Rectal metastasis from lobular breast carcinoma 15 years after primary diagnosis

Running head: Rectal metastasis from lobular carcinoma
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Abstract:

Background: Lobular breast carcinoma represents 2-20% of the infiltrative carcinomas of the breast. The incidence of extrahepatic gastrointestinal tract metastases observed in necropsy studies, varies from 6% to 18% and the most commonly affected organ is the stomach, followed by colon and rectum [1-4]. **Case report:** Reported herein is the case of a 67 year old woman who was primary diagnosed and surgically treated for a lobular carcinoma of the breast 15 years ago and refers now back pain and right hydronephrosis caused by a metastasis in rectum. **Conclusions:** Frequently, the absence of specific symptoms of the digestive metastases of the breast leads to a missdiagnosis of this pathology [5-7]. The treatment will be based on a detailed clinical history and histopathological findings.

Synopsis:

Metastases from breast cancer in GI tract tumours must be excluded in a patient with previous history of breast carcinoma, as in the case herein reported.

Introduction:

Breast cancer is the most frequent malignant tumour among female population, and is associated with an important morbidity a mortality rate. At the moment of diagnosis, 60% of the patients have lymph or distant organ metastases, and about

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30%-80% of the patients will develop metastatic disease following surgery and/or chemotherapy, radiotherapy or endocrine therapy [7,8]; lobular carcinoma tends to spread to bones, gynecological organs, peritoneum and retroperitoneum and is less likely to involve the gastrointestinal tract such us: gallbladder [8,9], colon [5,10], small intestine [1], ileocecal valve [11] or stomach [12,13] . Rectal metastasis from breast cancer is extremely rare [3,4,7] and the onset symptons may mimick a primary neoplasm, difficulting diagnosis. At this point, histologycal examination becomes very useful to obtain final diagnosis[14,15] and establish an adequate treatment. We intend to remark the importance of a correct clinical history when examining a patient presenting a gastrointestinal tumour with previous history of breast cancer, specially in the case of lobular carcinoma. We present the case of a 67 year old woman who was primary diagnosed and surgically treated for a lobular carcinoma of the breast 15 years ago and refers now back pain and right uretheral dilation caused by a metastases in rectum.

Case report:

A 67-year-old woman had undergone left radical mastectomy and axillary lymph node dissection in 1994 with adjuvant chemoradiotherapy due to lobular breast carcinoma. Histopathological examination revealed strands of tumour cells with moderate pleomorfism of the nuclei and lack of citoplasm; there were no glands or tubular structures. Occasionally, cells with "signet-ring" morphology were identified with PAS tinction (fig1). Oestrogen (ER) and progesterone (PgR) receptors were positive.

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Along the follow-up time the patient refered no other symptons, but 15 years later, she manifested back pain. An abdominal computerised tomography (CT) scan showed a pelvic mass arising from the rectosigmoidal junction and right hydronephrosis (fig2-3). The magnetic resonance (MR) revealed vertebral bone metastases. Blood tests for CEA and Ca 19.9 were low and CA 15.3 was 79,5. She underwent colonoscopy, wich showed a thickening of the mucosal with stenosis of the lumen 7cm above the anal verge. The pathology of the biopsy described a low-differentiated adenocarcinoma with "signet-ring" cells infiltrating the mucose with a linitis appearence (fig4). Inmunohistochemical staining for oestrogen and progesterone receptors were negative, as well as staining for CK20 and CDX2 markers (fig5), wich suggested a non-gastrointestinal origin of the tumour; presence of "signet-ring" cells in the previous lobular carcinoma similar to the cells observed in the rectal biopsy along with negativity for CK20 and CDX2 led to the diagnosis of rectal metastasis. Gastric or pancreatic primary tumour was excluded and bilateral mammography and ultrasonography were made to search for a primary metacronic breast tumour; a 2,3 cm node was found at the intern upper cuadrant of the right breast with fibroadenomatous pathology. The absence of new primary neoplasms and the inmunohistochemical examination excluding a primary neoplasm of the rectum concluded the diagnosis of rectal metastases with "signet-ring" cells from a lobular carcinoma of the breast treated 15 years ago. A double-J catheter was displaced at the right urether and the patient was sent to the Department of Oncology for chemotherapy. She died 2 months later due to medical complications.

