Clin Transl Oncol
DOI 10.1007/s12094-017-1750-y

BRIEF RESEARCH ARTICLE

Mucinous adenocarcinoma on perianal fistula. A rising entity?

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Received: 29 June 2017 / Accepted: 1 September 2017

Abstract
Introduction Mucinous adenocarcinoma on perianal fistula is a rare entity; it could be underdiagnosed because it behaves often as a regular perianal fistula.
Materials and methods We have recently treated four cases in our unit. We present them and review the literature, emphasizing on clinical characteristic and therapeutic options. The four patients were male with a mean age of 64. Three of them were classified as locally advances cases and therefore treated with neoadjuvant therapy.
Results All of them underwent laparoscopic abdominoperineal escisión. Surgical specimens are described and clinical characteristic specified. Review of the literature shows that this disease has a very high potential risk of local recurrence and we must be aggressive with the resection. Sometimes plastic surgery is needed to reconstruct the perianal wound.
Conclusions Mucinous adenocarcinoma associated with anal fistula is a rare disease. Neoadjuvant chemoradiotherapy followed by an adequate abdominoperineal excision may result in favourable outcomes.

Keywords Mucinous adenocarcinoma · Anal fistula · Neoadjuvant therapy

Introduction

Anal fistula is a prevalent pathology, but extremely rare its malignant degeneration, Rosser et al. first described seven cases in 1934 [1]. It represents 6.9% of all cancers of the anal canal [2]. Its origin is unclear. It may be due to either dysplastic degeneration in a long-standing recurrent fistula or seeding of granulating fistula by malignant cells arising from carcinoma originating from colorectal mucosa. Mucinous adenocarcinoma has typically been associated with benign inflammatory conditions such as chronic anal fistulas, perianal abscesses, TBC, diabetes, syphilis, venereal lymphogranuloma, or perianal Crohn's disease. Its diagnosis is late because it is sometimes confused with inflammatory pathology [3]. However, it is thought that these type of adenocarcinoma have greater potential of local aggression rather than systemic dissemination. In addition, neoadjuvant treatment has been shown to be effective, with a high response rate [4]. We found interesting to communicate our recent experience to pay more attention to the existing association between these two pathologies and their characteristics.

Patient and methods

During the last 20 months, until February 2017, of 80 patients treated in our unit for rectoanal carcinoma, we diagnosed four patients (5%) with mucinous adenocarcinoma of the perianal region.

Extension studies were done to all of them (complete colonoscopy, thoracoabdominal CT, and biological tumour markers). Once they were completed the multidisciplinary team decided the complete treatment based on the data we had.

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Published online: 19 September 2017

In case of deciding chemoradiotherapy, the regimen consisted on 4500 Gy of radiation during 5 weeks with 5 FU in continuous infusion in weeks 1 and 5. The interval between chemoradiotherapy and surgery was 10 weeks.

Case 1

- An 80-year-old man followed in the clinic since 1 year before for repeated ischiorectal abscess. During the last episode, irregular thick tissue was found and analysed resulting in positive biopsies for mucinous adenocarcinoma.
- The multidisciplinary team indicated neoadjuvant chemoradiotherapy.

Case 2

- A 40-year-old male with transsphincteric fistula of 2 years of evolution, recurred after surgical treatment. In the inflammatory tissue biopsy, appears mucinous adenocarcinoma.
- Preoperative studies showed a pT2N0M0 tumour so the multidisciplinary team directly indicated surgery (Fig. 1).

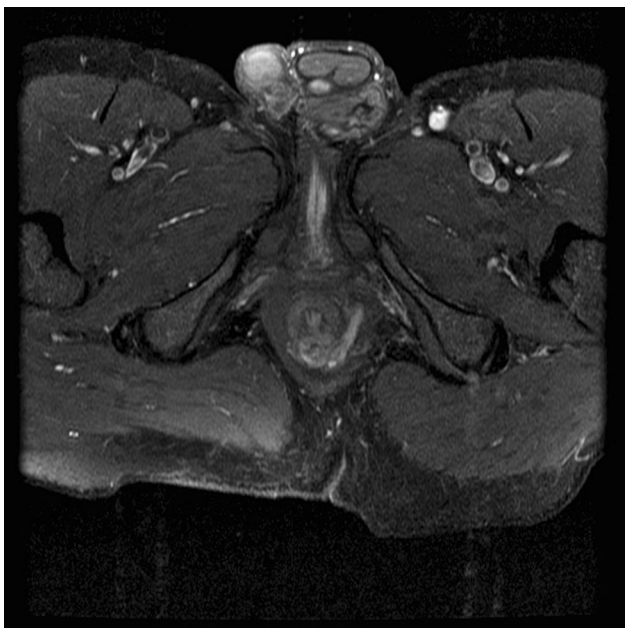

Fig. 1 MRI of anal fistula with signs of malignancy surgical specimen of abdominoperineal resection with extrarrectal mucinous adenocarcinoma on perianal fistula

Case 3

- A case of 66-year-old male, who have symptoms of perianal sepsis of months of evolution. Finally a MRI was performed showing a large multilobulated mass that invades both ischiorectal fossae.

