Novel treatment (new drug/intervention; established drug/procedure in new situation)

Sclerosing mesenteritis successfully treated with a TNF antagonist

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Summary

A 29-year-old female presented with intermittent nausea, vomiting, fevers, abdominal pain and fatigue. CT scans of the abdomen revealed inflammatory changes within the mesentery and small bowel. Histopathology of the mesentery and omentum showed chronic inflammation and fibrosis, supporting a diagnosis of sclerosing mesenteritis. Over the past 2 years, the patient suffered debilitating paroxysmal abdominal pain despite treatment with prednisone, azathioprine, sulfasalazine and narcotics. Additionally, she developed sacroiliitis diagnosed clinically and on radiographs. Intravenous infliximab (5 mg/kg intravenous) was initiated and continued every 6 weeks for 3 years. The patient has since had a dramatic improvement in her back and abdominal symptoms and has tapered off of prednisone, azathioprine and narcotics. Erythrocyte sedimentation rate, anaemia, leukocytosis and radiographic findings improved after initiation with infliximab. In conclusion, the authors report successfully treating sclerosing mesenteritis with sacroiliitis by the addition of infliximab. This may implicate a role for tumour necrosis factor α in disease pathogenesis.

BACKGROUND

The role of tumour necrosis factor α (TNF α) in the pathogenesis of sclerosing mesenteritis is unknown; however, it is known that TNF α is an important pro-inflammatory mediator of the systemic immune response. Specifically, TNF α has been identified as an important regulator of chronic inflammation in several other related disorders, including inflammatory bowel disease, rheumatoid arthritis and ankylosing spondylitis.¹ In a small open-label pilot study, five patients with symptomatic mesenteric panniculitis were treated with thalidomide and showed a trend toward improvement of symptoms, including a decreased erythrocyte sedimentation rate.² Among other effects, thalidomide is known to suppress TNF α , which may play a significant role in therapy. Consequently, we hypothesised that anti-TNF α therapy would be a good choice for this patient and safer than thalidomide.

Post-treatment initiation, the patient has had almost complete resolution of her abdominal pain, her laboratory markers of disease have significantly improved and she no longer uses chronic prednisone or narcotics for pain management. She also has improvement in the CT appearance of her disorder, which is not typically observed with other therapies.²⁻⁵ In conclusion, this case highlights an interesting presentation of a rare and elusive disease and introduces a new potential therapy that may suggest a role for TNF in the underlying disease pathogenesis.

CASE PRESENTATION

A 29-year-old female presented with recurrent, intermittent, non-localising abdominal pain. The pain was frequent,

but not always, associated with eating and coincided with subjective fever, nausea, vomiting, early satiety and fatigue. Over the course of a year, weight loss (9 kg) and food avoidance were observed without diarrhoea, blood per rectum or melena. While otherwise healthy, the patient suffered from these painful attacks lasting several hours with increasing frequency and duration.

Other pertinent medical conditions included childhood asthma in remission, allergic rhinitis, hypertension, a positive purified protein derivative that had been treated with isoniazid, and normocytic anaemia attributed to β -thalassaemia trait. The patient was a non-smoker, who did not drink excessive alcohol and was neither obese nor pregnant. She had a previous cholecystectomy for presumed biliary colic within a year prior to this presentation.

Physical examination revealed an abdomen that was soft, non-distended, with no masses palpable and diffuse tenderness. Abnormal laboratory assessments included an elevated erythrocyte sedimentation rate of greater than 100 on two separate occasions.

Occult malignancy, vasculitis or chronic mesenteric ischaemia was considered at this juncture. To evaluate further, a CT scan and an endoscopy of the abdomen were obtained. The patient had a normal colonoscopy and barium enema. Upper endoscopy was grossly normal; however, histopathology suggested Barrett's oesophagitis. The patient was treated with omeprazole without clinical improvement. A CT scan of the abdomen revealed non-specific inflammatory changes within the mesentery and small bowel thickening (figure 1A). A subsequent CT scan showed interval progression of inflammation in addition to

Figure 1 Inflammatory radiographic changes improve after initiation of infliximab (A) Three transverse CT images show extensive small bowel wall thickening (*) in multiple loops of bowel. Diffuse infiltration and stranding of adjacent mesentery (solid arrows) is also present. Intraperitoneal fluid (dashed arrows) is evident surrounding bowel loops and extending inferiorly into the pelvis (not shown). (B) Three transverse CT images, obtained 5 months after the images from (A) and after initiation of infliximab, reveal markedly decreased amounts of bowel wall thickening (*) and mesenteric infiltration and stranding (solid arrow). Intraperitoneal fluid (dashed arrow) persists.

