Primary squamous cell carcinoma of the most distal rectum: a dilemma in origin and management

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SUMMARY

Squamous cell carcinoma (SCC) of the rectum is a rare malignant entity that has been classically managed with a surgery-based approach, which included abdominoperineal resection for distal lesions. Recently there have been reports on the favourable outcomes achieved with the non-surgical management of these patients. We report a case of a 52-year-old woman who was diagnosed with a stage IIIa SCC located on the distal rectum. The patient was managed conservatively with a chemoradiation regime with mitomycin and 5-fluorouracil. Complete remission was achieved and she is currently alive, asymptomatic and disease-free after 30 months. This case adds to the existing evidence that supports the role of chemoradiation as a first-line curative treatment for the rare rectal SCC.

BACKGROUND

Colorectal cancer is the third most common cancer worldwide,¹ with the vast majority corresponding to adenocarcinoma. Squamous cell carcinoma (SCC) of the rectum is a rare malignant entity, with a reported incidence of 0.1–0.25/1000 colorectal cancers.² It was first described in 1933 by Raiford³ and has been reported in case reports and small case series ever since.

The diagnosis is not straightforward since it must be in accordance with Williams criteria⁴ that establish the need to rule out the presence of other primary SCC, fistulous tracts between the rectum and adjacent organs and the extension of SCC from the anal canal.

Therapeutic options have classically involved surgery with or without neoadjuvant chemoradiation (CRT).⁵ However there have been some reports^{6–8} where surgery was avoided and CRT was successfully used with curative intent, as in anal canal SCC.

We present a case of a woman with SCC of the lower rectum that was successfully managed conservatively with CRT with a 2-year disease-free follow-up.

CASE PRESENTATION

A 52-year-old Caucasian woman, mother of three and living in south of Portugal, was referred to the gastroenterology outpatient clinic for haematochezia, tenesmus and a mild non-specific abdominal pain for 3 months. She had a history of functional dyspepsia, chronic constipation, dyslipidemia, vitiligo and a breast fibroadenoma diagnosed by fine-needle aspiration 6 years earlier. The patient was on rosuvastatin, pantoprazole and used several laxatives on demand. Her grandfather had been diagnosed with colon carcinoma after the age of 60.

Figure 1 Endoscopic view of Paris 0-Is centrally ulcerated lesion with 15 mm diameter, located on the posterior rectal wall.

The physical examination was unremarkable apart from the digital rectal examination, which revealed a hard painful mass on the posterior wall of the rectum.

INVESTIGATIONS

The patient's blood tests, including haemoglobin and iron panel, were completely normal.

She underwent total colonoscopy which confirmed the presence of a sessile and centrally ulcerated lesion (Paris 0-Is) with 15 mm diameter and located in the rectum 5 cm proximally to the anal verge (*figure 1*). Multiple forcep biopsies were undertaken and the histology showed SCC proliferation (*figure 2*).

Both contrast-enhanced CT and fluorodeoxyglucose ¹⁸F(¹⁸F-FDG) labelled positron emission tomography (PET) scan of the thorax, abdomen and

Figure 2 Invasive squamous cell carcinoma (H&E x10).

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Figure 3 Positron emission tomography scan shows fluorodeoxyglucose uptake in a lesion located posterior to the bladder, compatible with a rectal tumour (black arrow).

pelvis failed to show metastatic disease, while confirming the rectal lesion (figure 3). As for local staging, endoscopic ultrasound (EUS) (figure 4) revealed invasion of the muscularis propria and two 6 mm regional lymph nodes with MRI identifying four regional lymph nodes at the mesorectum; no signs of fistulae and no involvement of the anal canal was documented on both. Exfoliative cytology of the uterine cervix was negative for dysplasia.

DIFFERENTIAL DIAGNOSIS

The lesion was staged as T1N1M0—stage IIIa in accordance with the American Joint Committee on Cancer (AJCC) for the anal canal cancer, since it was considered to be manageable analogously to a SCC from the anal canal.

TREATMENT

CRT was performed, with systemic chemotherapy based on mitomycin and 5-fluorouracil (5-FU) and with a radiotherapy (RT) dose of 52 Gy on the tumour and regional lymph nodes. Mild diarrhoea and urgency were noted during RT, which resolved with loperamide.

OUTCOME AND FOLLOW-UP

The CRT treatment was completed in May 2010. In July, a PET scan was performed and failed to show abnormal ^{18}F -FDG metabolism.

Figure 4 (A) Three dimensional endorectal ultrasound reconstruction showing a hypoechoic tumour in the right posterior wall of the inferior third of the rectum. (B) The muscularis propria (orange arrow) is invaded by the tumour (yellow arrow). There is no apparent extension beyond the wall, as the external contour remains regular. (C) The tumour presents 17 mm away from the anorectal junction (yellow arrow). (D) Presence of two hypoechoic, well-circumscribed, perirectal lymph nodes (red arrow).

The last colonoscopy was performed in October 2013 and it was unremarkable.

The patient is currently under close follow-up including yearly imaging evaluations by MRI. She is considered to be in complete remission at 40 months follow-up.

