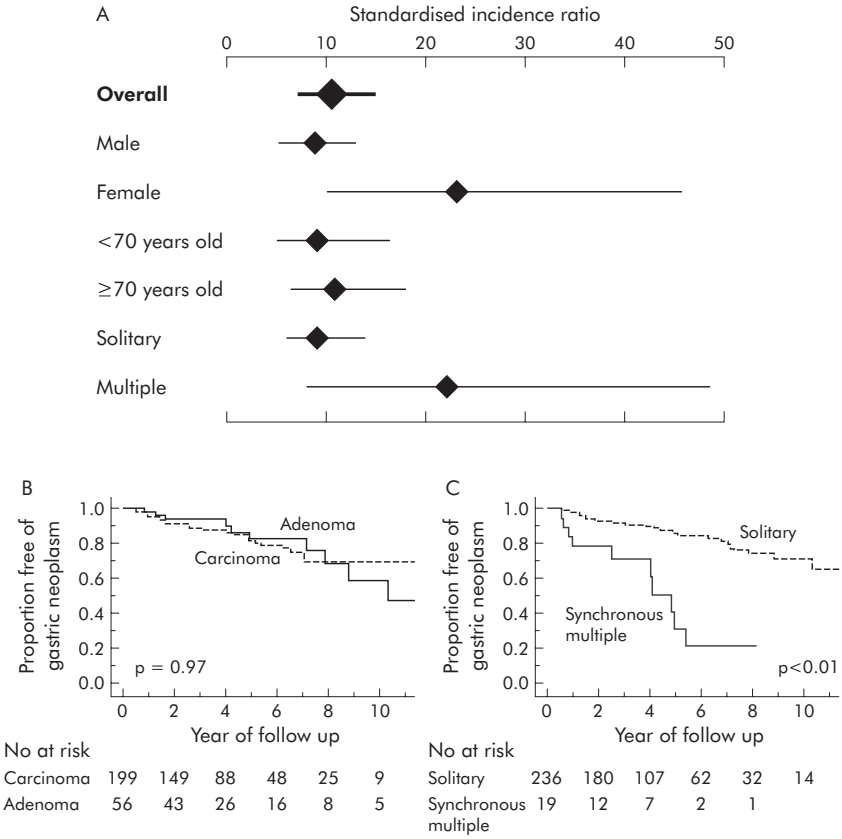

Figure 1 (A) Standardised incidence ratio (SIR) of newly developed gastric cancers according to sex, age, and multiplicity at the initial treatment. SIRs were calculated based on age, sex, and calendar year specific incidence rates of gastric cancer in the general population of Japan.[10] Values are SIRs (95% confidence intervals) calculated based on Poisson distribution. This analysis was restricted to 231 patients who received endoscopic mucosal resection (EMR) and whose subsequent gastric cancer developed before 1999 because data for the estimated incidence rate of gastric cancer in Japan was available only between 1975 and 1999.[10] (B, C) Cumulative incidence of subsequent gastric cancer after EMR. The Kaplan-Meier method was used to calculate the cumulative incidence. The cumulative incidence in patients with gastric adenoma did not differ significantly from the incidence in those with gastric cancer as the initial lesion (p=0.97) (B). The cumulative incidence of subsequent gastric cancer was significantly higher in patients with synchronous multiple lesions than in those with a single lesion as the initial neoplasia (p<0.01) (C). The log rank test was used to calculate p values.

should be considered to have an exceedingly high potential to develop cancers.

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Tumour necrosis factor α downregulation and therapeutic response to infliximab in a case of segmental colitis associated with diverticula

Inflammatory bowel disease (IBD) confined to the diverticular tract—defined as segmental colitis associated with diverticula (SCAD)—occurs in 3.8% of diverticular patients.[1] Recently, infliximab was reported to have a dramatic impact on severe Crohn's disease and ulcerative colitis therapy.[2 3] However, tumour necrosis factor α (TNF-α) involvement and the efficacy of anti-TNF-α in SCAD are unknown.

A 60 year old male smoker and non-NSAID user was admitted for severe bloody diarrhoea. At colonoscopy, the sigmoid and descending mucosa showed granularity, friability, and erosions confined to the diverticular tract, without alterations of the remaining ileocolonic mucosa. Histology of the inflamed tract revealed an ulcerative colitis-like picture. Therefore, a diagnosis of SCAD was made. After mesalazine and antibiotic failure, intravenous steroid therapy was successfully administered. After two years of steroid dependence, repeat endoscopy showed, in addition to the active SCAD, ulcerative colitis-like involvement of the proximal non-diverticular colon. Histology confirmed active SCAD, also showing severely active ulcerative colitis in the proximal colon, sparing the rectum and terminal ileum. A high dose steroid infusion achieved complete clinical remission, and azathioprine was started. After a further six months of steroid dependence, infliximab (5 mg/kg) was administered at 0, 2, and 6 weeks, and a steroid free complete clinical remission was achieved within one month. Maintenance treatment with infliximab every eight weeks has been successfully continued for up to 16 months of follow up. Ileocolonoscopy performed after one year from the beginning of infliximab revealed complete remission of SCAD, while a mild active colitis persisted in the proximal colon. Histology showed complete regression of SCAD but only a slight improvement in the proximal colon. TNF-α label index (percentage of positive stained stromal cells to the total number of lamina propria mononuclear cells[4]) appeared to be markedly reduced in SCAD (40% *v*15%) while

