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**Letter to the Editor**

# Ustekinumab as Induction and Maintenance Therapy in Patients with Inflammatory Bowel Disease and Type II Autoimmune Pancreatitis: Report of Two Cases

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## 1. Introduction

The association between inflammatory bowel disease [IBD] and autoimmune pancreatitis [AIP] has been described in up to 45% of patients, especially in ulcerative colitis [UC].[1] Treatment of type 2 AIP in IBD patients follows international guidelines, but no approved maintenance therapy for steroid-dependent patients is available.[2,3]

We report the first two cases of type 2 AIP in IBD patients treated with ustekinumab which is a safe and effective monoclonal antibody.[4,5]

The first patient [Figure 1, panel A–E] is a 53-year-old man with an apparently idiopathic early chronic pancreatitis [CP] at magnetic resonance imaging [MRI], then confirmed at endoscopic ultrasound [EUS] when referred to our Centre. For haematochezia, he underwent colonoscopy with biopsies. At histology, diagnosis of ulcerative pancolitis was made. Nine months later he experienced clinical, biochemical, and endoscopic relapse after treatment with oral mesalamine 4 g per day and budesonide MMX 9 mg per day. No pancreatic changes were found at MRI and the aetiology of CP was deemed probably autoimmune type II [AIPII]. Faecal elastase [FE] was <100 mg/g. After multidisciplinary discussion, ustekinumab [standard dose for IBD] was started. Clinical and biochemical colitis remission were achieved after 14 weeks and both endoscopic and histological remission after 6 months. EUS confirmed a stable picture of CP, but FE levels increased to the normal range [>200 mg/g].

The second patient [Figure 1 panel F–J] is a 34-year-old woman who had idiopathic acute pancreatitis and proctorrhagia and underwent ileocolonoscopy with biopsies. The patient was diagnosed with ileocolonic Crohn's disease [CD] with presence of granulomas at histology.

Budesonide 9 mg was started, but for a further pancreatic investigation she was then referred to our Centre and underwent an MRI with findings suggestive of autoimmune pancreatitis.

As the faecal calprotectin level was still elevated, we repeated colonoscopy which showed endoscopic activity and EUS which confirmed the suspicion of active AIPII.

After multidisciplinary discussion, she started ustekinumab. Clinical and biochemical CD remission was achieved after 16 weeks and endoscopic remission at 6-month colonoscopy. EUS was repeated, with complete remission of the previous acute flare.

In the first case, IBD diagnosis was made 6 years after AIP onset, and the use of ustekinumab at this time did not improve the CP morphological changes because of the irreversible destruction of the parenchyma. In the second case, IBD and type 2 AIP diagnoses were in a close, timely correlation, and ustekinumab led to a striking improvement in organ morphology in the pancreas too.

No definitive conclusions can be drawn due to the limited numbers of patients enrolled in this study. However, ustekinumab may represent a promising option in the presence of both IBD and AIPII. Larger studies on this population are warranted to confirm the efficacy and safety of ustekinumab in this specific setting.