She is still chronically constipated as before, occasionally with small haemorrhoidal bleeding as assessed by anoscopy.

DISCUSSION

SCC of the rectum is a rare entity. Therefore, unlike SCC of the oesophagus or the anal canal, little is known about its epidemiology, aetiology and optimal management strategy.

From the scarce literature on rectal SCC, it seems to affect women more frequently than men, with a mean age of 57 (32–93). The diagnosis is usually done at advanced stages, with 63% on stage III/IV.^{2 9 10}

Given the currently low quality of epidemiological data available it is hard to establish risk factors, however, a few reports have shown some possible associations, namely colorectal adenocarcinoma,¹¹ ulcerative colitis¹² and rectal infection with human papilloma virus (HPV), *Schistosoma*¹³ or *Entamoeba histolytica*.⁴ HPV is strongly associated with anal carcinoma, but evidence as a possible cause of rectal SCC is lacking, as search for HPV-DNA within squamous and adenosquamous cancers came out null.^{5 11 14} In our report there was no clinical evidence of any of these conditions. *Schistosoma* and *Entamoeba* are considered rare entities in Portugal.

Symptoms are similar to those of adenocarcinoma of the rectum. It usually presents with rectal bleeding, tenesmus, altered bowel habits, abdominal pain or anal pain while defaecating, anorexia and weight loss. Diagnosis is accomplished by endoscopic visualisation of a neoplastic lesion and forcep biopsies, abiding Williams criteria.⁴ Because of these, great care must be taken to document the absence of anal involvement. This is not an easy task, since it is not always straightforward to determine the origin of the lesion since anal SCC can extend proximally and the complexity of the transition zone of the rectal mucosa and the anal canal is still a matter of debate.^{15 16}

Owing to its rarity and absence of specific management recommendations, rectal SCC poses some problems regarding the staging system to use. Both rectal¹⁷ and anal cancer¹⁸ guidelines based on the AJCC TNM system¹⁹ can be adopted, with some differences regarding management and prognosis.

We chose to manage and hence, to stage this case based on the anal cancer staging system. In both staging systems, an intravenous contrast-enhanced CT of the thorax, abdomen and pelvis is performed. PET scan may be useful, specially to rule out other possible primary SCC sites. In selected cases, as in the absence of distant involvement, pelvic MRI and rectal EUS can aid in locoregional staging.²⁰

Squamous cell carcinoma antigen may be elevated in rectal SCC⁷ but lacks both sensitivity and specificity in order to be of clinical usefulness.

Similar to the staging systems, management has also been done either analogously to adenocarcinoma of the rectum or to the anal canal SCC. Most cases in the literature report surgical excision with adjuvant CRT, with 5-FU and mitomycin, due to the frequent advanced disease stage at presentation and also because of the rectal cancer experience for adenocarcinoma. For the latter, surgical options depend on the regional staging and location of the tumour. For superficial lesions, endoscopic or surgical excision may be attempted with endoscopic mucosal resection (EMR). For T2 or higher, an oncological resection should be performed and these include either low anterior

resection of the rectum for proximal tumours on the upper two thirds of the rectum, or abdominoperineal resection (APR) for tumours located 6 cm proximal to the anal verge or for more advanced stages that require a more aggressive approach. APR is a mutilating surgery that involves excision of the anus and a permanent colostomy and carries comorbidities and poor patient-satisfaction.²¹

As for the classic anal SCC management, the role of mitomycin and 5-FU-based CRT has been established by several randomised controlled trials (RCT)²² and embraced by current guidelines, relegating surgery to salvage therapy.¹⁸ Some centres have applied this principle to rectal SCC and recently there have been reports of conservative management using CRT with curative intent and showing promising results. Clark *et al*²³ reported seven rectal SCC cases treated with CRT with remission being achieved in six of them. Yeh *et al*⁶ reported a retrospective single centre review of six cases of rectal SCC of which five were treated with CRT (the sixth refused CRT) and two underwent salvage surgery, after 44 months of follow-up, four of them were alive and disease-free. Rasheed *et al*⁷ did a similar review and surgery was avoided in four of six patients with rectal SCC with disease-free survival on follow-up. No RCT has been performed to date and will be very hard to be successfully conducted given the low incidence of this specific type of cancer.

There seems to be a recent trend where non-operative management of rectal SCC is being preferred over more mutilating approaches, even though the evidence is scant. Indeed, the experience with anal SCC and the results from the small case series support the curative CRT approach as a first-line treatment, reserving surgery for cases of treatment failure.

We report a case of conservative management of rectal SCC with mitomycin and 5-FU-based CRT treatment. Surgery was successfully avoided and there is no evidence of recurrence with a follow-up of 30 months.

Learning points

- ▶ Squamous cell carcinoma of the rectum is a rare malignant entity.
- ▶ Chemoradiation may be an alternative to be considered, analogously to the anal canal cancer.
- ▶ Avoidance of mutilating surgery is possible with promising, albeit limited, results in the literature, with most evidence derived from case series.

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Competing interests None.

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