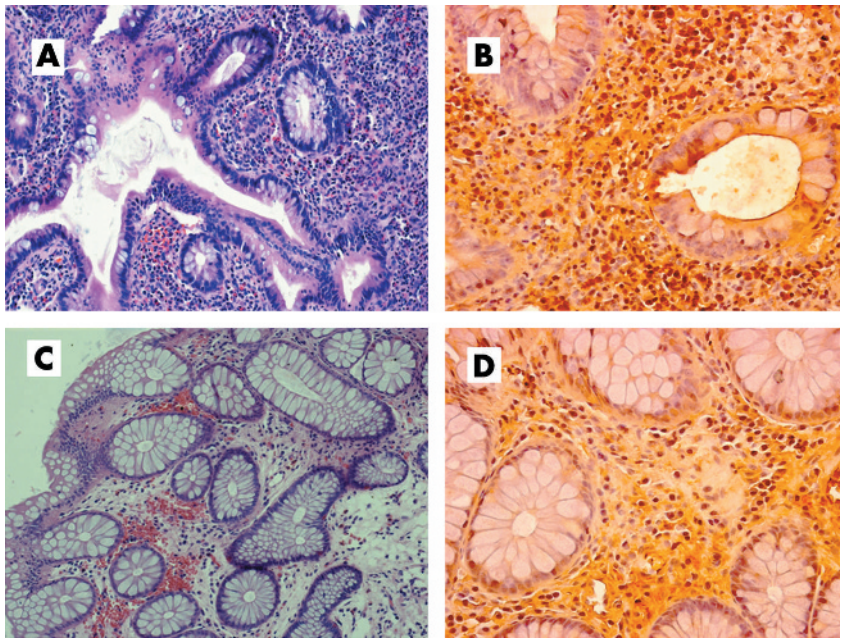

Figure 1 Histological changes in colonic biopsies and tumour necrosis factor α (TNF-α) expression before and after infliximab therapy (haematoxylin-eosin and immunohistochemical stains; original magnification 125× and 400×). (A) Active segmental colitis associated with diverticula (SCAD) characterised by a dense inflammatory infiltrate, disturbed crypt architecture, and epithelial damage, and by high TNF-α expression (B). (C) SCAD in remission characterised by regression of the inflammatory infiltrate, restoration of the epithelial damage, and profound downregulation of TNF-α expression (D).

remaining unchanged in the proximal colon (32% *v* 30%) (fig 1).

Increased TNF-α concentrations have been reported in both Crohn's disease and ulcerative colitis.[5 6] For the first time, this case report showed that TNF-α overexpression was also present in SCAD. It is known that high TNF-α levels detected in Crohn's disease are reduced by infliximab therapy.[7] Similarly, a dramatic decrease in histological activity with profound TNF-α downregulation in the SCAD tract occurred in our patient after infliximab. These observations suggest that SCAD pathogenesis may mirror the pathogenetic models proposed for IBD.

It has already been reported that SCAD can fade into a more classic ulcerative colitis picture.[8] In our case, although the two IBD pictures presented with similar TNF-α concentrations before therapy, complete endoscopic and histological regression was limited to the SCAD tract while only partial endoscopic improvement occurred in the non-diverticular ulcerative colitis-like picture. Interestingly, persistence of histological activity was associated with high TNF-α expression. This is the first case in which two simultaneous varieties of IBD have shown a different response to infliximab in the same patient. However, due to the more aggressive clinical behaviour of the SCAD, infliximab therapy was successful in annihilating the long term steroid dependence of our patient. This implies that a much deeper knowledge of the pathogenesis of IBD needs to be pursued before preventing a patient from a potentially life saving therapy.

In conclusion, our case report showed that the pathogenesis of SCAD can be sustained by TNF-α activity and reversed by specific therapy. Moreover, an associated ulcerative colitis may show a different degree of response to infliximab. Such different behaviours suggest that the more we struggle to unravel the inflammatory puzzle, the more puzzling the pathogenetic enigma of IBD appears to be.

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Life threatening intra-abdominal sepsis in patients on anti-TNF-α therapy

Tumour necrosis factor α (TNF-α) blocking drugs are used in the treatment of a number of inflammatory conditions. It is likely that the use of these drugs will increase. There have been reports of serious infections with these drugs.[1–3] Doctors need to be aware of the potential for sepsis, especially as they are increasingly likely to encounter patients on anti-TNF drugs. We present two cases of life threatening intra-abdominal sepsis in patients with rheumatological conditions receiving anti-TNF drugs.

Case 1

A 60 year old male with psoriatic arthritis resistant to treatment had benefited from etanercept for six months. In rheumatology outpatients he complained of a two week history of abdominal pain. On examination he was tender in the left upper quadrant with a palpable mass. A contrast enhanced computed tomography (CT) scan demonstrated a large multiloculated splenic abscess with subcapsular extension (fig 1). Blood cultures grew *Staphylococcus aureus*. Conservative treatment with high dose intravenous antibiotics, initially with cefuroxime, metronidazole, and gentamicin on microbiological advice, had no effect. The patient became increasingly septic and after one week of conservative therapy he proceeded to laparotomy and splenectomy (fig 2). Postoperatively he developed sepsis requiring ITU admission and high dose inotropic support for five days. Histopathology of the spleen showed multiple splenic abscesses that grew *Staphylococcus aureus*. The patient made a full recovery. He

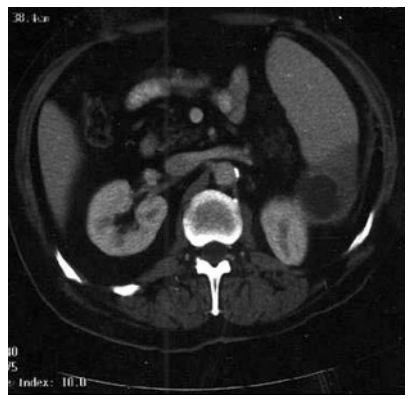

Figure 1 Computed tomography. Expansile predominantly cystic mass located within an area of hypodensity in the posterior pole of the spleen.