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Discussion:

Lobular breast carcinoma represents 2% to 20% of the infiltrative carcinomas of the breast.; multicentricity and bilaterality are present in about 30%. The incidence of extrahepatic metastases of the gastrointestinal tract observed in necropsy studies varies from 6% to 18%, affecting mostly stomach and less frequently colon and rectum [1-4]. Absence of specific clinical and radilological features of the metastases makes this entity be missdiagnosed [5-7].

Some studies suggest a relation between the histological type of breast carcinoma and the organs metastatised; Harris et al [16] reviewed 966 patients in which lobular breast carcinoma had a tendence to metastatise bone, gastrointestinal tract, gynecological organs, peritoneum and retroperitoneum, while ductal carcinoma was more frequently associated to lung metastases. In 1991, Lamovec [17] analised the necropsy of 261 patients with breast cancer; he concluded the same association; lobular carcinoma was more frequently spread to gastrointestinal tract, gynecological organs, peritoneum abnd retroperiotoneum, while ductal carcinoma metastatised lungs; he found no statistically significant differencies respecting metastases in bone and adrenal glands . Borst [18] in 1993 studied 2605 patients with metastatic breast cancer and arrived at the same conclusion. In this study, the metastases percentage oberved in small intestine was 2,2% in lobular carcinoma and 0,09% in ductal carcinoma.

The present case shows rectal metastases from lobular carcinoma presenting as back pain. Several complementary studies , and specifically, colonoscopy permitted to achieve a hsitological sample for final diagnosis. Although in some cases biopsy obtained during endoscopy will not reveal malignant cells [1,3] endoscopy still

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remains neccessary to establish diagnosis, in order to accurately detect the site of the lesions and because macroscopically, the features of the lesion identified, may help discriminate between a primary or a metastatic tumour; Bamias et al [7] suggest that metastases to the GI tract can appear as a difuse thickening and rigidity of the colonic wall mimicking *linitis plastica* of the colon, Crohn´s like apprearence and ulcerated or nodular areas rather than solitary, discrete massess [6,19-23]. In our case report "signet-ring" cells were observed in the rectal biopsy. "Signet-ring" cell carcinoma is a rare form of colorectal malignancy that usually affects young patients. Like its more common gastric counterpart, it usually presents grossly as a diffuse infiltration of the wall, although it has also been described arising in an adenomatous polyp. Micrscopically, the tumour grows in a diffuse fashion, with little if any glandular formation, as observed in our study. Most or all of the mucin is intracellular and this intracellular accumulation of mucin results in displacement of the nucleus and a typical signet-ring configuration of the cells. The possibility of the colorrectal lesion representing a metastasis from a gastric or mamary primary lesion should always be investigated; at this point, inmunohistochemistry will play an important role; CK7-/CK20+ profile favors a large bowel primary, whereas CK7+/CK20- favors a metastases. Recently, anothe marker has become more and more important: CDX2. CDX2 is a recently cloned caudal-type homeobox gene, encoding a transciption factor that plays an important role in proliferation and differentiation of intestinal epuithelial cells [14]. Robert et al in 2003 observed that CDX2 expression in neoplastic tissues was largely, but not absolutely, limited to adenocarcinomas of the gastrointestinal tract and among carcinomas outside of the GI tract, CDX2 expression was limited to mucinous ovarian adenocarcinomas and adenocarcinomas primary to the urinary bladder. He concluded the clinical utility of antibodies to CDX2 in the identification of

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adenocarcinomas of the gastrointestinal tract, particularly colorectal adenocarcinomas, in both the primary and metastatic setting and suggested that antibodies to CDX2 could play an important role in the inmunohistichemistry assessment of carcinomas of unknown primary. Therefore, organ-specific inmunostaging profiles using multiple markers may provide a high sensitivity, specifity and positive predictive value in detecting primary adenocarcinomas [15,24,25]. In this case report, "signet-ring" cell histology, along with the profile CDX2 -/CK20- pointed us to the diagnosis of mestastasis from a breast lobular carcinoma (fig.4-5). Due to high multicentricity and bilaterality of lobular carcinomas of the breast, it was mandatory to exclude the presence of a new primary tumour in the contralateral breast. On the other hand, the breast carcinoma treated 15 years ago was positive for oestrogen and progesterone markers, and the metastatis observed in the rectum was negative for both markers. This fact has also been described in other studies, suggesting that the biological characteristics of breast cancer can vary between primary tumours and asyncronous metastatic sites [26].

