Journal of Inflammation Research Dovepress

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Atypical Presentation of Small Bowel Crohn's Disease: Case Report of Musculoskeletal and Hepatic Complications Without Gastrointestinal Symptoms

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Abstract: Herein, we described a case of small bowel Crohn's disease with recurrent, unexplained fevers, pain in the right lower back, hip, and groin area over 20 months. The patient did not present any gastrointestinal symptoms and colonoscopy showed no abnormalities. Imaging revealed a liver abscess and multiple lesions with pneumatosis in the muscles of the right lower back region. Initially, disseminated infection was suspected and the antibiotics was administered without success. Subsequently, Magnetic resonance (MR) enterography suggested the possibility of a small bowel fistula which was confirmed during exploratory laparotomy. Inflammation was prominent in a 27-cm segment starting from 30-cm proximal to the ileocecal junction. The segment was resected and pathological examination confirmed Crohn's disease. Postoperatively, mesalazine was administered, but showed limited efficacy. After modifying the treatment plan to infliximab and azathioprine, the patient was symptom-free and no obvious inflammation was found in the colonoscopy reexamination.

Keywords: small bowel Crohn's disease, extraintestinal manifestations, inflammatory bowel disease, liver abscesses

Introduction

Crohn's disease, an inflammatory bowel disease, primarily affects the intestines and is characterized by abdominal pain, diarrhea and weight loss.[1] However, Crohn's disease is a multisystem disorder that can impact nearly every body system. Therefore, extraintestinal manifestations (EMIs) occur in up to half of patients, but rarely alone. EIMs include ocular (uveitis, episcleritis, scleritis), oral (aphthous stomatitis, periodontitis, orofacial granulomatosis), dermatological (erythema nodosum, pyoderma gangrenosum, psoriasis, Sweet's syndrome), respiratory (granulomatous disorder), hepatobiliary (primary sclerosis cholangitis, autoimmune hepatitis), pancreatic (acute idiopathic pancreatitis, autoimmune pancreatitis), and musculoskeletal (peripheral and axial spondyloarthritis and enthesitis) manifestations.[2,3] Moreover, EIMs in Crohn's disease may vary and manifest subtly, relying on factors such as site, presentation, and intensity. Consequently, this can lead to diagnostic delays.[4]

The diagnosis of Crohn's disease relies on a comprehensive approach including clinical symptoms, imaging findings, endoscopy and histopathological examination. Histopathology and endoscopy are considered the gold standard.[2] Microscopically, typical features of Crohn's disease include focal chronic inflammation, discontinuous crypt distortion, granulomas and irregular villous architecture.[5] Due to the colonoscopy only allows visualization of the terminal ileum, it

Received: 16 October 2024
Accepted: 10 December 2024
Published: 16 December 2024

may misdiagnose small bowel Crohn's disease. While capsule endoscopy (CE) and non-endoscopic techniques such as computed tomography enterography (CTE), magnetic resonance enterography (MRE), and intestinal ultrasound (IUS) have important diagnostic value for small bowel Crohn's disease.[6]

Previously, the treatment options for Crohn's disease were limited to 5-aminosalicylates, corticosteroids, and immunomodulators. However, the introduction of infliximab, an anti-TNF therapy, has shifted the treatment goal from clinical response to endoscopic healing.[7] Additionally, surgical intervention is necessary for patients with severe acute colitis, colonic stenosis or fistulas, as well as refractory cases.[8]

Case Presentation

A 47-year-old man presented with fever and aggravating pain involving the pelvic region and the right lower back for the past 20 months. A physical examination upon presentation revealed 38.7°C body temperature and tenderness of the right lower back. Lab testing revealed elevated hypersensitive C-reactive protein (CRP; 78 mg/L; normal reference range: <6 mg/L), elevated erythrocyte sedimentation rate (ESR; 39 mm/hr; normal reference range: 1–15 mm/hr) and increased ferritin (490 μg/L; normal reference range: 30–400 μg/L). The urine analysis showed slight proteinuria and positive urobilinogen (1+). Fecal occult blood test was positive. Blood routine and biochemical examinations were unremarkable. A close inspection of past history revealed recurrent fever and localized infection that involved the musculoskeletal system, urinary system and digestive system during the past 20 months.

