which causes hydronephrosis. Those conditions can lead to a predisposition to recurrent urinary tract infections (UTIs) and should be suspected in male patients with IBD. A 26-year-old male with a history of HSCR and multiple surgeries presented with recurrent UTIs over 3 months. Upon further evaluation, he was found to have hydronephrosis in both kidneys. An MRI of the abdomen with contrast showed thickening and fibrosis in contact with the posterior wall of the rectum, causing a narrowing of the bilateral ureter. This clinical case has been reported to raise awareness of urological complications in CD patients with a history of HSCR, with recurrent UTIs as the presenting symptom.

Keywords: *Chron's disease, Hirschsprung disease, hydronephrosis, ureteral obstruction.*

INTRODUCTION

Hirschsprung disease (HSCR) is a rare congenital intestinal disease characterized by the absence of ganglion cells in the myenteric and submucosal plexuses of the intestine.[1] Recent studies have shown that individuals with HSCR have a five-time higher risk for inflammatory bowel disease (IBD) than individuals without it.[2] Chron's disease (CD) is usually one of the more common types of IBD and is considered to have an incidence of 72.3%.[3,4] Although the pathophysiological link between the two diseases is not yet fully understood, there are similarities concerning altered microbiota and inflammatory responses.[5]

Extraintestinal manifestation of IBD occurs in 6–47% of patients and can involve almost all organ systems. There are several possible mechanisms for this involvement, including (1) systemic reactive manifestation directly related to intestinal inflammation and disease activity; (2) susceptibility to autoimmunity independent of IBD; (3) deposition or formation of an immune complex; and (4) secondary metabolic and anatomic disturbances (referred to as complications). In IBD patients, renal and urinary involvement was reported by 4–23% of patients, which manifested as urinary calculi, fistulas, and ureteral obstruction, which caused hydronephrosis.[6,7] These conditions can cause

a predisposition to recurrent urinary tract infections (UTIs) and should be suspected in male patients with IBD.[8]

We present a clinical case that highlights the urological complications in a CD patient with a history of HSCR, further complicated by recurrent UTIs.

CASE ILLUSTRATION

A 26-year-old male presented to the emergency department with complaints of persistent high-grade fever for a week prior. He also had abdominal pain, nausea, and a low appetite. Laboratory examinations found marked leukocytosis of 21.8 x 10^3/mcl, a procalcitonin level of 91.26 ng/mL, increased lactic acid of 4.4, and increased creatinine of 4.3 mg/dL. A urinalysis showed pyuria with positive leukocyte esterase and nitrite. He was diagnosed with urosepsis and started on a broad-spectrum antibiotic Meropenem 1000 mg BD (renal adjustment dose) for 5 days. His symptoms subsided and creatinine levels improved to 1.6 mg/dL. Urine culture and sensitivity (C/S) showed >100.000 CFU/ml of *Klebsiella pneumoniae* sensitive to Fosmoycin and resistant to Fluoroquinolone, Carbapenem and Cephalosporine and *Pseudomonas aeruginosa* sensitive to Gentamycin, Kanamycin, 4th generation Cephalosporine, Fluoroquinolone, and Carbapenem. Stool C/S was also performed and showed >100.000 CFU/ml of *Klebsiella pneumoniae* with the same sensitivity result. The blood culture was sterile. A kidney ultrasound showed a normal-sized kidney with increased echo density and no stone or cyst. He had a history of prior episodes of UTIs a month prior, which showed urine C/S with *E. coli* >100.000 CFU/ml sensitive for Cotrimoxazole, Tetracycline, Pipemidic acid, Cefotaxime, Ceftriaxone, Cefepime, Fosfomycin, Imipenem, and Levofloxacine. He was given a 5-day course of Ceftriaxone, which resulted in the resolution of his clinical symptoms.

The patient has a known history of HSCR, and he was diagnosed when at 1.5 years of age. He underwent a total of 6 surgeries, including a Duhamel procedure, colostomy procedure, stoma repair, and ileostomy procedure. The last procedure he had undergone was stoma closure at age 14. He had no significant symptoms until 7 months prior when he began experiencing bloody stools, diarrhea, and weight loss. The patient underwent a colonoscopy, which revealed a giant ulcer in his rectum and ileitis with multiple ulcers (**Figure 1**). An abdominal CT scan with contrast was performed, which showed a thickening of the mid-high rectal wall with stenosis, adhesions with the surrounding bowel, a suspected small bowel fistulation, suspected CD with fibro-stenosing, and fistulating disease. There was thickening, fibrosis, and soft tissue edema in the presacral space with infiltration of the posterior wall of the rectum, and bilateral ureters that caused hydro ureter and bilateral hydronephrosis (right grade II, left grade IV). A biopsy confirmed the diagnosis of CD, and he was started on Sulfazalazine 1000 mg TID.