We want to emphasize the fact that clinical presentation of metastatic disease to the GI tract is diverse and symptons may be non-specific or strikingly similar to that of primary GI malignancies. In this report, a long interval time between the primary lesion and the metastasis was summarized. Some authors report that the interval time between breast cancer and the peresence of metastases to the GI tract varies from 3 months to 30 years, with a higher incidence 4 to 5 years after primary diagnosis[3,7,12,27]. The interval of 15 years in our report is one of the longest in literature, although 10 years or more have rarely been reported [6,21,28,29].

Systemic treatment (chemotherapy, endocrine treatment or both) is usually

employed in patients with metastases to the GI tract, since patients usually present with involvement of multiple organs, despite not detecting extensive disease in preoperative investigations [7]. Remissions are observed in 32-53% patients. Surgical treatment is avaliable in case of complicactions such as perforation, haemorraghe or bowell obstruction. In the latter, paliative endoscopical stent can be placed.

In our case report, the patient underwent placvement of a double-J catherr at the right urether and was sent to the Deprtamnet of Oncology for ooncological mediacl tratment. She died 2 months later due to medical complications.

Conclusion

Rectal metastasis from breast carcinoma are very rare and represent the least frequent metastatic site in the gastrointestinal (GI) tract. When finding signet-ring cells at this site, differential diagnosis with metastases from pancreas, stomach and breast should be done. Inmunohistochemical profile is useful to differentiate both situations. Metastases from breast cancer in GI tract tumours must be excluded in a patient with previous history of breast carcinoma, especially in lobular variety. Systemic treatment is usually the choice.

Fig1.: *Histological feature breast carcinoma (PAS): cordones de células tumorales de carcinoma lobulillar infiltrando el estroma mamario. Algunas células presentan morfología de células en anillo de sello.*

