Learning Point for Clinicians

Renal amyloid is a rare complication of Crohn's disease (CD). Increased mortality is associated with increased serum amyloid A (SAA) protein concentration and reducing SAA improves survival. Anti-TNF-α may treat both renal amyloid and CD. NSAID use may precipitate a CD flare. Collagenous colitis is associated with CD and amyloidosis.

A 35-year-old butcher was admitted from the renal outpatient clinic for investigation and management of worsening peripheral oedema. He gave a past history of Crohn's disease (CD). This had been asymptomatic for many months and so the patient had weaned himself of immunosuppression (azathioprine) 4 months earlier.

On admission, serum albumin was <4 g/l (normal range 30–45) with proteinuria of ~20 g/d (0–30 mg/d). Serum creatinine was normal—41 μmol/l (40–125); C-reactive protein (CRP) was 23 mg/dl (0–5). Following a diagnosis of severe nephrotic syndrome, a renal biopsy was performed. This demonstrated AA amyloid (Figure 1A). Upper and lower gastrointestinal endoscopies showed no active inflammation. The patient was optimized on standard therapy for his nephrotic syndrome—maximal doses of an angiotensin converting enzyme inhibitor and angiotensin receptor blocker alongside high-dose diuretics.

Although the peripheral oedema improved slightly, serum albumin remained life-threateningly low. As this was considered to be largely due to urinary losses, it was felt that reducing the glomerular filtration rate (GFR) may help increase serum albumin and so improve the oedema further. Both medical (high-dose gentamicin) and surgical (bilateral nephrectomy) methods of reducing GFR were considered. On balance, the safest method was thought to be the use of a non-steroidal anti-inflammatory drug (NSAID) such as indomethacin, with concomitant gastric protection.

Following 2 weeks of NSAID use, the patient's clinical condition deteriorated. He developed a fever associated with abdominal pain and signs of peritonism. Serum creatinine was 124 μmol/l; white cell count was 16.7 × 10^9/l (4.0–11.0); CRP was 149 mg/dl. Although a computed tomography scan of the abdomen with contrast revealed no evidence of a perforation, it did show changes consistent with a terminal ileitis. The patient was transferred to the intensive care unit where he received supportive treatment—intravenous broad-spectrum antibiotics and steroids. When clinically stable, a magnetic resonance imaging scan demonstrated terminal ileitis.
in keeping with active CD. Repeat colonoscopy showed appearances of active terminal ileal CD. Gastrointestinal biopsies also showed AA amyloid deposition at multiple levels and a collagenous colitis.

The patient was started on prednisolone, azathioprine and the anti-tumour necrosis factor-α (TNF-α) agent, infliximab, targeting both the CD and renal amyloid. Over the next few months—and three doses of infliximab—the patient’s clinical state and supporting biochemistry improved (Figure 1B). Faecal calprotectin fell from 280 μg/g (0–50) to 60. The patient remains well at last review.

Systemic AA amyloidosis is a potentially fatal complication of CD, seen in ~0.9–2.5% of patients. Renal involvement is the commonest manifestation, often presenting with nephrotic syndrome. The deposited AA amyloid fibrils are derived from SAA protein. Increased mortality is associated with a reduced serum albumin and increased SAA concentration. Importantly, reducing and maintaining a low SAA concentration are associated with an increased survival.

Secondary amyloidosis is often due to chronic inflammation and is associated with persistently elevated levels of TNF-α. This ultimately leads to tissue accumulation of SAA. The patient was treated with infliximab with the goal of reducing SAA, potentially treating the renal amyloid and improving outcome. As a benefit, infliximab is also an established treatment for CD. There are a few reported cases of infliximab treatment for AA amyloid secondary to rheumatoid arthritis as well as active CD. The combination of treatment-resistant nephrotic syndrome due to AA amyloid and asymptomatic CD has not been previously reported.

NSAID use here was to reduce GFR and proteinuria. We balanced this risk against that of ulceration, given normal endoscopies and lack of symptoms. Our case highlights that short-term NSAID use may precipitate a severe flare of quiescent CD. Although infrequent, short and longer term use of NSAIDs have been associated with exacerbations of quiescent CD and ulcerative colitis. They may also trigger de novo colitis. The patient additionally developed a collagenous colitis. Long-term NSAID use may predispose to this, and there may be an association with other autoimmune diseases, including CD. However, there is no recognized association between collagenous colitis and amyloidosis.

Within a culture of evidence-based practice, our case highlights the importance of ‘out-of-the box’ thinking. Infliximab is an effective treatment for inflammatory bowel disease (IBD) although not first line. In this patient it had the additional benefit of treating the renal amyloid. Finally, we recognize that it would have been helpful to have access to our patient’s medical notes from the Czech Republic. With an increasingly migratory population across Europe, the sharing of medical information across borders, with the appropriate safeguards in place, is in the interest of patients and should be the focus of future health care budgets.

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References


