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## Non-responsive coeliac disease: Coeliac crisis vs. refractory coeliac disease with response to corticosteroids<sup>☆</sup>



### Enfermedad celíaca no respondedora: crisis celíaca vs. enfermedad celíaca refractaria con respuesta a corticoides

Coeliac disease (CD) is an immune-mediated enteropathy, triggered by the ingestion of gluten in genetically predisposed individuals, with various gastrointestinal and systemic manifestations.<sup>1</sup> Most patients respond to a gluten-free diet (GFD), but there is a percentage of patients with non-responsive CD, with the main cause being poor adherence to a GFD.<sup>2</sup> With lesser frequency, the lack of response is due to refractory coeliac disease (RCD).<sup>3</sup> Coeliac crisis (CC) is a rare and potentially fatal complication of CD.<sup>4</sup>

A 63-year-old woman with a history of hypertension and hyperthyroidism, undergoing treatment with carbimazole and torasemide. She was admitted to hospital for chronic diarrhoea with symptoms of severe malnutrition and an organic psychotic mania episode secondary to CD (diagnosis confirmed with intestinal biopsy consistent with Marsh 3a and positive tissue transglutaminase-IgA antibodies [tTG-IgA]: 45 U/ml [normal value: <20 U/ml]), which responded clinically and analytically to a GFD (tTG: 2 U/ml at 2 months after the episode). At 3 months from diagnosis, she was readmitted for disassociated psychosis and severe diarrhoea of rapid progression, with protein-calorie malnutrition, electrolyte imbalances and vitamin deficiencies, despite good adherence to the GFD. Intestinal infections were ruled out (negative faecal cultures and negative viral, bacterial and mycobacterial cultures in intestinal tissue samples). The tTG were determined at admission. They were positive at low titers (25 U/ml) and became negative on the fifth day of admission after GFD (9 U/ml). The genetic test was positive (HLA-DQ2) and the intestinal biopsies showed mucosal atrophy (Marsh 3b in the jejunum and Marsh 3c in the duodenum). During her stay, the patient required blood concentrate transfusions, electrolyte replenishment and parenteral nutrition. After one month without responding to the GFD, the patient developed pneumonia with severe

respiratory failure, which was treated with levofloxacin and linezolid, as well as intravenous corticosteroids (methylprednisolone 1 mg/kg), after which she had an excellent response both in the respiratory and digestive symptoms. At discharge, the corticosteroid treatment regimen was tapered off with good response. After one year of follow-up and good adherence to the GFD, the patient was asymptomatic with negative tTG (2 U/ml).

Non-responsive CD is defined as CD that does not respond after 6–12 months on a GFD.<sup>5</sup> Up to 10–20% of patients with CD develop non-responsive CD,<sup>2</sup> with non-adherence to the GFD being the main cause of the lack of response.<sup>3</sup>

tTG values tend to turn negative after a variable amount of time on a GFD. However, they can remain positive in up to 20–30% of patients with RCD despite good adherence to the GFD.<sup>3,6</sup> In our case, the patient had positive tTG values at low titers at admission which could be a false positive or contamination with trace amounts of gluten. The rapid negativisation of said values is notable, given that the antibody levels usually decrease gradually after removing gluten from the diet (half-life of 6–8 weeks).<sup>7</sup> These disparate levels in a short period of time caused confusion in the diagnosis.

Given the suspicion of contamination with trace amounts of gluten, the differential diagnosis of CC could be suggested. CC is a fulminant presentation of CD, with very few cases having been reported in adult patients. It is defined as an acute or rapidly progressing onset of the gastrointestinal symptoms attributable to CD, requiring hospitalisation and/or parenteral nutrition along with at least two objective signs of malnutrition, dehydration or electrolyte imbalance.<sup>4</sup> In this disease, tTG normally have high titers, since the majority of patients who have a CC did not have a prior diagnosis of CD and, therefore, did not follow a GFD, although others may develop it after diagnosis when they do not adequately adhere to a GFD.<sup>4,8</sup> The treatment for CC is a GFD, but some patients require steroids.<sup>4</sup>