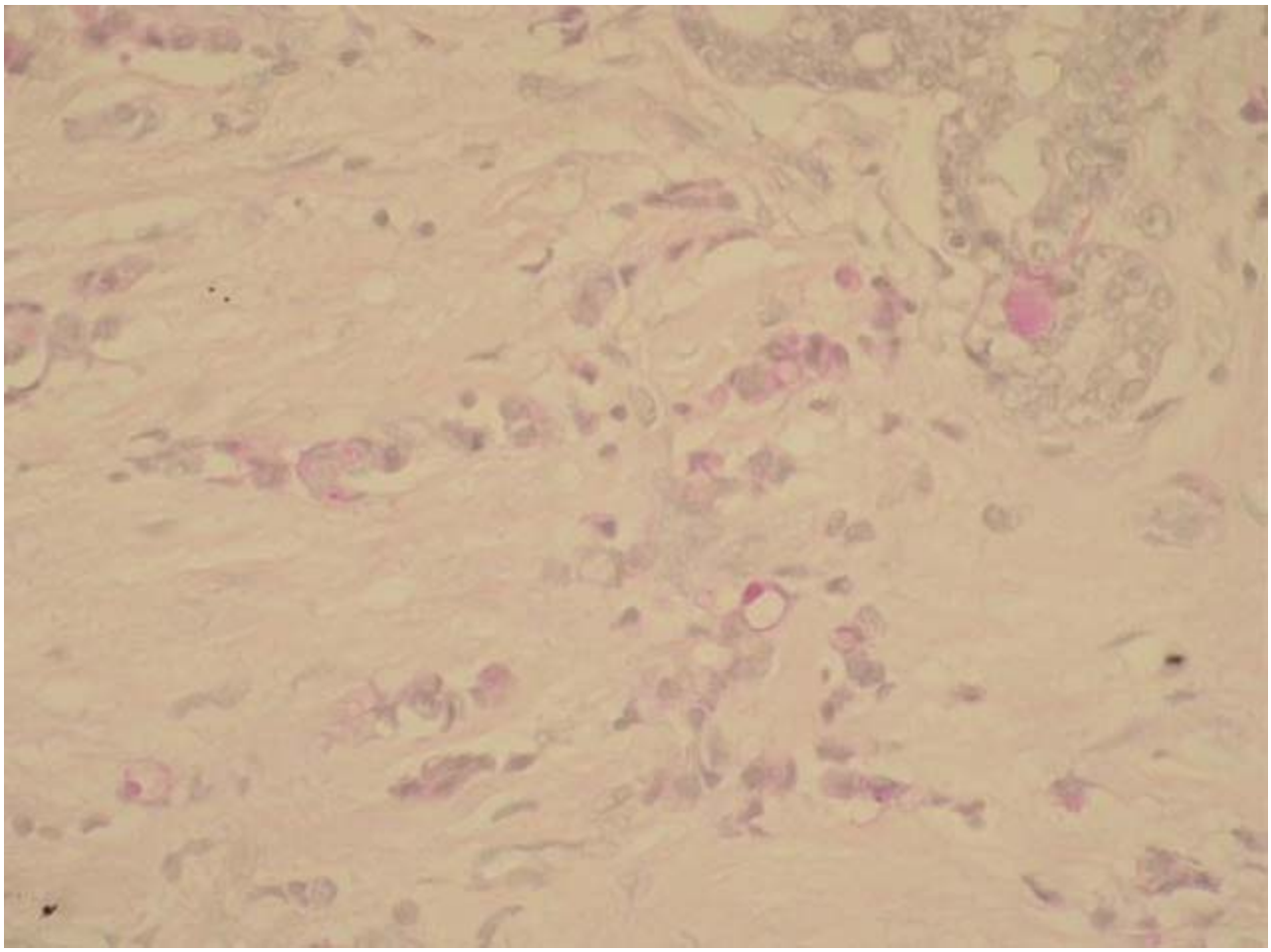

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Fig 2: *Right uretheral dilation.*

