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Gastrointestinal manifestations in patient with Common Variable Immunodeficiency Syndrome (CVID): A Case Report

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Case Report

A 57 yo male with a background history of common variable Immunodeficiency syndrome (CVID) on Immunoglobulin Infusion (Kiovig) 40mg three weekly was referred for investigation of diarrhoea and follow up from previous history of colonic polyps.
Colonoscopy showed an irregular looking ileocaecal valve (ICV) with an adjacent flat polyp (Paris IIa). Biopsies showed low grade dysplasia. There was also a duodenal polyp noted on gastroscopy and biopsy again showed low grade dysplasia. In light of the findings of upper and lower gastrointestinal tract polyps, a small bowel capsule endoscopy (SBCE) was arranged. This showed an irregular area of mucosa in the proximal small bowel with significant ulceration and inflammation (Figure 1). There were also multiple scattered lymphagiectasias and lymphoid hyperplasia in the distal small bowel (Figure 2).
Anterograde double ballon enteroscopy (ADBE) was subsequently performed to the distal jejunum about 8 weeks after the SBCE. The duodenal polyp seen at gastroscopy was visualised during ADBE (Figure 3). In addition, two diminutive (<3mm) jejunal sessile polyps were encountered and excised (Figure 4). There was no evidence of ulcerative enteritis as seen on SBCE. The enteritis features initially visualized on the SBCE was thought to be a transient phenomenon possibly related to his CVID background.
However, for completion, the distal point of enteroscopy insertion was marked and a repeat SBCE performed immediately after recovery from the ADBE. This again showed the known duodenal polyp as well as 2 further diminutive small bowel polyps and minimal distal patchy enteritis only, with complete resolution of the previously observed ulcerative jejunitis. The jejunal polyps' histology was reviewed at a histology multidisciplinary meeting, there were no adenomatous or hamartomatous features and biopsies were thought to have non-specific changes only.
The patient was referred for polyp resection and further follow up and surveillance will be arranged based on histology.

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Discussion

CVID is a heterogeneous primary immune deficiency disorder, characterized by a loss of B cell function leading to defective immunoglobulin production[1, 2]. It is associated with a high incidence of gastrointestinal (GI) manifestations (Table 1) and an increased risk of gastric malignancy. The age of onset of CVID is variable, presenting in both children and adults. The diagnosis is generally made between 20 and 40 years of age, but up to 20% may present before the age of 20 years. CVID should be considered in the differential diagnosis of patients with recurrent bacterial lung infections. In 20–50% of cases, interstitial lung disease, lymphoproliferative syndromes and auto-immunity are the presenting medical conditions[3]. The disease can affect multiple organs[4] (Table 2).

The diagnosis of CVID is confirmed by laboratory investigations showing a significantly low serum IgG associated with low IgM and/or IgA, and poor or absent serological response to vaccines. The majority of the GI disorders in CVID are thought to be caused by T-cell–mediated defects and not by the antibody deficiency[5].

Enteropathy

Small and large bowel enteropathies have been described in literature in patients with CVID. Gastrointestinal tract infections (*Campylobacter jejuni*, *Salmo- nella* sp, and *Giardia lamblia)* are common[3]. Non-infectious enteropathy occurs in 10 to 12% of CVID patients and may resemble other GI conditions such as Crohn's disease, ulcerative colitis or coeliac disease. In a large case series, Malamut et al. examined 50 patients with CVID, 40% of whom had chronic GI symptoms[6]. In this cohort, the mean age at CVID diagnosis was 36.8 years and mean age at the onset of GI symptoms was 34.5 years. Diarrhoea was present in two thirds of patients and abdominal pain in more than half of cases. As in our case the enteropathy can vary in severity over time.

CVID associated chronic enteropathy is a complex disorder that may include features similar to ulcerative colitis, proctitis, or severe small bowel disease that leads to weight loss and malnutrition which may require long-term parenteral feeding[3]. Small bowel disease in patients with CVID is associated with exudative enteropathy, chronic bacterial overgrowth, villous atrophy and inflammatory lymphocytic infiltrates.

For colonic lesions in CVID, the severity ranges from microscopic colitis (mostly lymphocytic but collagenous colitis is also found) to severe colitis with ulcerations [6]. The histopathological pattern may mimic ulcerative colitis or Crohn's disease including the presence of ulcers, crypt abscesses and crypt destruction. Alternatively, colonic lesions may show a mild inflammatory infiltrate. Follicular hyperplasia and GVH-like disease may be associated with acute or chronic colitis. Similarly, inflammation and ulcers may be seen, albeit at a lower frequency than in the small intestine[6].

Malignancy

Two to 10% of CVID patients may develop lymphoid malignancies[3, 7]. These are generally non-Hodgkin's B cell lymphomas and often involve extra nodal sites[8,] which in some cases include the GI tract. In the great majority of cases, these are EBV negative. CVID patients have a 10-fold increased risk of gastric cancer[9]. In our case both proximal duodenal and colonic advanced adenoma were detected and in the absence of a family history of gastrointestinal malignancy may represent another as yet unrecognized gastrointestinal association with CVID.

Although Immunoglobulin G [IgG] replacement is the hallmark of the treatment of CVID patients, it is ineffective for heterogeneous gastrointestinal pathologies associated with CVID. Most patients respond to steroids but often become steroid-refractory, and life-threatening malabsorption may develop. Immunosuppressants are not effective and

further increase infectious susceptibility.

