Eosinophilic esophagoduodenitis with unusual response to omeprazole in a teenager

Esofagoduodenitis eosinofílica con respuesta inusual al omeprazol en un adolescente

Dear Editor:

Eosinophilic gastroenteritis (EGE) represents one variety within the spectrum of diseases referred to as eosinophilic gastrointestinal disorders (EGIDs), which includes eosinophilic esophagitis (EoE), gastritis, enteritis and colitis.[1]

The EGE (beyond EoE) is a rare gastrointestinal disease, even more rarely happens to appear EoE along with ED in the same patient.

Twelve-year-old male patient, with a personal history of rhinoconjunctivitis and bronchial asthma due to allergy to grass and fungal allergens and subclinical sensitization to legumes since the age of 8. Gastroesophageal reflux disease (GERD) diagnosed by pH-metry at 10 years of age. The patient refered persistent abdominal pain, intermittent diarrhoea and symptoms of esophageal dysfunction – such as heartburn, vomiting, choking –, even though the therapy with omeprazole, 20 mg OD.

Esophagogastroduodenoscopy (EGDC)[1] with multiple biopsies/organs/sections oesophagus (3: upper, medium and lower), stomach (2: antrum and body), duodenum[2] was performed. Oesophagus with linear grooves and the appearance of some oesophageal rings were reported. The histological samples happened to contain 27 eosinophils/high power field (eos/hpf) in the duodenum with normal intestinal villi, 55 eos/hpf in the oesophagus, but no presence of eosinophils in the stomach was confirmed. After, the omeprazole dosage was increased to 40 mg BD for 2 months. Then the mentioned diagnostic procedure EGDC 2 was repeated, and no eosinophils were found in the samples of the biopsy of the duodenum, stomach or oesophagus (Table 1).

The patient continued with omeprazole (40 mg OD) and two years later. We repeated the EGDC 3 without evidence of eosinophilic infiltration in the 3 organs (Table 1). *Helicobacter pylori* was not detected in the in none of the three organs explored in the three EGDCs performed. We excluded other possible causes of tissue eosinophilia with thoracoabdominal ultrasound, performed 30 days before the EGDC1: normal; blood autoantibody levels and 3 stool cultures (intestinal parasitosis): negatives. Allergy study: Sensitization to pollen (grass and olive-tree) and legumes. The patient was diagnosed with eosinophilic esophagoduodenitis (EED), that responded omeprazole (very unusual response)

EGIDs was described by Kaijer in 1937.[2] These disorders characterized by gastrointestinal (GI) symptoms with eosinophilic inflammation (EI), most commonly in the GI mucosa but sometimes also of the muscular or serous layer. Other causes of these findings need to be ruled out. Symptoms may vary depending on both the location of EI (organ) and its extension (invasion of the bowel wall layers).[1] In addition to symptoms compatible with EoE, our patient had intermittent diarrhoea, suggesting EoE with EI of the intestinal mucosal layer. EI was confirmed in both organs with oesophageal and duodenal biopsies.

EGE is a rare disease, with poorly defined diagnostic criteria and treatment, therefore often responds poorly to therapy and there is no commonly accepted long-term treatment.[3] Except for EoE, consensus diagnostic criteria for the remaining EGIDs are lacking.[4] There is also no consensus in the number of eos/hpf for the pathological diagnosis of EGE: some authors set the cut-off point at 20 eos/hpf in the stomach and duodenum[2] while others set it at 25 eos/hpf.[5]

According to the 2007 consensus GERD had to be ruled out in order to diagnose EoE, but since the 2011 consensus there was no need to do so, since GERD can be associated with EoE, and both diseases are not mutually exclusive. Our patient had both EoE and GERD, what possibly contributed to the delay in the diagnosis of EoE. Since he was an atopic male with the symptoms persisted despite treatment of Omeprazole 20 mg OD, we considered the possibility that he had concomitant EoE,[1] and so it was.

In the EoE, neither the long-term treatment nor best maintenance doses for pharmacological therapies have been defined.[1] We agree with experts and the guidelines, which recommend an approach where the dose is progressively decreased to lowest dose that keeps the disease in remission; which in our patient were 40 mg OD.

There is controversy about the long-term efficacy of PPIs in children. A recent study has first shown that most children remain in clinical and pathological remission at one-year follow up on low maintenance dose; no data for >1 year of follow up are available yet; in our patient, sustained remission of EE for at least 2 years has been achieved with Omeprazole 40 mg OD. The systemic anti-inflammatory effect of Omeprazole could induce the remission of EI in the duodenum.

''In conclusion, we present the first case of eosinophilic esophagoduodenitis that responds to 40 mg of omeprazole and stays in remission with this dose for at least 2 years.

