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Early appearance of anal mucinous carcinoma in Crohn disease: Case report

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ABSTRACT:
Background*: The development of mucinous carcinoma within anal Crohn disease is highly unlikely, appear after several years of evolution of an anal fistula and its diagnosis is difficult as it may be masked by the inflammatory disease. The particularity in our clinical case is the appearance of the tumor rather early after less than 4 years of evolution of the anal fistula.*
Patient concerns*: Our patient is a 38-years-old female who is followed for ileo colic Crohn disease A2 L3 B2-3 evolving for 10 years and a complex anal fistula for less than 4 years having undergone a Seton drainage on multiple occasions and an anal stricture for less than 1 year; without sign of histology malignancy. She was treated by Azathioprine for 4 years before the appearance of anal fistula; and then Infliximab for few weeks.*
Diagnosis: *Then she developed an anal mucinous carcinoma on anal fistula Classified T4N0M0. This rare histological entity, which is very difficult to diagnose requiring in our case the recourse to a surgical biopsy, generally appears on a chronic anal disease evolving for more than 10 years The decision of multidisciplinary meeting was a palliative radiotherapy given the tumor volume and patient nutritional status while keeping a definitive stomy.*
Results: *The diagnosis retained is that of an advanced anal mucinous carcinoma developed on an anal fistula which has been evolving for less than 4 years and favored by taking azathioprine and antibiotics for infectious episodes and probably initiated by taking infliximab.*
Conclusion: *Through our case report we draw the attention of clinicians to the possibility of early appearance of anal mucinous carcinoma with aggressive evolution and poor prognosis; we should think about it in front of the atypical evolution of anal fistula in Crohn disease and requiring the realization of multiple and deep biopsies.*
Key Words: *Crohn disease, Mucinous carcinoma, anal fistula*

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I. INTRODUCTION

Crohn disease is a chronic inflammatory bowel disease that can affect the entire digestive tract from the mouth to the anus. Between 17 and 50% of cases, the disease presents with perianal involvement, mainly in the form of a fistula. [1] Cohort and population studies have shown an increased risk of intestinal cancer in Crohn's disease [2] [3]. Other neoplasms may also occur more frequently in Crohn's disease, including myeloid and lymphoid malignancies as well as carcinoid tumors [4] [5]. The features of colorectal cancers in Crohn's disease appear to include: old and extensive colonic disease, young age at cancer diagnosis, tendency to localize in the distal colorectum, and mucinous-like histopathologic features. [6]

The development of mucinous carcinoma within these fistulas is highly unlikely and its diagnosis is difficult as it may be masked by the inflammatory disease. This tumor is generally locally aggressive and its prognosis is poor. [1]

II. CASE REPORT:

This is a 28-year-old young patient who presented for the first time in November 2011 with chronic diarrhea associated with Koenig syndrome in whom the clinical examination, particularly proctologic, was without abnormalities. This is a 28-year-old young patient who presented for the first time in November 2011 with chronic diarrhea associated with Koenig's syndrome in whom the clinical examination, particularly

proctologic, was without abnormalities. Entero-MRI revealed an ileal multisegmental inflammatory with individualization of two ileo-ileal and ileo-transverse digestive fistulas. Colonoscopy showed a crossable stricture of the transverse colon with visualization of a fistulous orifice upstream of the stenosis, the rest of the colon appeared normal. The eso-gastro-duodenal fibroscopy was normal. At the end of the morphological assessment, the diagnosis of stenosing and fistulizing ileocolic Crohn's disease (CD) classified A2 L3 B2-3, without ano-perineal involvement, was retained. Surgical treatment was performed by performing a right ileocolic resection with ileo-transverse anastomosis. The anatomopathological study of the surgical specimen was compatible with Crohn's disease.

In May 2012, 6 months after surgery, a follow-up colonoscopy found an endoscopic appearance compatible with an anastomotic endoscopic recurrence of the disease classified I3 according to the Rutgeerts classification, and since then, a background treatment based on an immunosuppressant (Azathioprine) at a dose of 2.3 mg / kg / day was required after a correct pre-therapeutic assessment, for lack of anti-TNFα at the time. The patient was followed regularly in consultation for a period of 4 years during which she was asymptomatic and no side effects to the treatment were detected.

In August 2016, the patient was admitted for therapeutic reassessment. Clinically, she was asymptomatic but on endoscopic monitoring the appearance of the anastomotic recurrence of Crohn disease classified as Rutgeerts I3 was unchanged, resulting in a blood test for 6-TGNs in which the blood level was satisfactory. It was therefore concluded that the immunosuppressants had failed, hence their discontinuation. The patient was kept in therapeutic abstention with regular follow-up since the biotherapy was not available.