On the other hand, in light of the possibility that the initially positive tTG values could have been a false positive, given that they were negative a few days later, a differential diagnosis with RCD was suggested, after ruling out other conditions such as collagenous sprue, tropical sprue and bacterial overgrowth, among others.<sup>9,10</sup>

RCD is defined as the persistence of villous atrophy and clinical malabsorption that do not respond to a GFD. The refractory nature can be primary, if the patient never responded to the GFD, or secondary, if they had an initial response.<sup>5,10</sup> It is a rare condition (1–1.5% of patients with CD).<sup>2</sup> RCD can be classified as type I or type II. Type II RCD is characterised by abnormal T-cells in the intestines and is associated with a higher mortality than type I (56% vs. 7% at 5 years), mainly due to the risk of developing intestinal T-cell lymphoma.<sup>6</sup> With respect to treatment, steroids briefly

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improve clinical symptoms in most patients, but normalisation of intestinal mucosa is rarely achieved and in most cases a dependency on steroids is observed.<sup>3,9</sup>

The spectrum of disorders related to gluten constitutes a collection of complex diseases with limits that are not always defined. In our case, after having ruled out other causes of non-responsive CD and assuming that the initial tTG had actually been negative, the differential diagnosis with RCD was suggested. However, given an initially positive tTG and the excellent response to corticosteroids and, above all, having presented no relapses after the discontinuation of the corticosteroids, a diagnosis of CC is more probable.

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## Duodenal metastases from sarcomatoid renal cell carcinoma: Case report<sup>☆</sup>



### Metástasis a duodeno de cáncer renal de células claras con patrón sarcomatoide: reporte de caso

Renal cell carcinoma constitutes 3% of all neoplasms. At the time of diagnosis, 25% of patients have metastasis, reaching 51% in patients with nephrectomy.<sup>1</sup> Metastasis presents in the gastrointestinal tract in 0.2–0.7%.<sup>2</sup> There are few cases reported with metastasis of renal cell carcinoma to the duodenum, with the minority in women. The most common histology (75–85%) of these neoplasms are clear cells, with the sarcomatoid type variant being associated with poor prognosis.<sup>3</sup> There are no reported cases of duodenal metastasis of clear cell renal cell carcinoma (CCRCC) with sarcomatoid differentiation, with this being the first case in

a 48-year-old patient who came to the emergency department due to gastrointestinal tract bleeding.

A 48-year-old woman with a history of chronic exposure to wood smoke 200h/year, high blood pressure for the past seven years, and nephrectomy one year prior to her admission due to CCRCC carcinoma with sarcomatoid differentiation. She came in with symptoms of one-week evolution characterised by burning and sharp epigastric pain, haematemesis and melaena. At admission she had hypotension, tachycardia, and was febrile. Her admission analysis reported haemoglobin 6.5g/dl, thrombocytosis  $797 \times 10^3/\text{mm}^3$ , leukocytosis  $14.7 \times 10^3/\text{mm}^3$  with neutrophilia of  $12.9 \times 10^3/\text{mm}^3$  and elevated C reactive protein of 27.8 mg/l. An abdominal computed tomography (CT) was carried out, showing a mass in the second part of the duodenum, measuring 41 mm × 37 mm × 56 mm. An endoscopy was performed, showing a 10 cm tumour of neoplastic appearance in the second part of the duodenum, submucosal, with irregular and ulcerated surface with areas of haemorrhage, with 90% stenosis of the duodenal lumen (Fig. 1). The biopsy reported CCRCC with metastatic sarcomatoid differentiation (Fig. 2). The patient continued with gastrointestinal tract bleeding, requested voluntary discharge, and died one week later.

The most common metastasis locations for CCRCC are: lungs (75%), lymph nodes (36%), liver (18%), brain (8%) and skin (6%).<sup>4</sup> It causes invasion in the gastrointestinal tract

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