Case 4

- A 71-year-old male with no previous proctologic symptoms, complaining of anal pain, the MRI showed intersphincteric mucinous component.
- A biopsy was taken under local anaesthesia and an adenocarcinoma with high grade and undifferentiated component was found.
- Neoadjuvant treatment with chemoradiotherapy was indicated.

Results

Case 1

- After 10 weeks, APE was performed with non-affected margins and result of mucinous adenocarcinoma pT3pN1 (Fig. 2).
- Histopathology analysis showed normal rectal mucosa and below the mucosa mucinous adenocarcinoma with signet ring cells not affecting the mucosa (Fig. 3).
- Immunohistochemistry showed positivity for cytokeratin 7 (CK7), while normal mucosa was negative for cytokeratin 20 (CK20) and CDX2.

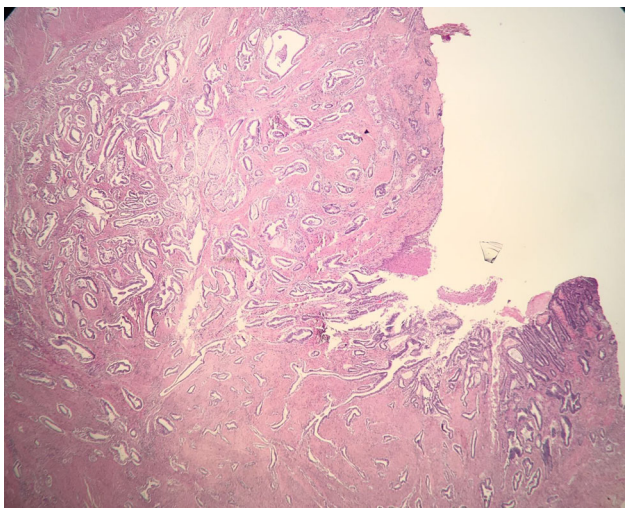

Fig. 2 Surgical specimen of abdominoperineal resection with extrarrectal mucinous adenocarcinoma on perianal fistula

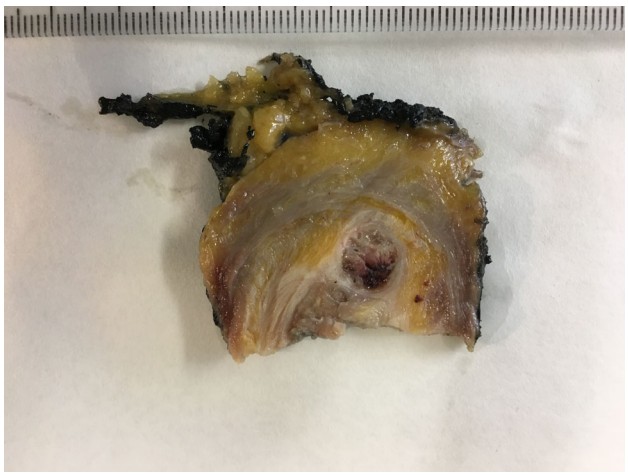

Fig. 3 Mucinous adenocarcinoma with signet ring cells under normal mucosa

- APE was practiced without any relevant event in postoperative period.
- Treatment was completed with adjuvant chemotherapy.
- After 2-year follow-up, no signs of recurrence were found.

Case 2

- Laparoscopic abdominoperineal resection was performed with pathologic result of adenomatous infiltrating adenocarcinoma pT2pN0.
- Histology showed normal squamous epithelium of the fistula with infiltrating mucinous adenocarcinoma. Postoperative period was uneventful.
- After 24 months, the patient attended to the clinic with pelvic pain and MRI showed a bone lytic lesion (Fig. 4), confirmed to be recurrence in the isquion by PET scan and biopsy. He is under consideration for bone resection.