In November 2017, the patient presented the first complex ano-perineal fistula with para-anal abscess caracterised by pelvic MRI (magnetic resonance imaging). The management consisted of the administration of an oral bi-antibiotic therapy, with fistulas drainage, the biotherapy still not available. The patient remained stable until 2019 when she presented two new active anal fistulas also drained.

In July 2020, she developed new fistula with anal narrowing with no sign of histological malignancy. After drainage, she was treated with Infliximab at a dose of 5 mg / kg at week 0, week 2 then week 6. At week 14, the patient presented a loss of gas through its vagina and anal incontinence (Wexner score =14). Pelvic MRI showed an inflammatory recto-sigmoid thickening with complex recto-anal fistulas and a 10 cm left para rectal abscess with the impossibility of studying sphincter given the significant ano-perineal involvement. Endoscopy demonstrated a relapsing CD with a CDEIS score of 18. The therapeutic approach was to perform a discharge colostomy with cessation of biotherapy treatment in October 2020.

In March 2021, she presented a budding ulcerative mass in the perianal region (figure 1) for which the exploration under sedation objectified a large cauliflower tumor infiltering the anal sphincters containing mucin. Surgical biopsy confirmed anorectal mucinous carcinoma. Imaging showed a large tumor occupying almost the entire pelvis with a double component, cystic and solid that mesures 107*93*172 mm with ano-recto-vaginal invasion (figure 2) classified T4N0M0.

The decision of multidisciplinary meeting was a palliative radiotherapy given the tumor volume and patient nutritional status while keeping the stomy

