Microscopic colitis
Studies of epidemiology, clinical features and nitric oxide

Martin Olesen

Akademisk avhandling
som för avläggande av medicine doktorsexamen vid Linköpings Universitet kommer att
offentligt försvaras i Wilandersalen, Universitetssjukhuset, Örebro,
fredagen den 23 januari 2004, kl. 09.00.
Fakultetsopponent: Professor Robert Löfberg, Karolinska Institutet

Department of Medicine, Division of Gastroenterology
Örebro University Hospital
S-701 85 Örebro, Sweden

&

Department of Molecular and Clinical Medicine
Division of Gastroenterology and Hepatology
Linköping University Hospital
S-581 85 Linköping, Sweden
2004
Abstract

Lymphocytic colitis (LC) and collagenous colitis (CC) are newly recognised inflammatory bowel diseases belonging to the group of microscopic colitides (MC). They are characterised clinically by chronic non-bloody and watery diarrhoea, and a macroscopically normal or near normal colonic mucosa where diagnostic histopathological abnormalities are found.

The aims of this thesis were to study the epidemiology of LC and CC in Örebro, the clinical features and outcome of treatment in a large Swedish cohort of patients with LC and the familial occurrence of MC. Further objectives were to study luminal levels of colonic nitric oxide (NO), plasma concentrations of the metabolites nitrate/nitrite and the epithelial expression of inducible nitric oxide synthase (iNOS) and endothelial nitric oxide synthase (eNOS) in patients with MC and correlate to clinical and histopathological status.

Whereas previously thought to be rare diseases, our epidemiological study in Örebro 1993-1998 showed that the annual incidence of LC and CC is close to the figures generally reported in Sweden in Crohn’s disease. The combined rates of LC and CC are nearly as high as the incidence of ulcerative colitis. Microscopic colitis was diagnosed in 10% of all patients referred for a colonoscopy due to non-bloody diarrhoea, and in almost 20% of those older than 70 years.

The clinical features and outcome of treatment in LC were studied retrospectively in 199 Swedish patients. Diarrhoea was the predominant symptom, followed by abdominal pain and weight loss. Forty percent had at least one associated autoimmune or inflammatory disease; the most common were thyroid disorder and coeliac disease. A single attack occurred in 63% with a median disease duration of six months. In 10% a drug induced disease was suspected. A sudden onset of disease was noted in 25% and a non-significant peak of disease onset was seen in December-January. The sudden onset, the single attack of limited duration, and the possible seasonality of the disease’s onset may indicate an infectious etiology in some cases.

Corticosteroids, prednisolone as well as budesonide, were the most effective therapy in our retrospective LC study and more than 80% of the patients improved short-term. However, the relapse risk was high after withdrawal of therapy. A response rate of 50-70% was noted for loperamide, cholestyramine, metronidazole and mesalazine.

A family history of bowel disease - ulcerative colitis, Crohn’s disease, CC or coeliac disease - was reported in 12% of the 199 LC patients, and ulcerative colitis or Crohn’s disease alone in 7%. We also report a familial occurrence of MC in five families, with two affected members in each family. In two families the members had different types of MC whereas in three families they all had CC.

Increased plasma levels of nitrate/nitrite and greatly enhanced levels of colonic luminal NO were found in MC patients. The NO levels were associated to the histopathological status and correlated with the clinical activity, indicating that NO is involved in the pathophysiology of MC. Expression of eNOS in the epithelium was not increased in patients with MC. An increased expression of iNOS was seen apically in the surface epithelium in MC patients, and a correlation between the staining intensity of iNOS and luminal NO levels, pointing towards the epithelial cells being the cellular source of the NO production.