The first episode occurred 20 months ago, with fever and pain in the right lower back, groin and lower limb. Plain computed tomography (CT) scan of the lumbar spine at the time showed swelling of presacral soft tissue and right iliopsoas muscle with pneumatosis, blurred anterior sacral foramina, and bone sclerosis adjacent to the lesion (Figure 1A–C). After treatment with anti-inflammatory and pain-relieving medications, symptoms alleviated but recurred after 3 months. A CT urogram revealed dilated ureter and kidney hydronephrosis on the left side (Figure 1D). Magnetic resonance (MR) of the lumbar spine revealed swelling and gas accumulation in the right psoas major muscle, and an abscess in the right iliopsoas muscle (Figure 1E–G). Plain abdominal CT scan suggested thickening of the small intestine wall and adhesion between adjacent segments of the small intestine in the presacral region (Figure 1H). Lab testing showed increased hypersensitive CRP (16 mg/L) and ESR (41 mm/hr), as well as red blood cells in the urine. Estimated Glomerular Filtration Rate (eGFR), creatinine, tumor markers, and routine stool tests were unremarkable. Since there was no history of exposure, no positive findings detected in the chest CT, and the results for QB-SPOT.TB and acid-fast culture were negative, intestinal tuberculosis (ITB) has been ruled out, eliminating the need for empirical anti-tuberculosis treatment. The patient has no epidemiological setting or recent travel history, no acute onset of symptoms, or positive results from fecal microbiological examination. Infectious enteritis has been ruled out as well. At that time,

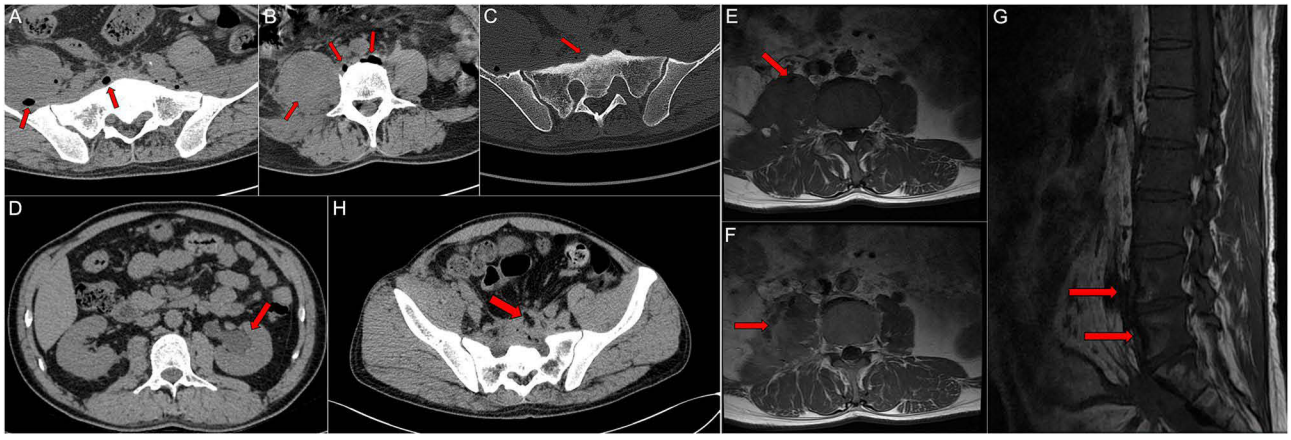

Figure 1 CT scan of the lumbar spine. (**A and B**), pneumatosis in the presacral and lumbar soft tissues and the right psoas major muscle. (**C**) bone sclerosis adjacent to the swollen soft tissue. (**D**) CT urogram showing dilated ureter and hydronephrosis in the left kidney. MR scan of the lumbar spine. (**E**) swollen right psoas major muscle. (**F**) axial view of enhanced MR showing gas accumulation in the muscle with peripheral signal enhancement. (**G**) sagittal view of enhanced MR showing inflammation and abscess formation in the right iliopsoas muscle. (**H**) abdominal CT scan showing indistinct demarcation between the thickened adjacent small intestine wall.

