CASE REPORT

Cryptogenic Multifocal Ulcerous Stenosing Enteritis: An Exceptionally Rare Disease

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Abstract:

Cryptogenic Multifocal Ulcerous Stenosing Enteritis (CMUSE) is a rare idiopathic disease of the small bowel. Its origin and pathophysiology has not been well described. Clinicopathologic features include unexplained ileal strictures with superficial ulceration. We present a case of a 31-year-old HIV positive lady who was admitted with complaints of recurrent abdominal pain and constipation. Laboratory investigations revealed iron deficiency anemia. Ultrasonography of the abdomen showed dilated bowel loops and a subsequent barium follow through showed five strictures in the ileum. Segmental small bowel resection with end-to-end anastomosis was performed. Grossly ileum showed five ileal strictures. The diagnosis of CMUSE was made on histopathology after ruling out other causes of strictures. The present case highlights the importance of considering CMUSE in patients with chronic or recurrent episodes of intestinal obstruction with multiple small intestinal ulcers and strictures after other common causes have been ruled out.

Keywords: Cryptogenic Multifocal Ulcerous Stenosing Enteritis, Small Intestine Strictures, Ileum

Introduction:

Small bowel obstruction can be a result of much pathology, the most common ones being adhesions, hernias, strictures and tumors. One of the rarest causes is Cryptogenic Multifocal Ulcerous Stenosing Enteritis (CMUSE). CMUSE is characterized by intermittent episodesof small-intestinal obstruction which is caused by benign non granulomatous ulceratedstenosis. CMUSE has been reported to localize in the jejunum or proximal ileum and is associated with shallow, rather than deep transmural ulcerations [1]. The location of the ulcers and the absence of any associated granulomatous inflammatory changes in resected bowel can differentiate it from Crohn's disease, tuberculosis etc.

Case Report:

A 31 year old HIV positive lady with history of diabetes on insulin presented with complaints of intermittent colicky abdominal pain with on and off vomiting and constipation for the past two years. There was no history of blood in stools, chemotherapy or radiation.

Abdominal examination showed distension of abdomen with tenderness over the right iliac and lumbar region. Abdominal x-ray showed multiple air fluid levels in the centre of abdomen (Fig. 1). Ultrasonography of the abdomen revealed dilated bowel loops. Barium meals follow through showed five strictures in the ileum. She was clinically diagnosed as a case of subacute intestinal obstruction and was treated symptomatically on

multiple hospital admissions. However the exact cause of the obstruction could not be established. She was empirically treated with anti-tubercular drugs two years ago with no improvement in symptoms. Hematological investigation revealed microcytic hypochromic anemia (Hb-10.8 gm %). The other biochemical investigations were within normal limits.

Exploratory laparotomy was performed for small bowel segmental resection with end-to-end anastomosis. Intraoperative and postoperative course was uneventful.

Grossly, the resected specimen of ileum measured 73 cms and showed five strictures. Cut section showed thickened firm transverse strictures with small ulcerations. Rest of the mucosa appeared normal (Fig. 2). Histological sections from the strictured area revealed superficial ulceration of mucosa. The muscularis mucosa was thinned out and the submucosa showed dense fibrocollagenous tissue (Fig. 3). There was diffuse mixed inflammatory infiltrate in the mucosa, lamina propria and sparse infiltrate in muscularis and subserosa. Few of the blood vessels showed features of vasculitis. The common causes for strictures like tuberculosis and Crohn's disease were ruled out because of the absence of any granulomatous lesions. Periodic Schiff stain, Gram's stain, Giemsa stain and Zeihl Neelson (ZN) stain were performed to rule out tuberculosis, fungi and other microorganisms. There was no evidence of villous atrophy or any viral inclusions. Thus, a diagnosis of Cryptogenic Multifocal Ulcerous Stenosing Enteritis (CMUSE) was offered.

