



## SCIENTIFIC LETTERS

## 2016: Inflammatory bowel disease epidemic in Asturias<sup>☆</sup>



### 2016: epidemia de enfermedad inflamatoria intestinal en Asturias

Dear Editor:

The term epidemic refers to the occurrence of a number of cases of a specific disease that exceeds the expected incidence in a given geographical area. The Hospital Universitario Central de Asturias (HUCA) is the regional referral centre for inflammatory bowel disease (IBD) for the paediatric population of the Autonomous Community of Asturias, Spain. Historically, the department of paediatric gastroenterology diagnosed an average of 2 new cases of IBD each year. However, in year 2016 the department diagnosed 15 new cases.

With the aim of finding an explanation to this striking increase in incidence, we reviewed the health records of children (aged 0–14 years) that received a diagnosis of IBD in the paediatric gastroenterology outpatient clinics of the HUCA between December 2015 and January 2017. We summarised the epidemiological, clinical and laboratory characteristics of these cases and compared them with those from previous years.

Fifteen new cases were diagnosed in the period under study. The mean age at diagnosis was 10 years, and one patient had onset at the atypically early age of 19 months. In previous years, the outpatient clinics of the HUCA had managed 23 patients with a median age of 11 years, the youngest of whom was 2 years old. The increase in the incidence of IBD was of approximately 650%, from 2 per 100,000 to 2 per 10,000 inhabitants per year. In 2016, 46.7% of new cases were diagnosed in male patients compared to 74% in the group of cases diagnosed in previous years ( $P = .03$ ). In 2016, most of the patients that received the diagnosis resided in an urban area (66.6%), and Oviedo and Gijón were the cities where the incidence increased most, while in previous year, the distribution of cases was more dispersed throughout the entire region of Asturias. In 2016, Crohn disease (CD) accounted for 66.7% of the cases, and the most frequent presenting symptoms were bloody stools and abdominal pain. In previous years, the distribution of

diagnostic categories was more even, with 52.2% of cases of CD, 43.5% of ulcerative colitis (UC) and 4.3% of indeterminate colitis (IC). In 2016, only one patient had a family history of IBD, while 46.7% had underlying diseases (57% asthma/allergy). The body weight was within the normal range in 73.3% of patients (body mass index between the 15th and the 85th percentiles), 1 patient was obese and 1 malnourished at the time of diagnosis. Eighty percent of patients had faecal calprotectin levels of 1000  $\mu\text{g/g}$  or greater, while only 5 patients had an erythrocyte sedimentation rate of more than 20 mm/h and 3 a C-reactive protein level of more than 5 mg/dL. Also, 26.7% tested positive for anti-*Saccharomyces cerevisiae* or anti-neutrophil cytoplasmic antibodies. Only one patient had an albumin level of less than 30 g/L. Thrombocytosis was present in 73.4% of cases. Except for one episode of severe colitis (Paediatric Ulcerative Colitis Activity Index [PUCAI] = 65 points) in the child aged 19 months, activity index scores in all patients (PUCAI and Paediatric Crohn's Disease Activity Index [PCDAI]) reflected mild disease at the time of diagnosis.

The causes of this increase in incidence have yet to be determined. The aetiology of IBD is multifactorial, and it is hypothesised that it results from the interaction of genetic vulnerability,<sup>1</sup> various environmental factors and the intestinal microbiota. When IBD is diagnosed in children aged less than 6 years, it is considered very-early-onset IBD (VEOIBD). Furthermore, diagnosis in children aged less than 2 years requires ruling out monogenic forms of IBD, as these children exhibit more disseminated inflammation, higher rates of treatment resistance and rapid disease progression.<sup>2</sup> In our patient aged 19 months, we ruled out immunodeficiencies that could present with an IBD-like phenotype (primary immunodeficiencies, autoinflammatory diseases, ...). However, we cannot rule out a genetic basis in this case, as a genetic investigation was not performed in this patient as part of the initial evaluation due to the presenting phenotype and the very favourable response to standard treatment. There are numerous articles in the literature on the influence of environmental factors in IBD.<sup>3</sup> There is an evidence of an association with diets rich in animal protein and additives, the excessive use of antibiotics and the increase in environmental pollution, among others, but the pathophysiology that underlies this association is not understood. We do know that antibiotic use can lead to dysbiosis in the intestinal microbiota, which in turn is associated with IBD.<sup>4</sup> The SPIRIT study<sup>5</sup> (a multicentre study conducted between 1996 and 2009) found that the incidence of CD had tripled, the incidence of UC doubled, and a north-south gradient in the incidence of IBD. There is evidence of an association between vitamin D deficiency and IBD,<sup>6</sup> which could partly explain the presence of this north-south gradient.