disseminated infection was considered. Symptoms and signs alleviated after empirical antibiotic treatment, initially with cefuroxime (1 g/d) and then cefdinir (0.3 g/d). Prescription upon patient discharge included linezolid (1.2 g/d) and amoxicillin (1.5 g/d). Mild symptoms persisted, and an enhanced abdominal CT scan showed pneumatosis in right psoas major muscle.

Seven months after the initial episode, the patient presented with worsening pain in the right hip and groin area, and claudication. A positron emission tomography (PET)-CT scan revealed multiple abscesses in the liver (Figure 2A), right psoas major muscle, quadratus lumborum muscle, left pararenal posterior space, lumbosacral vertebral body and anterior soft tissue, bilateral iliopsoas muscle, piriformis muscle, and lumbosacral vertebra. Bacteria culture and next-generation sequencing (NGS) of the liver abscess drainage revealed the presence of streptococcus intermedius. The finding was consistent with severe gingivitis of the patient. Gastroscopy and colonoscopy revealed chronic non-atrophic gastritis and a few small polyps in the transverse colon. The results of antinuclear antibody (ANA) profile, HLAB27 gene determination, anti-cyclic citrullinated peptide (anti-CCP) antibody, vasculitis-related tests were all negative. Additionally, IgG4 levels were within normal range. Therefore, main rheumatic diseases have been ruled out. Chronic streptococcal infection derived from digestive tract combined with anaerobic infection was considered. The patient was treated with ceftriaxone (2 g/d) and metronidazole (1.5 g/d), and symptoms rapidly alleviated. A repeated CT showed dissipation of pneumatosis and reduction in hepatic abscess. The patient remained well for about one year before the current episode.

Based on the findings of abdominal CT scan and the presence of multiple infection sites, we considered the possibility of small intestinal perforation and fistula formation. A MR enterography revealed thickening of the distal small intestine wall and sacrococcygeal paravertebral empyema, but failed to identify intestinal fistula (Figure 2B–C), suspecting Crohn's disease. The patient underwent exploratory laparotomy. It revealed a segment about 30-cm proximal to the ileocecal junction adhered tightly to the right pelvic floor, accompanied with sinus and local ulceration (Figure 2D). A 27-cm segment was resected followed by side-to-side anastomosis, abscess incision and drainage, and indwelling D-J tubes (Figure 2E–F). Pathological examination revealed features that were consistent with Crohn's disease, including cobblestone appearance, overt inflammation, local lymphoid follicular hyperplasia, active ulcers, non-caseous granuloma, as well as pyloric gland metaplasia (Figure 3). After the surgery, the patient was treated with mesalazine (4 g/d) for anti-inflammatory purpose for a month. However, CT enterography (CTE) indicated inflammation at the anastomosis site and multiple segments of ileum. Consequently, the revised treatment plan included a combination of infliximab (400 mg) and azathioprine (50 mg/d). The CTE 4 months later indicated minimal inflammatory. At the last follow-up, two years after surgery, the patient was free of symptoms and signs.

Discussion

The patient presented with recurrent infection that primarily involved the muscles in the right lower back and hip, which later progressed to muscle and liver abscesses, but never had gastrointestinal symptoms. A diagnosis of small bowel Crohn's disease was not made until 20 months later during exploratory laparotomy.

