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PHOTO QUIZ

Oedema and Crohn's disease

J. Heidt[1]*, S.D.J. van der Werf[2], E.C.M. Ooms[3], J.H.M. Groeneveld[1]

Departments of [1]Internal Medicine, [2]Gastroenterology, [3]Pathology, Medical Centre Haaglanden, Lijnbaan 32, The Hague, the Netherlands, *corresponding author: tel.: +31 (0)70-330 20 00, fax: +31 (0)70-380 94 59, e-mail: jeroenheidt@yahoo.com

CASE REPORT

A 43-year-old man was admitted to the hospital for analysis and treatment of severe oedema. He had suffered from Crohn's disease since 1988, which had responded well to prednisolone in the past. However, he did not tolerate treatment with azathioprine and treatment with infliximab was unsuccessful. His Crohn's disease was not well controlled, due in part to the patient's poor follow-up, non-compliance and intolerance for medication, resulting in (peri)anal fistulas and frequent exacerbations. In 1993, the terminal ileum had to be resected.

Blood tests at admission showed a creatinine of 78 µmol/l (50-95 µmol/l), urea of 2.3 mmol/l (2.5-6.4 mmol/l), sodium of 147 mmol/l (135-145 mmol/l), potassium of 3.1 mmol/l (3.2-4.7 mmol/l) and albumin of 15 g/l (32-48 g/l). There was proteinuria of 5.28 g/24 h; in 1989 the urine dipstick was negative for protein. Liver tests were abnormal, with ASAT 216 U/l (11-35 U/l), ALAT 266 U/l (15-35 U/l), alkaline phosphatase 372 U/l (40-120 U/l), γGT 709 U/l (8-35 U/l) and bilirubin 13 µmol/l (5-19 µmol/l). The urinary sediment was acellular.

Our patient was admitted with nephrotic syndrome. Treatment with diuretics and ACE inhibition was started. In regard to the abnormal liver tests, we suspected primary sclerosing cholangitis (PSC). Both liver biopsy (*figure 1*) and kidney biopsy (*figure 2*) were performed.

Figure 1. *PAS staining of liver biopsy*

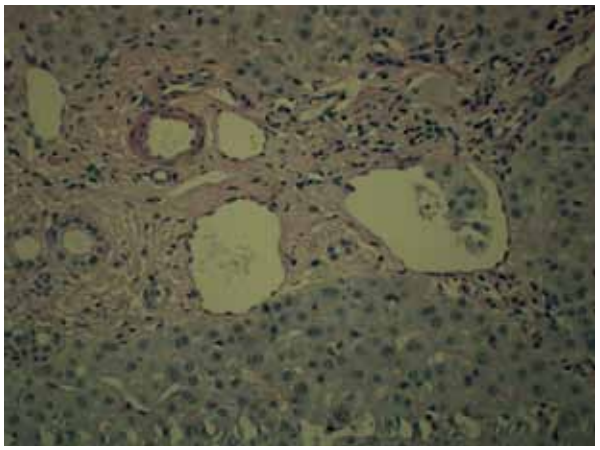
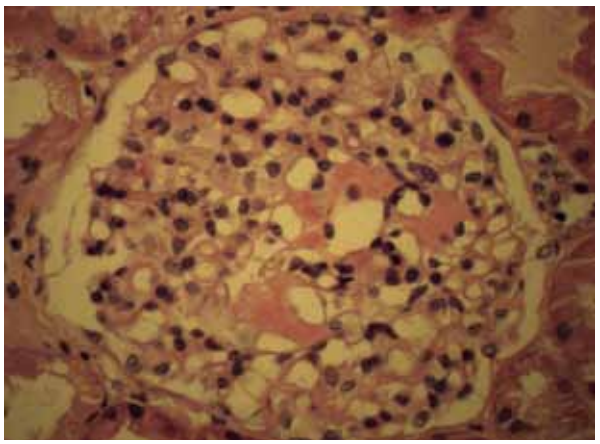


Figure 2. *PAS staining of kidney biopsy*



WHAT IS YOUR DIAGNOSIS?

See page 98 for the answer to this photo quiz.

