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Original Article

Primary anal adenocarcinoma: a caution for conservative treatment

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Abstract

There is evidence that a conservative approach with chemoradiotherapy can achieve long-term local control in patients with anal adenocarcinoma. Identification of suitable patients for this approach remains a problem. We describe a patient with a clinically staged T2N0 tumour, who achieved a complete clinical response on magnetic resonance imaging and positron emission tomography after chemoradiotherapy, but was noted to have residual disease with evidence of lymph node metastasis on pathological examination in the abdominoperineal resection specimen. A complete clinical response does not necessarily equate to pathological response.

Keywords

Anal tumours; adenocarcinoma; radiotherapy; chemotherapy; surgery

INTRODUCTION

Anal adenocarcinoma is a rare tumour, accounting for <5% of all anal cancers. Treatment outcome appears to be poorer than that for anal squamous cell carcinoma, or rectal adenocarcinoma. Conventional treatment involves abdominoperineal resection. The success of chemoradiotherapy in the management of anal squamous cell carcinoma has led us to explore a similar approach for anal adenocarcinoma. The goal of treatment is to achieve local control equivalent to abdominoperineal resection while maintaining ano-rectal function and reserving surgery for salvage. In this report, we describe a case that illustrates the difficulty in identifying a group of patients that can be managed by chemoradiotherapy alone.

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CASE REPORT

A 68-year-old man presented to his local doctor with a 1-year history of intermittent faecal incontinence and a 3 month history of fresh blood per rectum with some tenesmus. An ulcerating anal canal lesion was detected, and he was referred to our centre for further management after anal biopsy showed an adenocarcinoma. A rectal examination with rigid sigmoidoscopy revealed a tumour in the anal canal. The tumour extended from 12 o'clock to 10 o'clock in the lithotomy position. Computed tomography (CT) of the abdomen and pelvis showed no lymphadenopathy or hepatic metastases. A magnetic resonance imaging (MRI) showed asymmetrical mucosal thickening along the right lateral aspect of the anal canal, which measured 8 mm in thickness and 37 mm in length, with no associated lymphadenopathy. Positron emission tomography (PET) using ^{18}F-fluoro-deoxy-D-glucose radiotracer (FDG) showed increased FDG uptake in the primary

lesion, but no evidence of nodal or distant disease. Examination under anaesthesia confirmed the lesion extending from 1 cm above the ano-rectal ring to the anal verge. Endo-anal ultrasound showed it to be involving the internal but not the external anal sphincter. The anal cancer was therefore staged T2N0M0.

The patient received megavoltage radiotherapy via a CT-planned three-phase shrinking field technique. He was treated in the prone position on a belly-board. A total radiation dose of 50.4 Gy in 28 fractions in 1.8 Gy/fraction over a period of 5 weeks and 3 days was delivered (in accordance to ICRU-50). This plan delivered 39.6 Gy to the true pelvis and bilateral inguinal lymph nodes via a parallel opposed anterior–posterior approach. It was followed by 5.4 Gy to the true pelvis using two lateral fields and a posterior field. The final phase delivered 5.4 Gy to the gross tumour including a 2 cm margin from gross tumour volume to planning target volume in all directions. Concurrent chemotherapy consisted of continuous infusional 5-fluorouracil (5-FU) (225 mg/m^2/day) for the duration of the radiotherapy and mitomycin-C (10 mg/m^2) on day 1. The chemoradiotherapy was well-tolerated and the course was completed without a treatment break.

Six weeks following completion of chemoradiotherapy the patient achieved a clinical complete response, with no gross tumour palpable per-rectum. Restaging MRI, CT and PET also showed no evidence of residual or metastatic disease. The patient proceeded to abdominaoperineal resection 12 weeks after the completion of chemoradiotherapy. Histopathology showed a 14 × 7 mm focus of residual adenocarcinoma invading the muscularis propria at the primary site (Fig. 1). In addition, there was a previously undetected sub-centimetre lymph node within the mesorectum completely replaced with tumour. The remaining specimen, including 12 lymph nodes, showed no evidence of disease. Adjuvant chemotherapy in the form of weekly 5-FU and folinic acid for 4 months was given.

There was no evidence of local recurrence or distant metastasis when the patient was last assessed at 20 months after presentation.