Figure 2 (A) Mesenteric and (B) omental biopsy show fibrosis with chronic inflammation. Differential diagnosis includes infection versus sclerosing mesenteritis.

two peripheral portal vein thromboses in the left and right hepatic lobe. Abdominal, mesenteric, bilateral renal and ileocolic arteriograms showed no vasculitis or renal arterial stenosis. Her hypercoagulable investigation revealed heterozygosity for factor V Leiden and a slightly decreased antithrombin III (ATIII) level. The patient began anticoagulation with warfarin.

Despite anticoagulation and resolution of the thrombosis, the patient's symptoms did not improve. Consequently, the patient was hospitalised for an exploratory laparotomy. Histopathology of the mesentery and omentum showed

chronic inflammation and fibrosis consistent with sclerosing mesenteritis (figure 2). Cultures of the peritoneal fluid grew two organisms, *Morganella morganii* and *Enterococcus faecalis*, for which the patient was treated with imipenem (1 g every 8 h). After antibiotic completion, the patient was treated with prednisone (40 mg/day), azathioprine (75 mg/day) and oxycontin (10–20 mg/day).

Despite immunosuppression, the patient was hospitalised eight times over the next year for severe abdominal pain. The frequency of hospitalisations increased as the patient's steroid doses were reduced, thus rendering her

Figure 3 Markers of disease and treatment course with prednisone and infliximab. Infliximab infusions (arrows) were given at 5 mg/kg intravenous. Separate prednisone tapers were initiated during disease course, the first starting at 40 mg four times a day and the second starting at 20 mg four times a day before increasing to 40 mg four times a day. Azathioprine was started at 75 mg four times a day, increased to 150 mg four times a day and halted on day 565. Sulfasalazine was given at 500 mg by mouth twice daily and increased to 1000 mg by mouth twice daily on day 565. Shown are white blood cell count (WBC) (reference range $4.5\text{--}11 \times 10^9/\text{l}$), erythrocyte sedimentation rate (ESR) (reference range $<20\text{ mm/h}$) and haematocrit (HCT) (reference range $36\text{--}46\%$).

steroid and narcotic dependent. CT scans showed worsening inflammation, fluid in the midabdominal and pelvic regions and wall thickening and inflammatory changes of the jejunum. Inflammatory markers that correlated with the patient's abdominal symptom included a reactive leukocytosis ($11.3\text{--}26.5$; reference range $4.5\text{--}11 \times 10^9/\text{l}$), elevated erythrocyte sedimentation rate ($26\text{--}61$; reference range $<20\text{ mm/h}$) and anaemia (haematocrit $26\text{--}35.9$; reference range

$36\text{--}46\%$) that was independent of her known β -thalassaemia trait (figure 3). High-dose prednisone ($1\text{--}0.5\text{ mg/kg}$) became necessary to control the patient's symptoms despite additional azathioprine (100 mg) and sulfasalazine (1000 mg). The patient then developed severe intermittent low-back pain. The musculoskeletal exam was initially normal, but radiographs revealed periarticular sclerosis at the sacroiliac joints and sacroiliitis (figure 4).

Figure 4 Anteroposterior (left) and cephalically angulated (right) projections of the sacroiliac joints demonstrate sclerosis and subchondral erosions along the lateral portions of both sacroiliac joints.

INVESTIGATIONS

- ▶ CT scan of the abdomen (figure 1)
- ▶ Histopathology of the omentum and mesentery (figure 2)
- ▶ White blood cell count (figure 3)
- ▶ Haematocrit (figure 3)
- ▶ Erythrocyte sedimentation rate (figure 3)
- ▶ Radiographs of the sacroiliac joints (figure 4).

DIFFERENTIAL DIAGNOSIS

- ▶ Cholecystitis
- ▶ Occult malignancy
- ▶ Occult infection
- ▶ Vasculitis
- ▶ Chronic mesenteric ischaemia
- ▶ Fitz-Hugh-Curtis syndrome
- ▶ Endometriosis
- ▶ Inflammatory bowel disease.

TREATMENT

The patient began intravenous infliximab infusions (5 mg/kg on weeks 0, 2 and 6 followed by infusions every 8 and then 6 weeks thereafter).

