Split-course chemoradiotherapy: an effective alternative treatment of anal cancer in elderly patients

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Objective

Combined Chemotherapy and Radiotherapy (CRT) results in better local control and colostomy-free survival than radiotherapy alone in squamous cell carcinomas (SCC) of the anus. Full dose CRT of 50.4Gy in 28 fractions with concomitant chemotherapy in anal SCC can result in a 3-year relapse free survival (RFS) of 75%.(1) However, frail elderly patients or those with co-morbidities and poor performance status cannot tolerate full-dose CRT due to toxicities.

Our objective was to assess the effectiveness of a modified split course CRT regimen in the radical treatment of anal SCC in patients over the age of 70 in whom poor performance status, co-morbidity or a combination precluded full dose radical CRT.

Method

Retrospective review of all 27 patients with biopsy-proven squamous carcinoma of the anal canal or margin treated at Addenbrooke’s Hospital, Cambridge, UK from 1995 to 2011 with radical intent with a modification of the split-course regimen described by Cummings.(2)

Radiotherapy consisted of 26Gy in 13 fractions (Phase1), followed by a minimum 2 week break, then 26Gy in 13 fractions (Phase 2) to a planned tumour volume and involved nodes, with concurrent chemotherapy, 5-fluorouracil 1000 mg/m²/day on days 1-4 and Mitomycin-C 8 mg/m² bolus day 1 in each phase.

Results

- Total number of patients in the study = 27
- Median age was 83 years (range 70 - 92 years)
- 9 patients (33%) were male
- 15 patients (56%) had stage 2 disease
- 8 patients (30%) had stage 3 disease
- Median overall treatment time - 59 days (range 17–74 days)
- Median follow up from start of radiotherapy was 19 months (range 1 – 114 months)

- 26/27 of the patients completed both phases of radiotherapy
- 3 patients (aged 86, 90, 92) received no chemotherapy but all 3 had a complete response (CR), 1 patient later had a local recurrence (LR) and died
- 2 patients only had chemotherapy during Phase 1
- 3 patients did not receive Mitomycin C, but had 5-FU

- 25/27 (93%) of the patients achieved CR at 3 months
- 1 patient had persistent disease – treatment time was 59 days, time from end of treatment to death was 3 months.
- 1 patient died 8 days after phase 1 (non-neutropenic death)

- 4/25 (16%) patients who achieved CR then relapsed and died of anal cancer
  - 2 patients developed LR with no distant metastases (DM)
  - 2 patients developed DM with no LR despite chemotherapy

- 17/27 (63%) patients who started treatment have died
  - Only 7/27 (26%) died of anal cancer since starting treatment
  - 3 within 1 year, 1 within 2 years, 2 within 3 years, 1 within 4 years

  - 1 patient was not reported to have disease recurrence, but the death certificate stated Anal Cancer as the cause of death – this is most likely to be incorrect

Kaplan Meier curve of the relapse free survival (RFS), red line demonstrates the 2 year RFS

The 2 year results since the start of treatment were:

- Overall survival (OS) - 68% (95% CI 46 – 82)
- Anal cancer specific survival - 83% (95% CI 60 – 93)
- Once achieved CR, RFS - 87% (95% CI 59 – 95)
- The median OS was 33.5 months

- These results are comparable or better than those seen with some other split course regimens using different fractionation schedules.(3) Our outcomes are similar to certain continuous lower dose regimens (30Gy) used in the elderly. (4)

Conclusion

Although radiobiologically a break in treatment is thought undesirable, allowing accelerated repopulation, continuous CRT can cause unacceptable skin reactions and unplanned breaks in treating frail and elderly patients.

We have found this alternative regimen of split-course CRT to be effective and well-tolerated in the frail or elderly, allowing a radical dose delivery and high local control.

References