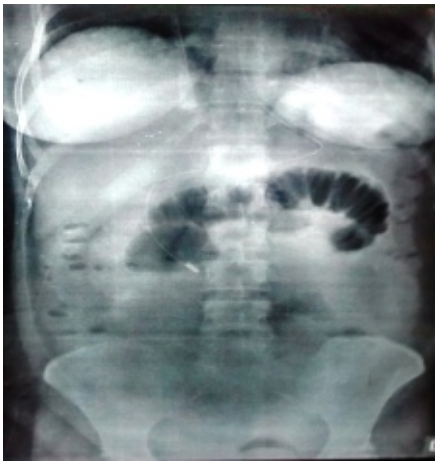

Fig. 1: X-Ray showing Multiple Air Fluid Levels

Fig. 2: Cut Section of the Ileum Showing Stricture (Arrow)

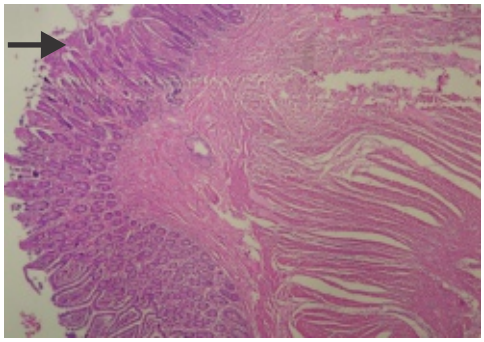

Fig. 3: Mucosa of the Ileum shows Superficial Ulceration (Arrow) and Submucosa Shows Increased Fibrocollagenous Tissue, (H & E stain, x40)

Discussion:

CMUSE was first described by Debray *et al* in 1964 [2]. It is a poorly understood entity of the jejunum and ileum characterized by the presence of multiple small intestinal strictures that often require surgical intervention or therapy with steroids (or both). No association with any of the other forms of inflammatory bowel disease has been reported [3]. Only about fifty cases of CMUSE have been published so far, although this entity is probably misdiagnosed, mostly with Crohn's disease and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) induced enteropathy [4].

The origin and pathophysiology of this entity has not been well described. However, Brooke *et al*. identified mutations in PLA2G4A as a cause of CMUSE in two of the affected siblings [3]. Vasculopathy has also been suggested as the cause of CMUSE. Perlemuter reported 17 cases in France where he suggested that CMUSE could be related to vasculitis [5]. Chang *et al* classified CMUSE into CMUSE-I (idiopathic) and CMUSE-V (vasculitis-related) suggesting that all the cases may not be associated with vasculitis. The present case infact didshow features of vasculitis. Some authors have suggested that the overstimulated fibrous tissue and disturbance of collagen degradation could play a role in pathogenesis of CMUSE. Fibroblast proliferation can be augmented by pro-inflammatory cytokines (IL-6, IL-8, TNF-alpha), granulocyte / macrophage colony-stimulating factor (GM-CSF), fibroblast growth factors (FGS II), platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-beta) [4, 6]. Fraile *et al.* diagnosed CMUSE in a man with a diagnosis of X-linked reticulate pigmentary disorder [7].

CMUSE typically has a relapsing clinical course even after surgery [2]. Matsumoto from Japan reported 12 cases where he described chronic intestinal bleeding, anemia and ulcers in the intestine with the tendency to stenose as the predominant features [8]. The diagnosis of CMUSE should be considered after ruling out other differentials such as Crohn's disease involving the small intestine, lymphoma (especially invading the mucosa only), infections (including Tuberculosis, CMV), drug-induced small bowel disease, traumatic injury, and ischemic ulcers as these diseases have similar clinical and radiological presentation [9]. When compared with Crohn's disease, CMUSE is not associated with any clinical and laboratory feature of systemic inflammation. Crohn's disease shows transmural ulceration and non caseating granulomas whereas in CMUSE the ulcers are localized to the mucosa and sub mucosa as was seen in the present case [10]. The mucosa on both sides of the ulcer was normal and there was no villous atrophy which ruled out any mala-bsorption syndrome. NSAID induced enteropathy was ruled out as there was no history of long term intake of NSAIDs. Absence of caseating granulomas and negative ZN stain ruled out tuberculosis as the cause.

CMUSE remains as a diagnosis of exclusion as there are no specific laboratory tests to diagnose CMUSE. The treatment of CMUSE is sympto-matic and it responds to glucocorticoids, but can

result in dependence. In patients with mechanical intestinal obstruction who do not respond to medical treatment, surgery is the treatment of choice [10]. Nowadays, they have even been treated endoscopically by means of double balloon enteroscopy [4]. The prognosis remains poorly understood and it has a propensity to recur even after surgery. So, the patient should be followed up closely [10].

Conclusion:

Although CMUSE is a rare cause of small intestine obstruction, it should be considered in cases of chronic or relapsing episodes of small intestinal obstruction resulting from multiple small intestinal strictures and multiple shallow ulcers. However, other causes of small intestinal strictures should first be ruled out before considering the diagnosis of CMUSE.

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