Due to suspected fistulating disease, an abdominal MRI with contrast and fistulography was performed. It showed visible contrast thickening and fibrosis accompanied by foci of air obliterating the presacral fat space. They measured approximately 1.5 x 5.5 x 5.1 cm and were in contact with the posterior wall of the rectum, causing a narrowing of the bilateral ureter (**Figure 2**). Neither an abscess nor a fistulation were observed. A repeat colonoscopy 4 months later showed a normal result (**Figure 1**).

A urology consultation was made due to the hydronephrosis of both kidneys. A cystoscopy and anterograde and retrograde pyelography revealed partial stenosis on the ureterovesical junction and S4 kinking on the right side, causing mild-to-moderate hydronephrosis and total stenosis at the sacroiliac (SI) joint on the left side. A cystoscopy showed hyperemic mucosa, minimal trabeculation and no diverticula, mass, or stone. He underwent a double J stent procedure on his right ureter and a percutaneous nephrostomy (PCN) on his left kidney.

Surgery was initially considered for a more definite diagnosis and treatment of the suspected mass and fibrosis around the presacral space, but it was considered high risk in his condition. Medical treatment with an anti-tumor necrosis factor (TNF), Infliximab, was going to be administered due to the fibro-stenosing nature

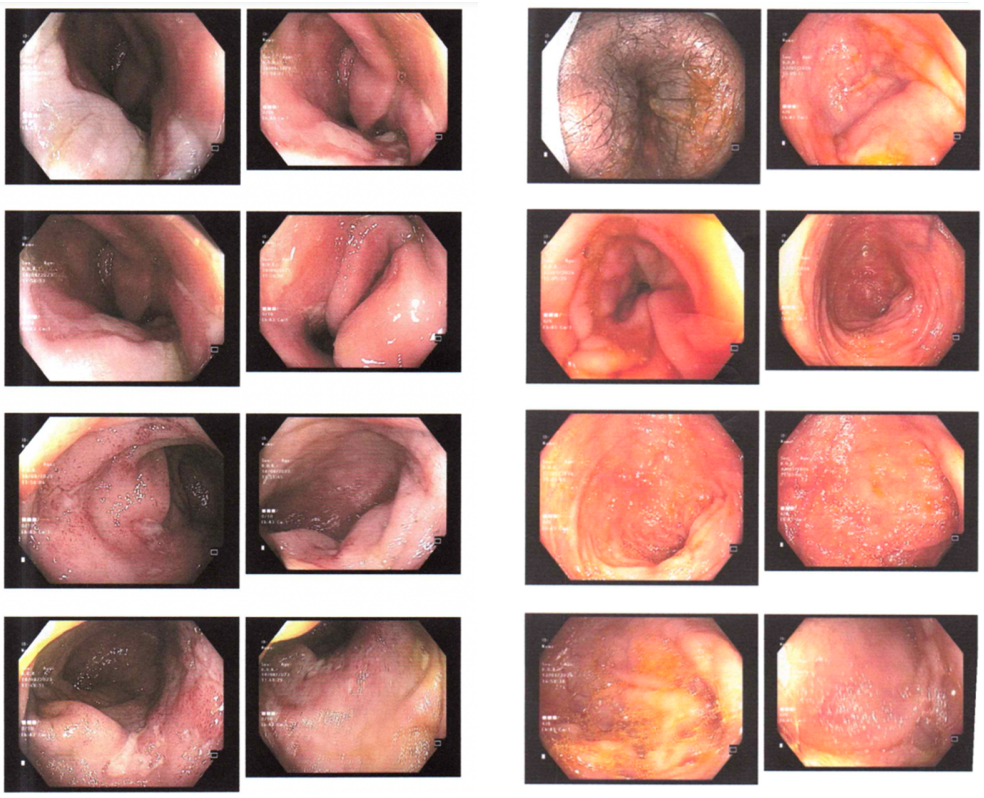

Figure 1. Right side: An initial colonoscopy showed a giant ulcer in the rectum with a clean base and ileitis with multiple ulcers. Left side: Repeat colonoscopy 4 months after medical treatment showed a normal colonoscopy.