OUTCOME AND FOLLOW-UP

To date, the patient has received infliximab for more than 3 years with remarkable improvement of her back and abdominal symptoms both clinically and radiographically. She has been able to taper off prednisone, azathioprine and narcotics and has had one brief hospitalisation for abdominal symptoms since her first infusion. An abdominal CT scan taken after infliximab initiation showed marked improvement in the abnormal mucosal thickening of the small bowel and resolution of the thickened colonic mucosa when compared to previous scans (figure 1B). In addition, laboratory data show a reduction of the erythrocyte sedimentation rate and normalisation of the white blood cell count and anaemia (figure 3).

DISCUSSION

Sclerosing (retractile) mesenteritis is part of a spectrum of rare, idiopathic diseases, including mesenteric panniculitis and mesenteric lipodystrophy.⁶ The diagnoses are differentiated by the predominant pathological finding; sclerosing mesenteritis is defined by marked fibrosis, whereas mesenteric panniculitis describes patients with inflammatory lesions as the primary pathologic finding, and fat necrosis indicates a diagnosis of mesenteric lipodystrophy. Controversy exists as to whether these diseases are separate entities or simply a progression of the same pathophysiologic process.⁶

Part of the controversy over the aetiology and classification of this disorder is due to its rarity. About 300 cases have been reported in the literature, all heterogeneous in terms of natural history, clinical presentation and effective treatment. The most recent study of the clinical features of sclerosing mesenteritis reported on 92 cases diagnosed at the Mayo clinic.⁷ In this series, the disorder most commonly affected males (70%) in the fifth, sixth and seventh decades of life; however, other reviews have found no such gender association.^{6 8} The most common symptoms included abdominal pain (70%), bloating and distension (26%), diarrhoea (25%) and weight loss (23%), though there are several reports of asymptomatic sclerosing mesenteritis, that have been incidentally diagnosed either through autopsy or abdominal CT.^{7 8}

Sclerosing mesenteritis is both a biopsy confirmed diagnosis and one of exclusion. In our patient, cholecystitis may have been the initial cause of her abdominal symptoms; however, abdominal surgery has been hypothesised as a trigger of sclerosing mesenteritis, with 41% of patients from the Mayo Clinic case reviews having had abdominal surgery prior to the onset of symptoms.⁷ Consequently, sclerosing mesenteritis may be the result of abnormal healing or a non-specific symptom complex leading to a surgical intervention.

Occult malignancy with a desmoplastic and inflammatory response of the peritoneum was considered in our patient, which led to the definitive pathologic specimen. The CT appearance of sclerosing mesenteritis and lymphoma can be similar;⁹ however, pathology from our patient's laparotomy ruled out malignancy, highlighting the importance of a biopsy, in order to arrive at the appropriate diagnosis.

Treatment of sclerosing mesenteritis has been reported by several sources, though most are anecdotal, lending to no consensus. Surgical intervention has rarely shown to have a positive impact on the chronic disease.⁷ Medical intervention including steroids, colchicine, thalidomide and tamoxifen have all been reported to give clinical improvement, though CT improvement was rarely seen.^{2–5} In the present case, high-dose prednisone provided some symptomatic relief; however, the symptoms rebounded during taper periods despite additional therapy with azathioprine and sulfasalazine.

Axial skeletal involvement is not typical of this disease with only one patient described in a recent review of 92 cases by Akram *et al* with coexisting ankylosing spondylitis.⁷ The presence of radiographic and symptomatic sacroiliitis prompted commencement of anti-TNF α therapy with infliximab. Anti-TNF α agents have been shown to be well tolerated and significantly effective in treating ankylosing spondylitis^{10–11} where sacroiliitis is a profound component of the disease.¹² Moreover, infliximab is effective in treating the inflammatory bowel manifestations of patients with Crohn's disease and ulcerative colitis,^{13–14} as well as their coexisting axial arthropathies.¹⁵

Learning points

- ▶ Sclerosing mesenteritis is a rare disease consisting of inflammation of the omentum and mesentery that requires biopsy confirmation and exclusion of other disorders.
- ▶ Patients with sclerosing mesenteritis may develop other autoimmune disorders.
- ▶ Anti-TNF α agents are beneficial in treating autoimmune disorders including seronegative spondyloarthropathies, inflammatory bowel disease and rheumatoid arthritis.
- ▶ Anti-TNF α agents may be beneficial in patients with sclerosing mesenteritis, and TNF α may be important to disease pathogenesis.

Competing interests None.

Patient consent Obtained.

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