Mesenteric fat as a source of C reactive protein and as a target for bacterial translocation in Crohn's disease

Laurent Peyrin-Biroulet, Florent Gonzalez, Laurent Dubuquoy, Christel Rousseaux, Caroline Dubuquoy, Cecilia Decourcelle, Alain Saudemont, Mickael Tachon, Elodie Beclin, Marie-Francoise Odou, Christel Neut, Jean-Frederic Colombel, Pierre Desreumaux

Gut. 2012 Jan;61(1):78-85.

PETER BOSSUYT
Department of gastroenterology
Imelda general hospital
Bonheiden, Belgium

Peter Bossuyt
is gastroenterologist focusing on IBD and principal investigator at the Imelda GI clinical research centre in Bonheiden.

Introduction

The CRP response in Crohn's disease (CD) is stronger than in ulcerative colitis (UC). For current treatment decisions in Crohn's disease, the level of C-reactive protein (CRP) is a major biochemical guide. However, CRP and endoscopic findings correlate poorly. The mechanism of CRP production is still poorly understood. Recently, adipocytes were identified as a source of CRP aside the liver. Since CD is characterized by mesenteric fat hyperplasia, the authors focused on the role of mesenteric fat in CRP production and the inflammatory process CD.

What this is this study about?

In the present study the role of mesenteric fat in the inflammatory reaction was examined in three steps.

First, the authors demonstrated an overexpression of CRP both on the mRNA and protein level in mesenteric fat. This seems to be a specific property of the mesenteric fat in CD since it is not seen in mesenteric fat in UC and control patients, nor in subcutaneous fat or in the adjacent inflamed intestinal wall of CD, UC or control patients. The fact that there is a positive correlation between transcription levels and plasma CRP concentration suggests that in CD mesenteric adipose tissue is an important source of CRP.

Second, the authors investigated possible triggers of CRP overexpression. Since CD is a transmural inflammatory process, they stimulated adipose tissue in vitro with pro-inflammatory cytokines, which are associated with CD. They found that this triggers the expression of CRP, dependent on the stage of adipocyte maturation. An additional key feature of CD pathogenesis is bacterial translocation, which the authors tested using Gram-negative bacteria. Indeed, stimulation of mesenteric adipocytes with Gram-negative bacteria induces CRP biogenesis. Combined stimulation of mesenteric fat by both pro-inflammatory cytokines and bacteria has a synergistic effect on CRP production and the inflammatory process.

Third, after unraveling the mechanisms of CRP expression in mesenteric fat, the authors explored whether there is a direct translocation of bacteria to the mesenteric adipose tissue. In experimental animal models of colitis and ileitis, bacterial translocation to mesenteric fat and lymph nodes occurred significantly more than in controls. In humans, a higher rate of bacterial translocation to the mesenteric fat and lymph nodes was seen in CD compared to non-CD patients.

What are the key points of this paper?

First of all, this paper highlights the fact that creeping fat is not just an innocent bystander in CD. It demonstrates that adipose tissue is an active player in the inflammatory process. The extent to which mesenteric fat contributes to CD still to be established but it is clear that adipose tissue can sense and react to both bacterial and inflammatory stimuli. As such, it may influence or even drive the inflammatory process in CD. Further research needs to be done to know whether this influence may be protective. Mesenteric fat may be a first line of defense.

A second important message from this paper is the confirmation that CRP is a poor marker for mucosal lesions. CRP does not originates form the bowel wall but from the mesenteric fat and the liver. In this view CRP is an extraluminal marker of inflammation not an intraluminal one.

Finally elucidating the role of adipose tissue in CD can provide new therapeutic targets. By blocking receptors in the mesenteric fat it may be possible to influence the inflammatory cascade.