ANSWER TO PHOTO QUIZ (PAGE 97)

OEDEMA AND CROHN'S DISEASE

DIAGNOSIS

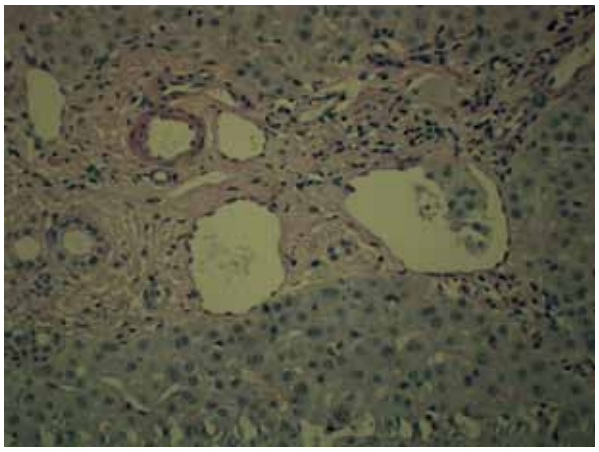
Liver biopsy showed no PSC but depositions of amyloid (*figure 1*). Kidney biopsy also showed depositions of amyloid (*figure 2*). CT imaging and colonoscopy showed no active Crohn's disease, but leucocyte scintigraphy showed activity in the anastomotic area of the ileocaecum. He was treated with prednisolone and 6-mercaptopurine. The oedema diminished, proteinuria declined to 4 g/24 h and the albumin increased to 20 g/l.

Chronic inflammatory disease can be complicated by systemic amyloidosis. Proteins accumulate in tissues as nonsoluble fibrils, resulting in progressive organ failure and eventually death.[1] In this reactive type of amyloidosis, the serum amyloid A protein (SAA) plays an important role. It is synthesised by hepatocytes under regulation of proinflammatory cytokines.[2] The fibrils are derived from these acute phase proteins via a process of cleavage, misfolding and aggregation.[1] The mean plasma concentration of SAA in healthy persons is 3 mg/l, while the concentration during an acute phase response can increase to more than 2000 mg/l.[3] Overproduction of SAA increases the risk of development of AA amyloidosis; it is unclear why this affects just a small group of patients with chronic inflammatory disease.[4,5] The kidney is the organ most affected.[6] Deposition of amyloid results in proteinuria and progressive loss of renal function. Other sites of deposition can be the digestive tract, the liver, the autonomic nervous system and the heart.[7] Treatment consists of removing the stimulus, in this case preventing the persistence of the acute phase response by effectively treating the inflammatory bowel disease.[8] No treatment has a direct effect on the development of SAA,[3] although a recent study showed treatment with eprodisate to be promising.[7]

The Crohn's disease of our patient was difficult to treat, partly due to erratic care and multiple intolerances. This resulted in ongoing inflammation. The end result is manifest AA amyloidosis, presenting as nephrotic syndrome. The SAA plasma concentration was not determined prior to the treatment with prednisolone and 6-mercaptopurine. It was normal during treatment, an indication of improved control of the Crohn's disease.

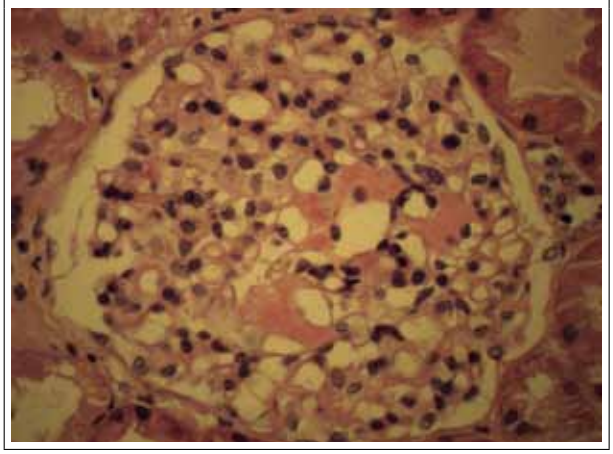
In case of nephrotic syndrome in patients with inflammatory bowel disease, amyloidosis as a rare complication should be considered.

Figure 1. *PAS staining of portal tract in liver biopsy*



The arterial wall shows amorphous depositions which stain positive in amyloid stains (Congo red, SAB, Thioflavine, immunoperoxidase for AA amyloid). There is no intrasinusoidal amyloid deposition.

Figure 2. *PAS staining of kidney biopsy, showing mesangial depositions of amyloid*



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