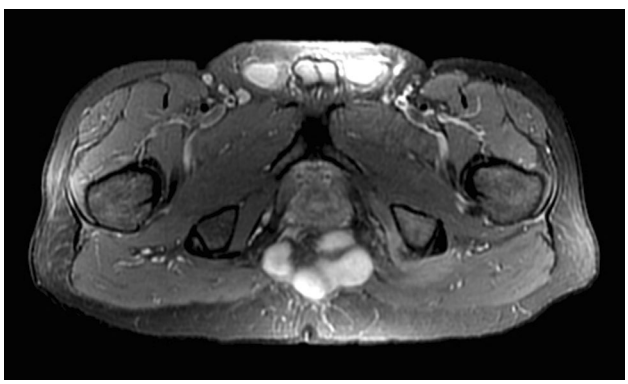

Fig. 4 MRI of bone lytic lesion confirmed to be metastases of adenocarcinoma

Case 3

- Neoadjuvant chemoradiotherapy followed by laparoscopic abdominoperineal resection: Rectal mucinous adenocarcinoma with perianal extension pT4bpNx.
- Adjuvant chemotherapy completed the treatment.
- After 18 months, advanced local recurrence showed up in the complementary studies practiced at follow-up.
- Only palliative treatment could be given.

Case 4

- Ten weeks after, laparoscopic abdominoperineal resection was performed with mucinous adenocarcinoma result on perianal fistula pT3N1.
- After 30 months, no signs of recurrence are shown in the image studies.
- After a median follow-up of 24 months, local recurrence was diagnoses in 50%.

Discussion

It is known the relationship between chronic anal fistula and adenocarcinoma of the anal canal since long time [1].

Primary adenocarcinoma of anal fistula would be caused by dysplastic degeneration of a long-term fistula and should be suspected in any recurrent fistula [5]. Secondary adenocarcinoma of anal fistula develops because the implantation of malignant tissue from cells of the anal canal in the fistula or transformation of inflammatory tissue into malignant directly in the fistula tract or abscesses cavity. The dissemination of tumour cells from a colon cancer through a fistula prior to tumour development is well described [6].

Chronic inflammatory condition due to perianal fistula is easily treatable, so surgery should not be delayed, biopsies should be performed to rule out malignancy. In particular, mucinous adenocarcinoma on perianal fistula is the malignant pathology that must be suspected in an anal fistula with atypical and recurrent clinical features.

T2-weighted MR images revealed symptomatic features; that is, the hyperintense heterogeneous content looked like a gathering of various sizes of granules. This is due to the fact that mucinous adenocarcinomas usually consist of the gathering of many small mucous lakes [7]

Once malignancy has developed, the indicated treatment is radical surgery; it appears that neoadjuvant treatment

improves the prognosis of this type of tumour when it is associated with radical surgery. Surgery must be radical, so abdominoperineal resection is the technique of choice, with extension to the extra-levator component in case of being affected or threatened by the circumferential margin [2]. Although some authors have published series with less overall survival than patients with anal canal adenocarcinoma, most of them were not treated with neoadjuvant treatment [8].

Some clinical features are characteristics of these tumours:

- The background of a chronic perianal fistula is usually present.
- Although clinical examination results usually in a thick tissue touch, endoscopic studies could be normal because mucosa could not be affected.
- Hyperintense heterogeneous content in T2 weighted MR.
- Good response to neoadjuvant chemoradiotherapy.
- Few percentage of systemic recurrence.

The clear circumferential margin is the most important data on its histopathology exam.

The incidence of this type of tumours seems to be rising but in our opinion it is probably because the effect of a more accurate diagnose taking into account that MR is wide spread in the last years for staging rectal cancer.

The present series is too limited to establish conclusions about long-term outcomes but it is very important the issue that it seems to be clearly curable if the disease is diagnosed within sufficient margin to make a good and aggressive local treatment combining chemoradiotherapy and aggressive surgery to achieve R0 resection.

After 24 months of follow-up, 50% of recurrence confirms the bad prognoses of this disease. One of this recurrence occurred in the only patient that did not underwent neoadjuvant treatment, so we may consider these patients as a special type with high recurrence risk and we should put all of them in neoadjuvant treatment because of this fact.

Conclusion

Mucinous adenocarcinoma on perianal fistula is a unique clinical entity with specific clinical characteristics, it must be suspected in any fistula with atypical course or recurrence. Rectoscopy may be normal, and MRI and biopsies of the fistula tissue should done in order to make the correct diagnose. Chemoradiotherapy followed by a correct surgery is the main treatment options in the majority of cases. Long-term outcomes seem to be good with low rate of systemic dissemination. We need larger series to learn more about this very specific type of anal adenocarcinoma.

Compliance with ethical standards

Ethical standards The manuscript does not contain clinical studies or patient data.

Conflict of interest Authors declare that we have no conflict of interest.

Informed consent Informed consent was obtained from all patients.

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