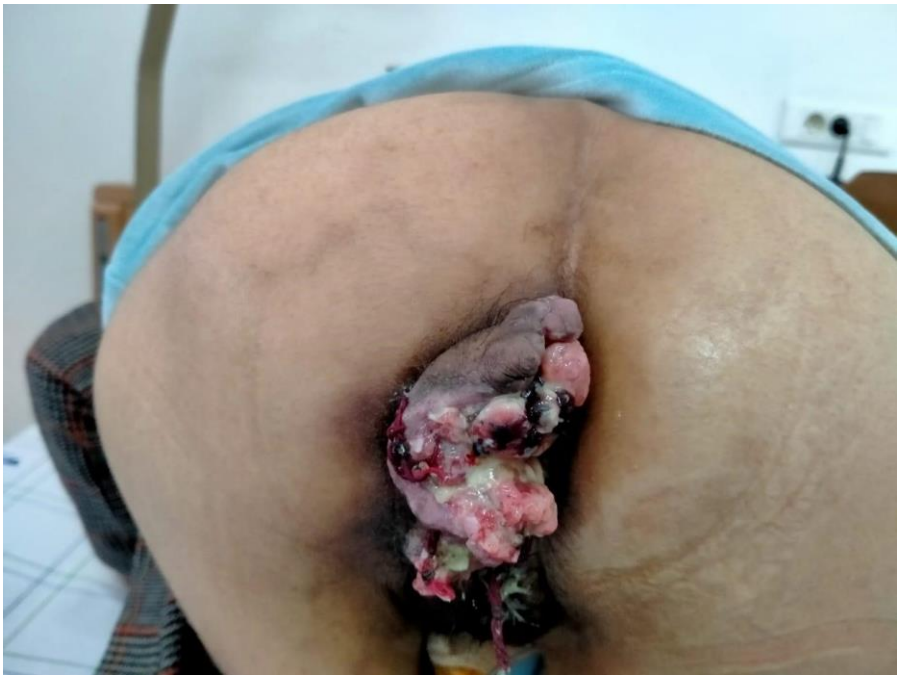

Figure 1: Ulcerative Budding anal Mass

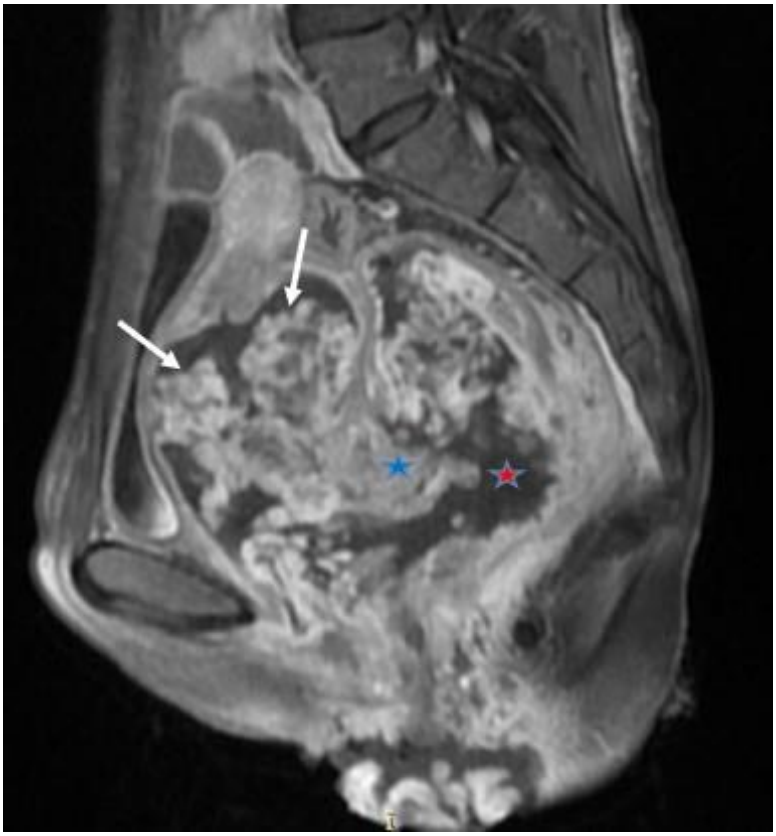

Figure 2: Sagittal T1 FAT SAT sequence image after gadolinium injection showing the pelvi-perineal tumor with double component, cystic (red asterisk) and solid (blue asterisk). Notice the large endovaginal extension (arrows)

III. DISCUSSION:

Anal cancer accounts for 2 to 3% minority among neoplasms of the gastrointestinal tract. [7] [8] Three types of anal canal cancer have been described; intestinal adenocarcinoma, squamous cell carcinoma and mucinous adenocarcinoma. Only 5 to 11% of anal cancers correspond to anal mucinous adenocarcinoma. [7] [8]

There is no consensus on its origin, pathogenesis or biological behavior. However, there is an increase in its incidence when there are concomitant chronic inflammatory conditions, such as chronic anal fistula in a patient with Crohn disease. In 1934, Rosser and al, pioneered the description of perianal carcinoma from chronic fistula. Some authors, such as Traube et al, have postulated that this association is due to the need for constant regeneration of the mucosa. [1]

Mucinous carcinoma of the anal canal is estimated to have an incidence of 0.7% in patients with Crohn's disease. [1] [9] If associated with chronic anal fistula, the average age at which it occurs is between 43 and 53 years old. The average duration of fistula in a patient with Crohn disease before cancer diagnosis is 10 to 20 years. [8]

Our patient had developed mucinous carcinoma at a younger age, 38 years old, and her ano-perineal disease was not very old (4 years before the cancer development).

The risk factors for fistula malignancy are the degree of associated inflammation, the location and, most importantly, the time of progression. Cancer often goes unnoticed due to the inflammatory disease itself, so strong diagnostic suspicion is needed, with biopsy being the gold standard of diagnosis. [1]

The mucinous carcinoma could be attributed to the underlying Crohn disease, possibly related to "adenomatous epithelialization" of the fistula tract with progression from the dysplastic epithelium to the carcinoma. The neoplastic change could be the result of long-term exposure to drugs such as metronidazole or azathioprine. However, the potential long-term effects of biological agents in this context must also be taken into account. [10] [11]

Biotherapy treatments could play a role in the initiation of cancers, but in old and widespread Crohn's disease where the risk of neoplasia is already increased, these treatments could also affect the progression of this process or influence its aggressiveness. [10]

Therapeutically, there is no standardized treatment for this specific type of tumor. On the one hand, direct surgery is suggested in local early-stage tumors; on the other hand, if the tumor is locally advanced, some case series such as Gaertner and al recommend neoadjuvant chemoradiotherapy before surgery. Sometimes, due to extensive resection of the levator ani muscle, pelvic floor reconstruction is advised.[12] Radiotherapy as the only treatment is an alternative in fragile patients who cannot undergo radical surgery. [1]

In our case, given the extensive nature of the tumor and the malnutrition state of the patient, treatment with radiotherapy alone was recommended by the multidisciplinary meeting.

IV. CONCLUSION:

In conclusion, anal mucinous carcinoma is a rare malignant tumor that can complicate old Crohnian anal fistulas, but also recent ones (the case of our patient), the diagnosis of which remains difficult to establish given the inflammation that can mask the tumor. Long-term exposure to metronidazole or azathioprine may play a role in the development of these tumors. Biotherapies could play a role in the initiation but also affect the progression and aggressiveness of anal mucinous carcinoma.

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