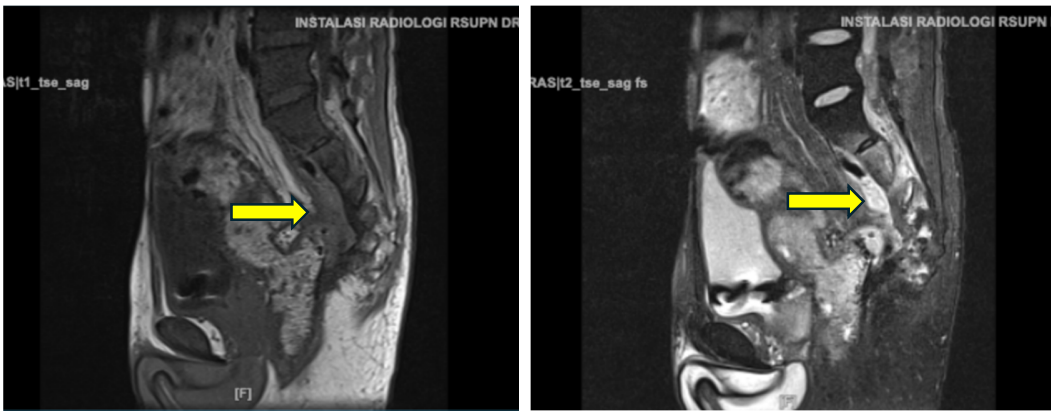

Figure 2. MRI abdomen with contrast showing visible contrast thickening and fibrosis accompanied by foci of air obliterating the presacral fat space measuring approximately 1.5 x 5.5 x 5.1 cm (arrow).

of his CD, however, he had another episode of UTI with the multi-drug resistant *Klebsiella pneumonia.* He was treated with another course of antibiotics and, after his symptoms subsided, he was given 3 grams of Fosfomycin every 10 days as a prophylaxis antibiotic.

DISCUSSION

Inflammatory bowel disease in patients with HSCR is a rare condition with a reported incidence of 2%, with a predominance of CD.[9] It may present around the same age as a patient without HSCR, usually in adolescence or adulthood after neonatal surgical HSCR treatment.[10] This case is of a young adult male who presented with IBD at the age of 25. Other, similar cases also reported adolescent and young-adult presentations of IBD with a history of HSCR diagnosed at 17[11] and 34 years of age.[12] However, one study with 55 patients showed an

earlier age of onset, with 50% of patients being under the age of 5.[9]

It is still unclear whether IBD in HSCR patients is a consequence of the disease or a separate disease etiology entirely; however, they share the same pathophysiology of altered microbiota and inflammatory response.[5] These mechanical factors might affect the gut microbiome and allow colonization overgrowth or alterations in patients with HSCR, which may predispose them to chronic inflammatory changes.[13] As a result, it could disrupt host–gut microbiome interactions, which are likely to contribute to the development of IBD.[13,14]

One of the key findings in this case was the thickening and fibrosis of the soft tissue in the presacral space, which caused ureter stenosis. This condition might be attributed to the patient's history of multiple surgeries, or it could be an extraintestinal manifestation of IBD that exacerbated the underlying pathology. The first hypothesis is less likely, as the patient had been symptom-free for the past ten years following the last surgery, with urinary symptoms only emerging after IBD diagnosis. Extraintestinal manifestation of IBD occurs in 6–47% of patients and can involve almost all organ systems, including the urinary tract,[6,7] And can be followed by fistula formation. It is considered that 35–40% of patients will develop at least one fistula throughout their disease.[15]

In this case, a fistula was initially suspected due to the recurrent UTI, and the same organism was found in the patient's urine and stools. A CT scan supported this possibility. The pathogenesis of fistulas is complex, involving a combination of the upregulation of pro-inflammatory cytokines, genetic susceptibility, epigenetic changes, and the possible influence of intestinal microbiota on a chronic, transmural inflammation-creating sinus tract.[15] However, further tests, including an abdominal MRI with contrast and a fistulography, ruled out the presence of a fistula. MRI has the sensitivity and specificity of 100% and 86% to detect fistula tracks and 96% and 97% for abscesses.[16] Additionally, a cystoscopy and colonoscopy did not reveal any fistulae, but their diagnostic yield is low, with a sensitivity of 34% and 7%, respectively.[17] The patient also did not exhibit the typical symptoms of an entero-urinary fistula, such as pneumaturia, fecaluria or hematuria.

