GASTROINTESTINAL COMPLICATIONS OF SYSTEMIC SARCOIDOSIS. V. Defosse, L. de Leval, A. De Roover, O. Detry, P. Honoré, J. Boniver. (1) CHU Liège.

The incidence of systemic (extra pulmonary) sarcoidosis is underestimated. The gastrointestinal complications of this disease are even more ignored. We present here the cases of three patients who had developed severe abdominal sarcoidosis. The first one is a 45-year-old woman who developed sarcoidotic uveitis in 2000. Bronchial biopsy realised in 2001 revealed the presence of multiple epithelioid granulomas of sarcoidotic type. Liver blood tests have been abnormal since 2004, rapidly increasing. In 2006, serum bilirubins were over 400 mg/l. Clinical examination and further explorations revealed chronic cholestatic syndrome, portal hypertension and a Budd-Chiari syndrome. Liver biopsy confirmed granulomatous involvement of the parenchyma. A liver transplant was performed. The study of the liver explant (2100 g) revealed the presence of florid granulomatous and sclerosing involvement of the liver parenchyma, severely evolutive and admixed to cholangitic sclerosis, sub-hepatic vessel sclerosis and porta vena thrombosis. It was associated with a diffuse aspecific lobular hepatitis, and with portal hypertension histological proofs. The second case was a 56-year-old woman, who also needed a liver transplant for severe cholestatic syndrome due to liver sarcoidosis, refractory to corticosteroids. The study of the liver explant revealed granulomatous vasculitis. The third one is a 46-year-old woman under observation since 1988 (diagnosis of pulmonary sarcoidosis, asymptomatic). Liver biopsy performed in 2001 had revealed granulomatous involvement, associated with abnormal liver blood tests. In 2005, she complained about asthenia, weight loss and hypochondric pain. Further explorations showed increasing liver blood test abnormalities, and heterogenous splenomegaly at CT-scan. Splenectomy was performed. Histopathologic study of the surgical specimen (1300 g) confirmed non-caseating granulomatosis. Another liver biopsy was performed in June 2006, showing cirrhotic evolution. Systemic sarcoidosis is a multisystemic pathology the aetiology of which remains uncertain, characterised by multiple non-caseating granulomas. Though pulmonary or lymphatic involvement is well documented, gastrointestinal manifestations still remain underestimated. The three patients reported illustrate the dramatic possible issues of these involvements. Large autopsy series have researched granulomas in the whole gastrointestinal tract, and have found a higher incidence than diagnosed by other routine techniques, including CT-scan. For example, among 117 patients referred for autopsy (with a pre-mortem diagnosis of sarcoidosis), hepatic granulomas were found in 66.5% of cases, splenic granulomas in 49.5% of cases, and pancreatic, gastric and enteric granulomas in a small percentage (compared to 77% for pulmonary and mediastinal involvement).


Background & aims: The intestinal bacterial flora is involved in the pathogenesis of Crohn's disease (CD). Bacterial translocation may be required for the development of chronic transmural inflammation. Three single nucleotide polymorphisms (SNPs) of the CARD15 gene are associated with an increased susceptibility to develop CD and a decreased expression of alpha-defensins in ileal Paneth cells. We questioned whether the CARD15 gene status influences the type and ultimate distribution in the bowel wall of translocating bacteria in CD patients.

Methods: 4 CD patients were selected on the basis of their status for the Arg702Trp, Gly908Arg, and Leu1007IleSNPs of the CARD15 gene (1 wild type; 1 heterozygous and 1 homozygous for Arg702Trp; 1 compound heterozygous for Arg702Trp and Gly908Arg). Normal and pathological mucosa, myenteric plexus and mesenterial lymph node tissue were microdissected from snap-frozen ileal biopsies taken from the surgical bowel specimens. Extracted DNA was used as template in a 2-round PCR using universal primers for the 16S rDNA gene. Purified PCR products were subcloned, sequenced and subjected to a BLAST-search against the GenBank-, EMBL- and RDPII-databases.

Results: PCR and cloning of 16S rDNA was successful in all samples. Sequence analysis revealed the presence of typical bowel bacteria (Enterobacteriaceae; Clostridia; Bacteroidetes) at all levels of the bowel wall, but there was no relation between the CARD15 gene status and the type of translocating bacteria. There was also no difference between the types of bacteria detected at the mucosal level and deeper in the bowel wall. Interestingly, 2 samples of the myenteric plexus in macroscopically involved bowel segments contained DNA derived from Legionella species.

Conclusions: The majority of translocating bacteria in CD belong to the typical bowel microflora. The status of the CARD15 gene for the Arg702Trp, Gly908Arg, and Leu1007IleSNPs does not influence the type and ultimate distribution in the bowel wall of these bacteria. Interestingly, this is the first report that demonstrates the presence of Legionella species deep in the bowel wall in CD patients. Further exploration of additional biopsy samples will be needed to confirm this finding.