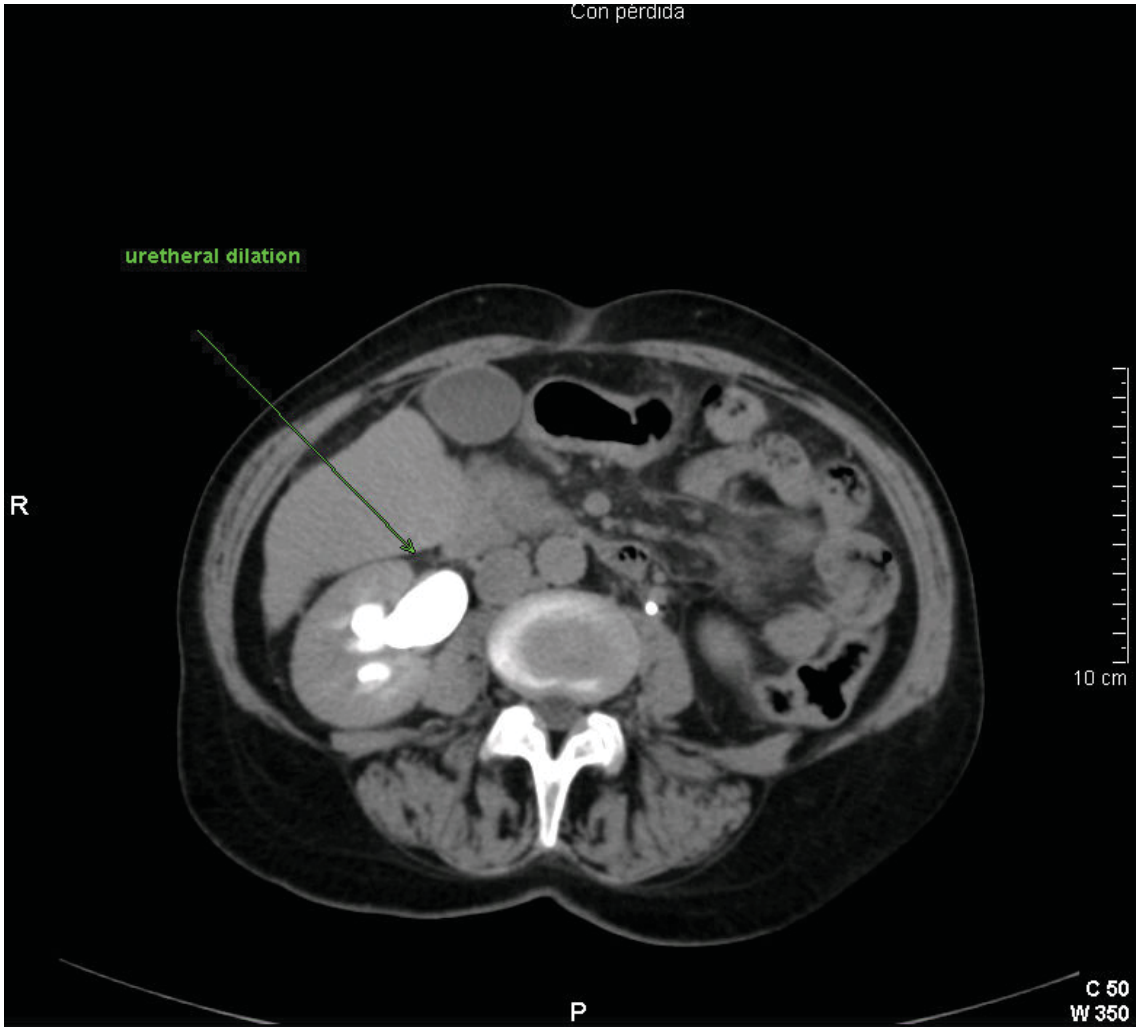

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Fig.3: Tumor invasion of the right urether.