<sup>☆</sup> Please cite this article as: Pascual Pérez AI, Díaz Martín JJ, Jiménez Treviño S, Bousoño García C. 2016: epidemia de enfermedad inflamatoria intestinal en Asturias. An Pediatr (Barc). 2018;89:183–184.

The increased incidence of IBD observed in our region in 2016 has the characteristics of an epidemic. Although we found no differences in the age at onset or disease severity, we did find a significant increase in the incidence of IBD in female patients. Performance of epidemiological studies would be useful to try to determine the underlying causes of this phenomenon.

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2341-2879/

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## Faecal microbiota transplant in a child with very early onset inflammatory bowel disease<sup>☆</sup>



### Trasplante de microbiota fecal en niño con enfermedad inflamatoria intestinal de inicio muy precoz

Dear Editor:

The intestinal dysbiosis found in patients with inflammatory bowel disease (IBD) has partly guided the development of treatment strategies. Faecal microbiota transplantation (FMT), which consists in the infusion of a faecal suspension from a healthy donor into the gastrointestinal tract of a recipient to cure a specific disease associated with changes in the intestinal microbiota, has proven efficient in the treatment of recurrent infection by *Clostridium difficile* in adults and children. This treatment modality could also contribute significantly to the control of IBD. Diverting ileostomy is a surgical intervention that has been used as a temporising therapy in children with refractory colitis to stabilise symptoms, improve nutritional status and taper or discontinue steroid therapy.<sup>1</sup> We describe the first paediatric case of FMT via diverted ileostomy performed in Spain.

The patient was a boy aged 6 years and 7 months whose mother had Crohn disease. He had received a diagnosis of inflammatory bowel disease unclassified (IBDU) at age 2 years based on a history of recurrent episodes of

bloody diarrhoea, anaemia and hypoalbuminaemia. Tests for the differential diagnosis of immunodeficiencies and monogenic inflammatory diseases were negative, and diagnostic tests for detection of infection including tuberculosis and cytomegalovirus were repeatedly negative, except in the assessment of 3 episodes of bloody diarrhoea, when the patient tested positive for *C. difficile* toxin. Three endoscopic examinations with histological examination of biopsy specimens did not provide significant findings that would

**Table 1** Donor screening criteria.

Age >18 years
BMI within normal range
No personal or family history of autoimmune disease
No evidence of current transmissible disease
No evidence of psychiatric disorders
No use of antibiotic agents or proton pump inhibitors in the past 3 months
Food diary to verify healthy diet
Stool cultures negative for pathogenic bacteria, parasites, <i>Clostridium difficile</i> , rotavirus, adenovirus
Faecal calprotectin <50 µg/g of faeces
Negative for <i>Helicobacter pylori</i> stool antigen
Negative serologic tests for hepatitis A, B and C, HIV, syphilis and CMV
Normal blood panel results (complete blood count, creatinine, electrolytes, transaminases, cholesterol, triglycerides, ferritin, albumin, immunoglobulins, CRP and vitamin D3)
Absence of high-risk sexual behaviour (multiple partners, sex work)
No history of travel to endemic regions with a high prevalence of diarrheal diseases

<sup>☆</sup> Please cite this article as: Sierra Salinas C, Vicioso Recio MI, Blasco-Alonso J, Serrano Nieto MJ, Navas-López VM. Trasplante de microbiota fecal en niño con enfermedad inflamatoria intestinal de inicio muy precoz. *An Pediatr (Barc).* 2018;89:184–186.

BMI, body mass index; CMV, cytomegalovirus; CRP, C-reactive protein; HIV, human immunodeficiency virus.