The patients of Crohn's disease may only present as EIMs, leading to missed diagnosis. EIMs as the initial and main clinical features have been previously reported in several case reports. George et al reported a 20-year-old Indian woman with 18-month pain and muscle cramps in all 4 extremities and progressive weakness.[9] A diagnosis of osteomalacic myopathy was made based on the extremely low vitamin D level until eventual diagnosis of Crohn's disease based on colonoscopy biopsy. After receiving intestinal anti-inflammatory treatment and vitamin supplementation, the patient's symptoms were alleviated. Cutaneous metastatic Crohn's disease is a frequently overlooked condition. Among them, the diagnosis of vulval Crohn's disease can be challenging, as reported by Forward et al. They observed 8 cases where the genitalia showed swelling or induration without any gastrointestinal involvement. The diagnosis was delayed until a gastrointestinal biopsy or vulvar biopsy was performed, and combining systematic treatment brings more benefits to patients.[10] Therefore, the manifestations of Crohn's disease are very complex, sometimes even presenting solely as EIMs, leading to delayed diagnosis. In such cases, diagnosis usually relies on pathological biopsy. In addition to conventional treatment of Crohn's disease, patients also need symptomatic treatment.

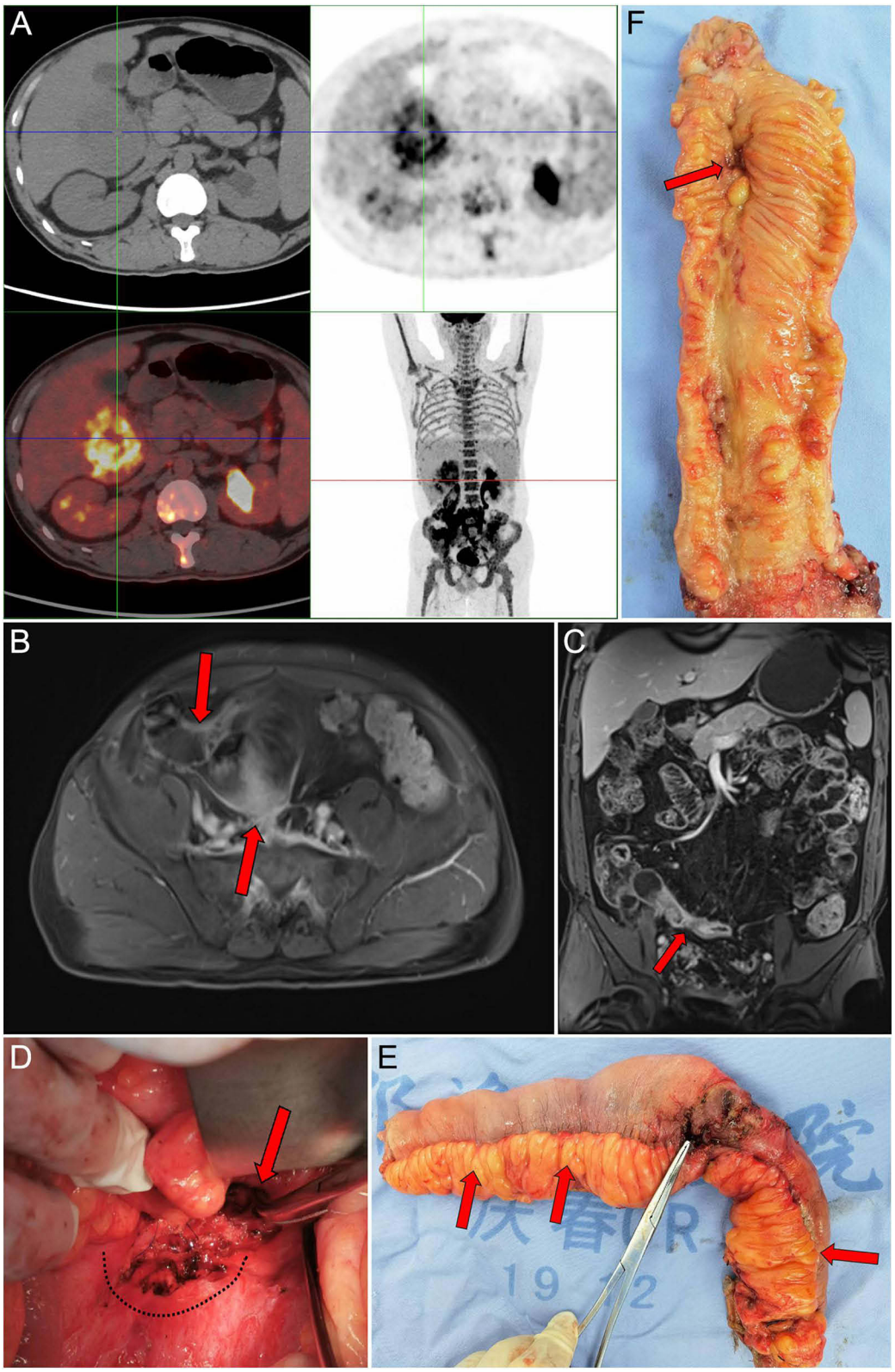

Figure 2 (A) PET-CT. Uneven increase of 18F-deoxyglucose uptake in the right posterior lobe mass of liver. MRE. (**B**) sacrococcygeal paravertebral empyema and thickened intestinal walls. (**C**) lateral wall of the small intestine in the lower right anterior pelvic cavity. (**D**) view during surgery: ulceration, sinus formation and tight adhesion of intestine to the right pelvic floor. (**E and F**) a 27-cm resected segment with perforation and creeping fat.