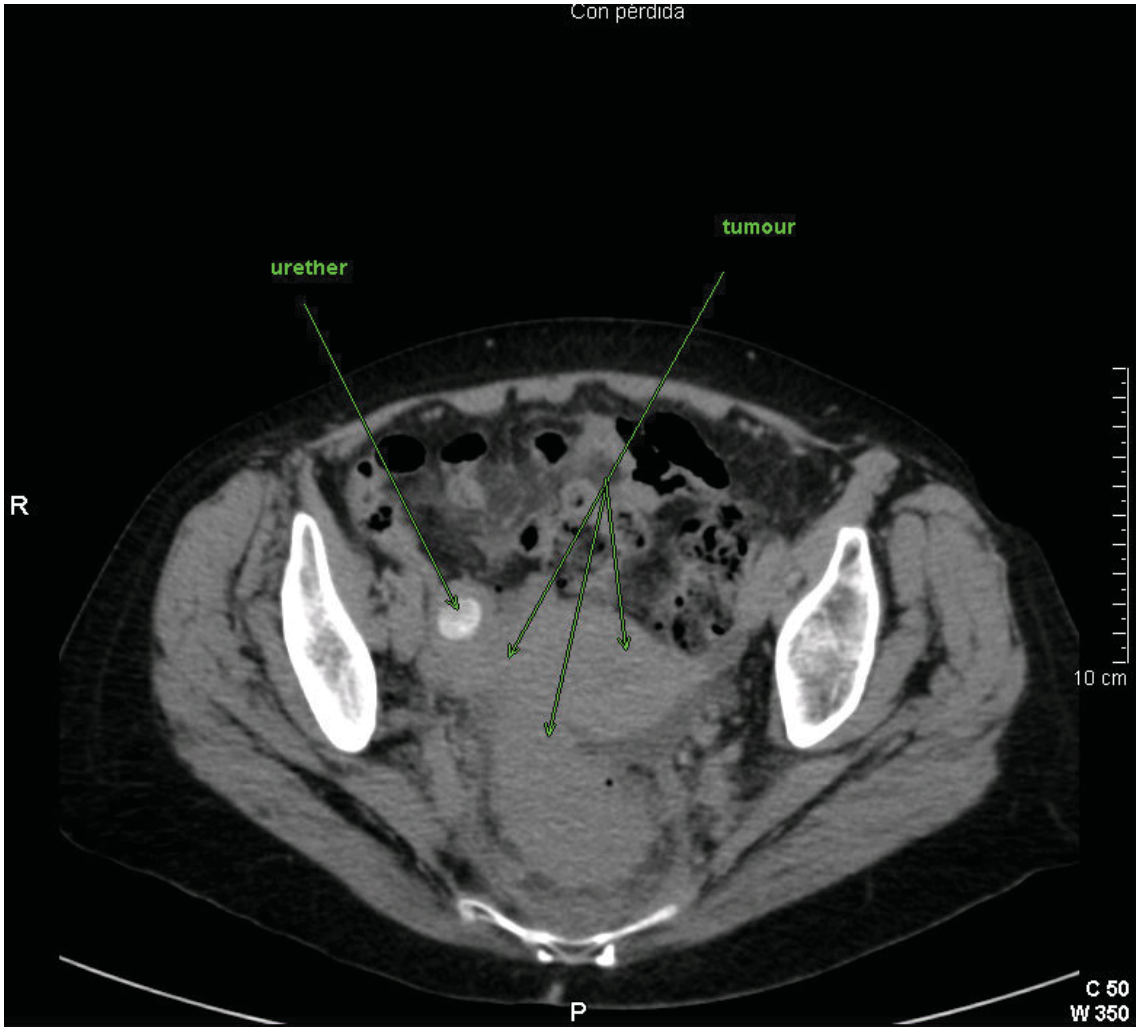

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Fig.4: *Histological feature of colon biopsy: infiltración por algunas células tumorales con morfología en anillo de sello entre dos glándulas rectales respetadas.*