Conflict of interest

The authors declare that they have no conflict of interest.

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Elisa Gómez Torrijos[a,*], Alejandro Raúl Gratacós Gómez[b], Alba Mª Extremera Ortega[a], Oscar Gonzalez Jimenez[a], Juana Bautista Joyanes Romo[a], Rosa Garcia Rodriguez[a]

[a] *Allergy Section, Hospital General Universitario, Ciudad Real, Spain*

[b] *Facultad de Medicina, Universidad de Castilla La Mancha, Ciudad Real, Spain*

[*] Corresponding author.
E-mail address: egomezt.cr@gmail.com
(E.G. Torrijos).

Inflammatory bowel disease and inherited colorectal cancer: Is there a genetic link?☆

Enfermedad inflamatoria intestinal y cáncer colorrectal hereditario: ¿existe un vínculo genético?

Inflammatory bowel disease (IBD) is associated with an increased risk of developing dysplasia and cancer. This is mainly due to the chronic inflammation, which is an independent risk factor linked to the duration and extent of the disease.[1]

The risk of colorectal cancer (CRC) in IBD has decreased in recent years, probably due to the optimisation of medical treatment and endoscopic surveillance. However, despite these advances, there is a lack of consensus on the optimal strategies for surveillance and the decision to resort to surgical intervention.[2]

We present the case of a patient with a diagnosis of CRC and long-standing ulcerative colitis (UC). Genetic testing confirmed he was a carrier of the familial BRCA1 pathogenic mutation, raising the possibility of a genetic link between the two diseases.

This was a 35-year-old male with a 15-year history of pan-ulcerative colitis on treatment with mesalazine. Onset had been at age 20 with a mild-to-moderate flare-up. He was initially treated with azathioprine, but it was discontinued after three months due to gastrointestinal intolerance. Since then he has been on monotherapy with mesalazine and remained in clinical remission at check-ups.

The first endoscopy for CRC surveillance ten years after diagnosis detected a flat polyp (0-IIa) of about 2 cm in the transverse colon which was biopsied and tattooed, as it exhibited the *non-lifting* sign (Fig. 1). He was referred to surgery and had a total proctocolectomy, with examination of the surgical specimen confirming ulcerative-invasive adenocarcinoma.

As the patient had a family history of breast cancer diagnosed at a young age (mother died at age 40, sister diagnosed at 35 and carrier of the BRCA mutation), he was referred to the Genetic Counselling Unit, where he was diagnosed as having a mutation in BRCA1, with particular susceptibility to breast and prostate cancer and, in his case, to CRC due to his history of IBD.

Inflammatory bowel disease develops in patients who are genetically predisposed and then exposed to environmental factors, which are not fully understood. These patients have an increased risk of CRC, attributable to the carcinogenic effect of chronic mucosal inflammation.

The risk of colorectal cancer for any patient with ulcerative colitis is high, estimated at 2% after 10 years of disease, 8% after 20 years and 18% after 30 years.[3]

There are reports in the literature of various different genetic factors being involved in the development and severity of IBD. However, the potential for simultaneous predisposition to UC and CRC has not been studied from a genetic point of view.

Alterations in the expression of the E-cadherin gene (CDH1), DNA methylation (mainly its promoters p14 and p16) and microRNA can act as oncogenes and favour the development of CRC in this type of patient.[4]

BRCA 1/2 mutations are associated with an increased risk of breast, ovarian, pancreatic and prostate cancer. However, no association with colorectal cancer has been demonstrated to date.

In the case of our patient, there was a double risk factor for developing CRC: long-standing extensive UC or pan-UC, and being a carrier of the familial BRCA1 pathogenic mutation.

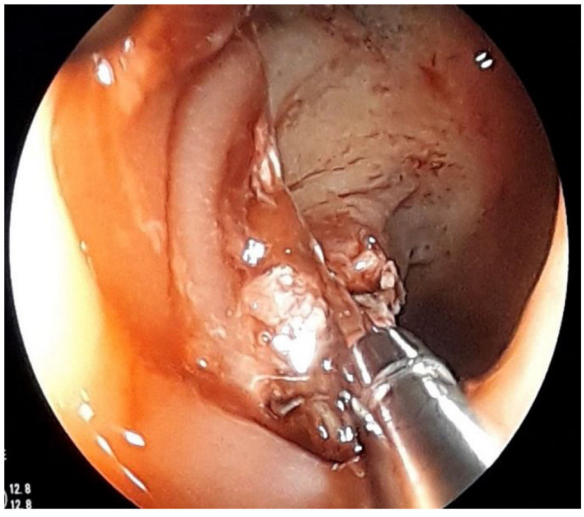

Figure 1 Non-lifting sign after injection techniques.

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