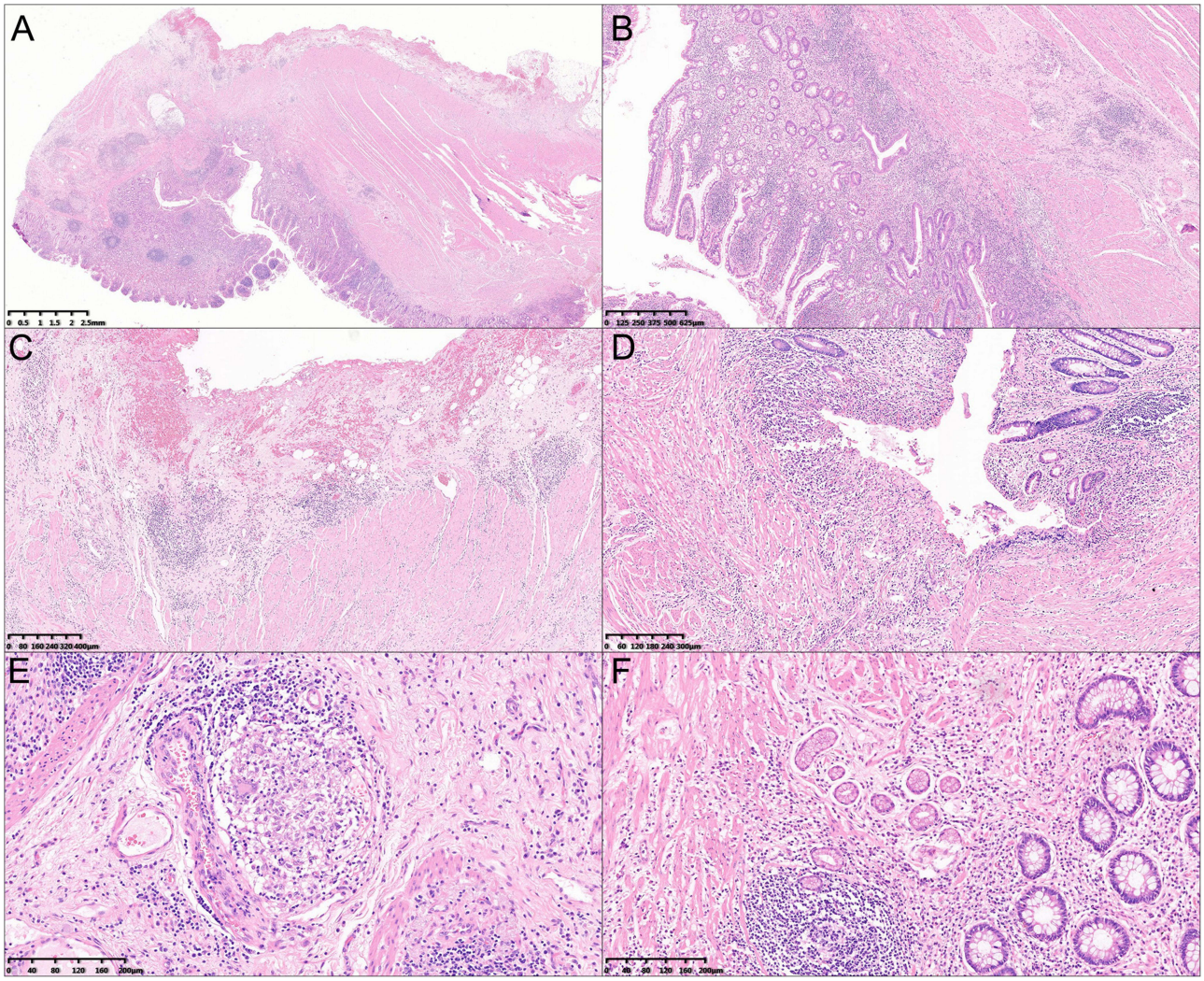

Figure 3 Pathological findings. (**A**) thickened intestinal wall, pan-mural inflammation, lymphoid follicle hyperplasia. (**B**) mucosal atrophy, hypertrophy. (**C**) the subserous lymphatic follicles are beaded. (**D**) ulcer. (**E**) non-caseous granuloma. (**F**) pyloric gland metaplasia.

The terminal ileum and surrounding colon are the most common sites affected in Crohn's disease. However, it is important to note that the entire digestive tract can be involved from mouth to anus. Small bowel Crohn's disease accounts for a significant proportion. In this case, due to the lesion being distant from the terminal ileum, colonoscopy was not accessible. Additionally, the patient had no gastrointestinal symptoms, resulting in a 20-month delay from initial consultation to definitive diagnosis. Upper gastrointestinal CD is also notable, occurring in 0.5%-16% of all patients.[11] Out of all the types, duodenal Crohn's disease is extremely rare and can lead to specific complications such as gastric outlet obstruction stenosis or pancreatitis, posing challenges for diagnosis and treatment.[12]

The patient underwent exploratory laparotomy due to unclear etiology, protracted disease course, abscesses formation, the possibility of intestinal perforation and fistula consistent with indications. In addition, surgery is also necessary when patients experience severe complications such as persistent or recurrent intestinal obstruction, bowel perforation, intractable gastrointestinal bleeding, dysplasia, or cancer.