The patient presented with a urological complication from CD, manifesting as bilateral hydronephrosis. Previous studies have reported that urological complications in CD mainly arise due to (1) the development of phlegmon with inflammation and retroperitoneal fibrosis; (2) the presence of abscesses or fistulas in the anterior retroperitoneal compartment; (3) a dense cicatrix encasing the ureter.[7,18,19] The patient presented with a right ureter stenosis at the level of S4 and a left ureter at the level of the SI joint. This is under the literature, which indicates that obstruction typically occurs at the level of the linea terminalis, predominantly on the right side.[18]

The patient experienced three episodes of UTIs within three months, meeting the criteria for recurrent UTIs.[20] Particularly in males, recurrent UTIs may indicate underlying structural abnormalities or immunological disorders.[8,20] The patient has several risk factors for recurrent UTIs, including a suspected entero-urinary fistula due to CD, the presence of a double J stent, and a percutaneous nephrostomy (PCN). These factors, along with diarrhea from CD, increase the risk of infection. [21]

The primary treatment for CD-related ureteral obstruction is drainage of the affected kidney using a double J stent or PCN.[7] However, these devices can become colonized by microbial flora, leading to infections like pyelonephritis, abscesses, and, potentially, sepsis.[22,23] Infections associated with catheters in the upper urinary tract (CUUT) are associated with significant morbidity due to multidrug-resistant (MDR) organisms, with *Pseudomonas spp., E. coli*, and *K. pneumoniae* being common pathogens.[22,23] This patient's urinary culture confirmed the presence of MDR *K. pneumoniae, E. coli*, and *P. aeruginosa*.

Due to the high frequency of UTI recurrence, antibiotic prophylaxis may be considered in this case with a duration ranging from 6 to 12 months. Commonly used antibiotics are Trimethoprim-Sulfametoxazole (40 mg/200 mg once daily, 40 mg/200 mg thrice weekly), Nitrofurantoin

(50–100 mg daily), Cephalexin (125–250 mg daily) and Fosfomycin (3 grams every 10 days), however, due to increased concerns regarding antibiotic resistance, non-antibiotic prophylaxis, such as cranberry extract, can be considered for this patient. Due to its proanthocyanidins (PACs) that prevent the adhesion of bacteria to the urothelium, cranberry extract has been the subject of interest in several randomized control trials (RCTs). Other alternatives with insufficient evidence to support their efficacy were lactobacillus, D-mannose, methenamine, herbs/supplements, intravesical hyaluronic acid/chondroitin, biofeedback, and immunoactivity therapy.[24]

Depending on the severity of the presenting symptoms, CD requires medical management or surgical intervention. For fibro-stenosing disease caused due to CD, medical treatment is the first choice, with surgical resection being the definite treatment.[25,26] Treatments with corticosteroids can be considered, and anti-TNF agents have shown high clinical results in patients with CD and strictures.[26] Absolute contraindication of anti-TNF drugs is concomitant with abscesses, as it can facilitate sepsis progression.[27] In this current case, Infliximab was considered to treat the patient's condition, however, recurrent UTIs complicated the timing of therapy. Infliximab is also not covered by Indonesia's National Insurance Policy and is expensive.

The patient was considered for surgery to evacuate the mass on the presacral space as the underlying pathology of ureter stenosis. Surgery should be considered in symptomatic CD strictures and remains the standard treatment, with sustained remission achieved in 99% of patients.[25,26] However, surgery treatment is complex and can be extremely demanding, due to dense adhesions. Chronic inflammatory processes can also cause large inflammatory masses.[27] In this case, while surgery is normally the definitive treatment, the high-risk nature of the procedure made medical management the preferred option.

CONCLUSION

Patients with HSCR-related IBD are at an increased risk for urological complications, which underscore the interplay between gastrointestinal and urological systems, especially in this case. Recurrent UTIs, especially in male patients, can be caused by multiple factors and should be treated according to the underlying cause. It also emphasizes the importance of early recognition and treatment of urological complications to prevent long-term renal damage.

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