Conclusions

Gastrointestinal involvement, common in CVID, could be the dominant disease manifestation in a subset of patients. GI symptoms can mimic other GI diseases such as celiac disease and IBD. Early diagnosis and treatment are important for a favorable outcome. The multiorgan involvement warrants a multidisciplinary specialists' care with close collaboration with specialized immunodeficiency centers.

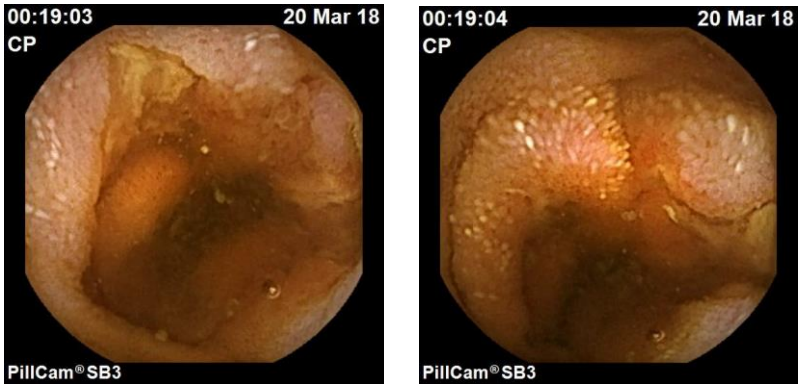

Figure 1: Proximal small bowel with significant ulceration and inflammation seen on SBCE

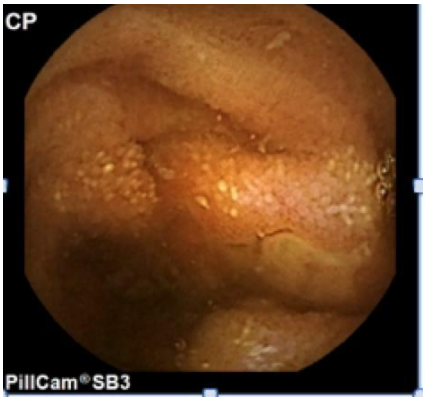

Figure 2: Scattered lymphagiectasias and lymphoid hyperplasia in the distal small bowel seen on SBCE

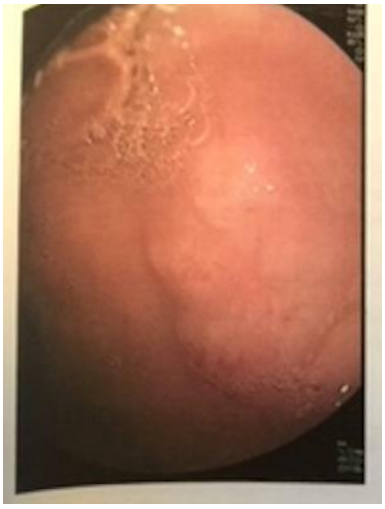

Figure 3: Duodenal polyp seen at ADBE

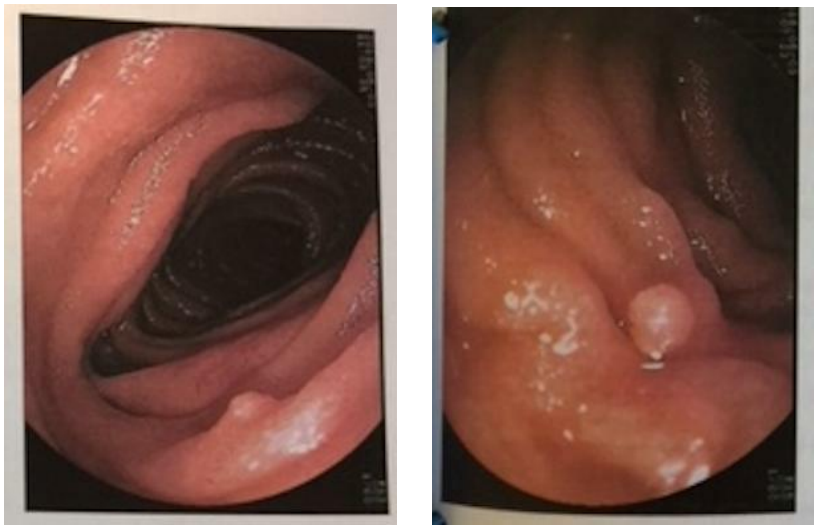

Figure 4: Jejunal sessile polyps seen at ADBE

Table 1: Gastointestinal manifestations of CVID (Non-malignant and non-infectious CVID related GI disorders)

GI organ	Manifestation	Clinical features
Stomach	chronic gastritis	nausea, vomiting abdominal pain
Small intestine	villous atrophy bacterial overgrowth chronic enteritis chronic exudative enteropathy	malnutrition chronic diarrhoea chronic diarrhoea abdominal discomfort malnutrition features as above with anasacra
Colon	chronic colitis	abdominal pain bloody diarrhoea

Table 2: Multi-system manifestations and frequencies of CVI (ESID - European Society for Immunodeficiencies)

Manifestations	Mount Sinai Hospital (n=473, 2012)[3](%)	ESID Database (n=902, 2014)[7](%)
Infections	94	Not specified
Pneumonia	40	32
Bronchiectasis	11	23
GI involvement	>15	9
Splenomegaly	Not specified	26
Cancers	7	5
Lymphoma	8.2	3
Granuloma	9.7	9

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