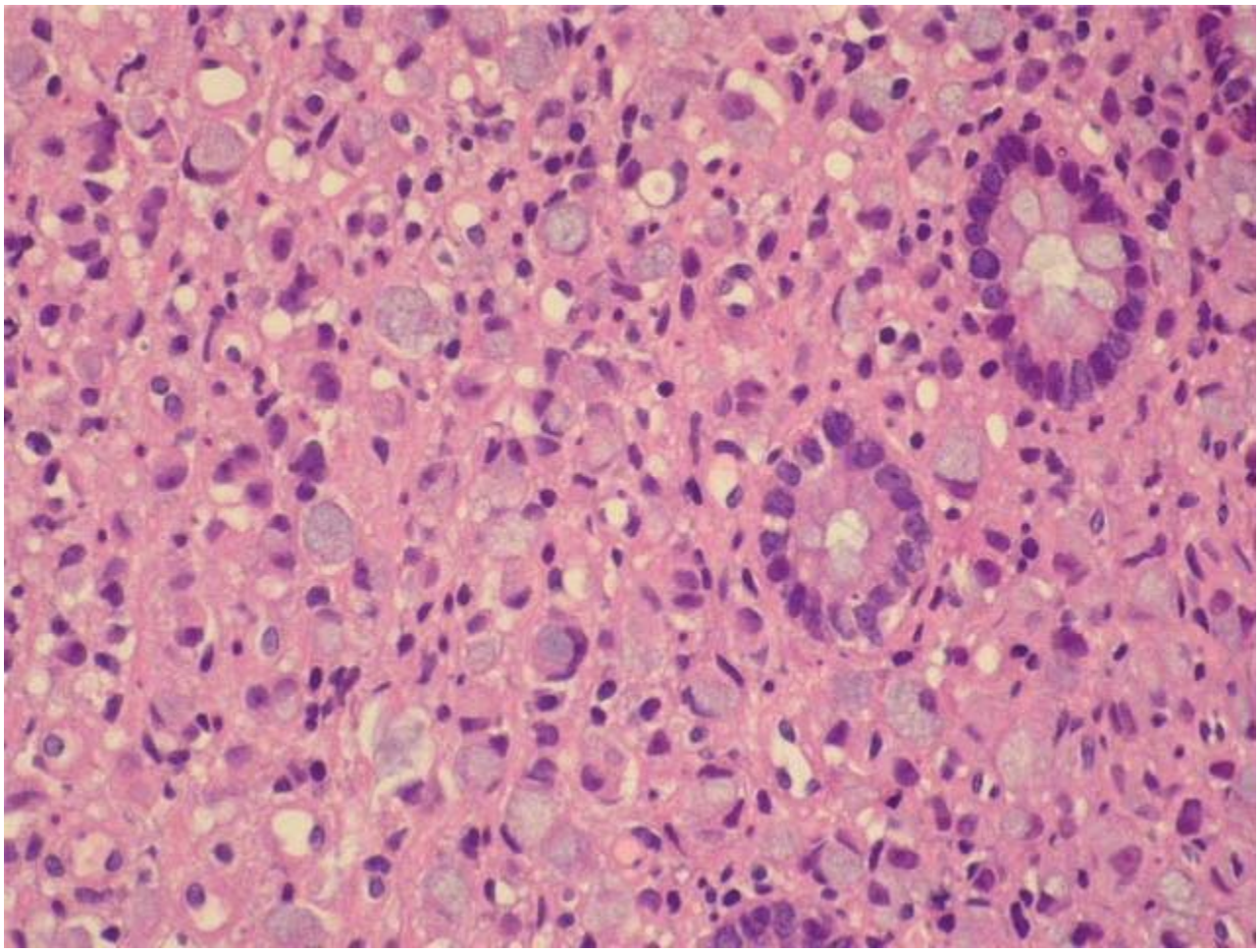
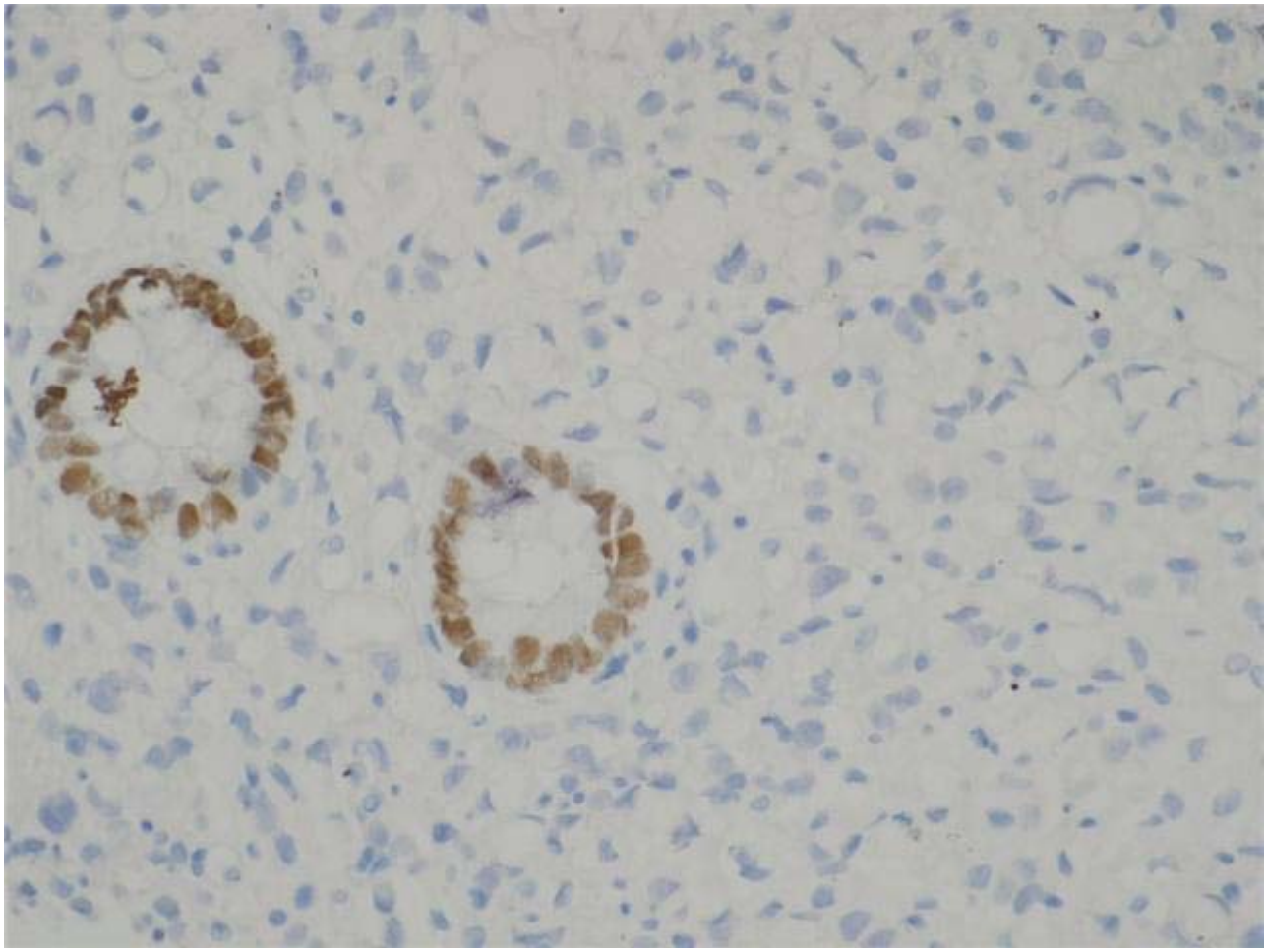


Fig.5: *Histological feature of rectal biopsy: células tumorales con CDX2 negativo entre glándulas CDX2 positivo.*



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