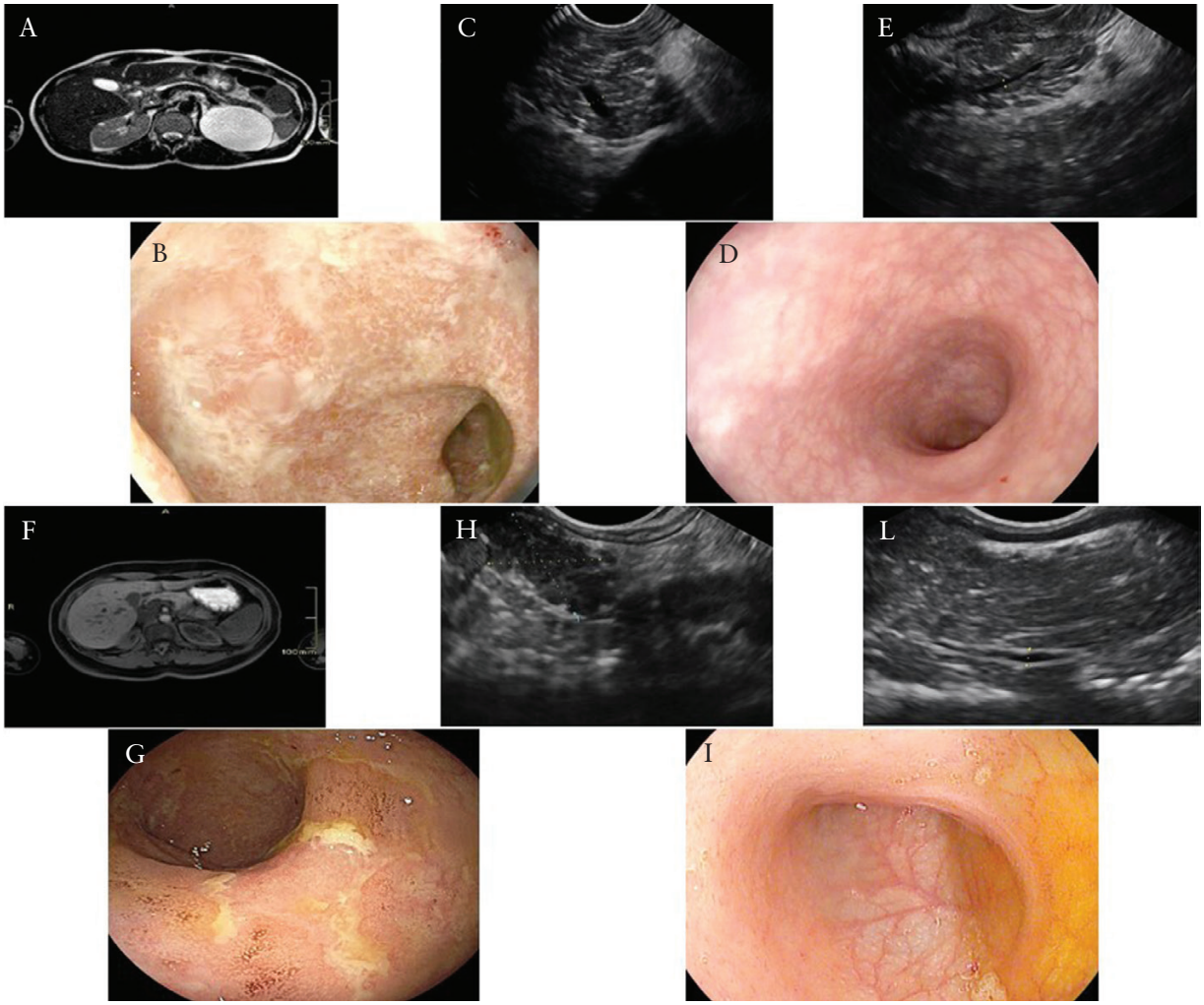


**Figure 1.** Magnetic resonance imaging, endoscopic and endoscopic ultrasound findings before and after ustekinumab therapy in a patient with type II autoimmune pancreatitis and ulcerative colitis [Panel A–E] and in a patient with type II autoimmune pancreatitis and Crohn's disease [Panel F–J] [A] Axial T2 weighted image demonstrating a slightly dilated Wirsung duct. [B] Multiple erosions and ulcers located in sigma, with loss of mucosal vascular pattern and friability. [C] Hypotrophic pancreas, with inhomogeneous hyperechoic echostructure and multiple hyperechoic spots and strands. At the isthmus dilated Wirsung [4 mm], with hyperechoic walls. [D] Endoscopic remission 6 months later, having started therapy with ustekinumab. [E] Stable chronic pancreatitis 6 months later, having started therapy with ustekinumab. [F] Axial T1 weighted image with fat suppression showing hypointense signal of the pancreatic tail when compared with the normal pancreatic parenchyma, corresponding to hyperintense signal in both T2 and, above all, diffusion weighted images, strongly suggesting autoimmune aetiology. [G] Aphthous lesions in the ileum. [H] Enlarged and swollen pancreas, with inhomogeneous echostructure with hyperechoic spot and strands. Pancreatic tail appears more hypoechoic and swollen compared with the rest of the organ, regular Wirsung. [I] Endoscopic remission 6 months later, having started therapy with ustekinumab. [J] No more swollen or oedematous parenchyma, with only few hyperechoic spots without strands 6 months later, having started therapy with ustekinumab.

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## Conflict of Interest

GL declares no conflict of interest. FD'A has served as a speaker for Sandoz, Janssen, Galapagos, and Omega Pharma. MA received consulting fees from Nikkiso Europe, Mundipharma, Janssen, Abbvie, and Pfizer. EDT declares no conflict of interest. PGA declares no conflict of interest. GC has served as a speaker, consultant, and advisory board member for AG Pharma, Viatris, and Bayer. SD has served as a speaker, consultant, and advisory board member for Schering-Plough, AbbVie, Actelion, Alphawasserman, AstraZeneca, Cellerix, Cosmo Pharmaceuticals, Ferring, Genentech, Grunenthal, Johnson and Johnson, Millenium Takeda, MSD, Nikkiso Europe, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos, UCB Pharma, and Vifor.

## Author Contributions

SD and GC conceived the study. GL and FD wrote the manuscript and created the tables. SD, MA, EDT, PGA, and GP revised the manuscript. All the authors approved the final version of the manuscript

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