[13] The patient initially tried mesalazine for managing Crohn's disease, but it proved ineffective. Subsequently, the treatment plan was switched to a combination of infliximab and azathioprine, yielding good therapeutic results. Infliximab has been proven effective in treating Crohn's disease with perianal involvement or axial spondyloarthritis, preventing recurrence after surgery and reducing inflammation burden.[14,15] Moreover, the early use of biologics was associated with improved clinical outcomes. Additionally, the combined use of azathioprine helps resist immunogenicity.[16]

Conclusion

Small bowel Crohn's disease may not always present with digestive symptoms, but instead manifests as complications caused by infections around the segment of the small intestine, such as those affecting skeletal muscles and liver. When the affected area cannot be reached in time by colonoscopy, diagnosis and treatment may be delayed. For postoperative Crohn's disease involving axial bones, infliximab and azathioprine can effectively alleviate symptoms.

Ethics Approval

This article was performed in accordance with the principles of Declaration of Helsinki. The Ethics Review Board of Sir Run Run Shaw Hospital granted ethical review and approval.

Consent for Publication Statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Acknowledgment

The authors thank the patient and her family for signing informed consent for publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was funded by National Natural Science Foundation of China (32200593) and key research and development program of Zhejiang province(2022C03032).

Disclosure

The authors report no conflicts of interest in this work.

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