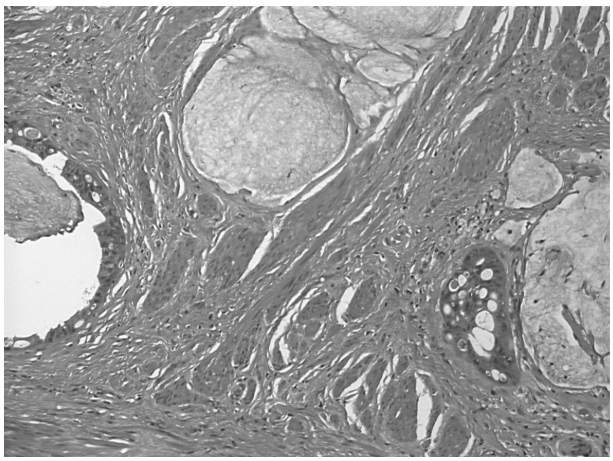

Figure 1. Histopathology following resection showing residual tumour after chemoradiotherapy in the presence of a complete response clinically, radiologically and functionally. The image shows moderately differentiated adenocarcinoma, as well as pools of acellular mucin, infiltrating muscularis propria. Haematoxylin and Eosin, original magnification ×100.

DISCUSSION

Conventional treatment of anal adenocarcinoma involves abdominoperineal resection. The success of organ preserving chemoradiotherapy in the management of anal squamous cell carcinoma has led to the investigation of a similar approach for anal adenocarcinoma. The goal is to achieve local control equivalent to abdominoperineal resection while maintaining ano-rectal function and reserving surgery for salvage. We have described a case that illustrates the difficulty in identifying a group of patients that can be managed by chemoradiotherapy alone.

Because primary anal adenocarcinoma is rare, there is no standard treatment approach for these tumours. Treatment policy is therefore shaped by local practice, extrapolation from multi-modality management of rectal adenocarcinoma and anal squamous cell carcinoma, and conclusions from relatively small retrospective series.

Primary anal adenocarcinoma should include tumours that arise in the anal canal distal to the upper border of the anal sphincter. This definition has been controversial, given the difficulty of distinguishing between a low rectal tumour and an anal primary. A pragmatic definition has been proposed

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to include tumours involving the anal canal (0–4 cm from the anal verge), but with <50% of its total length proximal to this region.[1]

The location of anal adenocarcinoma is similar to the much more common anal squamous cell carcinoma. Results from three randomized trials treating squamous cell carcinoma confirm the utility of combined modality chemoradiotherapy using mitomycin-C and 5-FU, and reserving surgery for salvage.[2] Outcomes with this treatment result in local control rates of 58–61%, and overall survival of 65–80%.

We have previously reported the results of our retrospective review of anal adenocarcinoma.[3] The main conclusion from this series of 15 patients was that chemoradiotherapy was an effective curative treatment modality. However, this series focused on the 6 patients treated with radical intent, all of whom had early stage disease T1/2N0, and would be expected to have a better prognosis. The remaining 9 patients had a median survival of 10 months.

A multi-centre European retrospective study reported outcomes for 82 patients.[4] Superior outcomes were observed in the group that received combined chemoradiotherapy. Chemoradiotherapy was recommended as standard treatment, with surgery being reserved for salvage. However, the median radiation dose was only 35 Gy for those patients receiving surgery and adjuvant radiotherapy, which was <10 Gy in the chemoradiotherapy group. It is therefore difficult to compare the two groups directly. Furthermore, no group received true trimodality therapy with chemoradiotherapy and surgery.

A third series reported the outcomes of 16 patients from M.D. Anderson Cancer Centre.[1] Results were consistently poorer than a contemporary series of patients with anal squamous carcinoma from the same centre. This series included radiotherapy to a dose of 55 Gy to all patients, concurrent chemotherapy for 11 patients, and surgery reserved as a salvage procedure. They concluded based on the poor locoregional control that trimodality therapy was indicated initially, and that the high rate of distant failure justified consideration of adjuvant chemotherapy.

An article from Memorial Sloan-Kettering Cancer Centre reported a series of 13 patients treated over a period of 12 years.[5] Three general treatment approaches were employed including preoperative combined modality therapy followed by abdominoperineal resection (n = 5), with four of the five receiving postoperative chemotherapy; local excision followed by postoperative radiation alone or combined modality therapy (n = 5); and abdominoperineal resection followed by combined modality therapy (n = 3). With a median follow-up of 19 months, the median survival was 26 months, the local failure rate was 37%, and the 2-year actuarial survival was 62%. It was concluded that the combination of abdominoperineal resection and combined modality therapy is a reasonable approach.

It would appear that the overall local control rate with chemoradiotherapy alone for anal adenocarcinoma is lower than for anal squamous carcinoma. Chemoradiotherapy alone can achieve permanent control in some patients with anal adenocarcinoma, however, identification of this group of patients remains a challenge.

The patient described in this case report had residual tumour in the resected specimen 12 weeks after completion of chemoradiotherapy, despite a complete metabolic response on PET and complete resolution of tumour mass on MRI. A previously undetected metastatic perirectal lymph node was revealed. Extrapolating once again from rectal adenocarcinoma treatment, adjuvant 5-FU based chemotherapy was commenced. Although tumour viability is unknown, the pathological findings reinforce the rationale that surgery remains an essential part of the treatment package of even early, optimally staged tumours until a more effective chemoradiotherapy regimen becomes available.

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