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Trimodality therapy for superior sulcus tumours: Evolution and evaluation of a treatment protocol

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Abstract

Aim: We studied the clinical outcomes of a trimodality protocol used for the treatment of superior sulcus tumours (SST) in a tertiary referral centre.
Methods: The details of all patients who underwent treatment for a SST between January 2003 and December 2009 were retrospectively analysed. Following pre-treatment staging, all patients underwent concurrent chemoradiotherapy with cisplatin/etoposide, followed by surgery. Outcomes studied were treatment-related complications, pathological response rates, recurrence rates and survival.
Results: Fifty-four patients were treated by chemotherapy (cisplatin/etoposide) and concurrent radiotherapy (46–66 Gy) followed by surgical resection. Minimum follow-up was 23 months. No 30-day mortality was observed. A complete (R0) resection was performed in 44 out of 54 patients. None had an R2 resection. Two-year survival was 50% (95%CI: 36.7–63.3). Patients who achieved a pathological complete response ($n = 16$) had a 2-year survival of 81% (95%CI: 62.1–100.0) versus a 37% 2-year survival (95%CI: 21.5–52.1) in patients with remaining vital tumour in their resection specimens ($n = 38$; $P = 0.003$). Five patients developed a local recurrence, and 23 patients a distant metastasis, mainly to the brain ($n = 15$). Two patients died from causes unrelated to cancer.
Conclusions: Trimodality treatment of SST in accordance to our protocol achieved results comparable to previous reports. Pathological response rates to induction were an important prognostic factor, and distant metastasis remains a major problem.

Keywords: Pancoast; Superior sulcus tumour; Trimodality treatment; Survival; Outcome

Introduction

Superior sulcus tumours (SST) or Pancoast tumours represent a subgroup of non-small cell lung carcinomas (NSCLC) arising near the pulmonary apex or superior sulcus, and invade the chest wall, brachial plexus, and occasionally the spine or subclavian vessels. Since 2003, chemoradiotherapy followed by surgery has been the recommended treatment approach for SST.[1] However, considerable variation exists between centres with regards to patient selection, extent of staging and pre-treatment regimens.[2–8] For example, some reports have excluded patients who present with N2 disease,[2] and an ^{18}fluorodeoxyglucose (FDG) – positron emission tomography (PET) scan for staging has not been uniformly used.[2–8]

We implemented a regional clinical protocol to standardize the staging and treatment of SST, and present the results of the first 54 patients that were treated in this fashion. In addition, an analysis of the prognostic factors influencing disease free and overall survival in this cohort of patients.

Materials and methods

Patient selection and staging

This retrospective analysis was approved by our institutional Medical Ethics Committee. Data on all patients with

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a SST, who were operated between January 2003 and December 2009 at our institution, were retrieved from a patient database. The diagnosis of SST was established after review in a multidisciplinary lung cancer board and in accordance with established clinical and radiological criteria.[9] All patients were uniformly staged (TNM6 classification was retrospectively converted to TNM7)[10] by: history, physical examination, laboratory investigations, chest X-ray, bronchoscopy, lung function tests, computed tomography (CT) scan of the chest and upper abdomen and a whole body FDG-PET scan. Patients with suspected or cytologically proven metastasis to N2 lymph nodes (N2 disease), were eligible for this study.

Induction therapy and restaging

All patients underwent concurrent induction chemoradiotherapy followed by surgery. Chemotherapy consisted of 1 cycle of cisplatin 80 mg/m^2 on day 1 and either gemcitabine 1250 mg/m^2 on day 1 and 8, in case of squamous histology or pemetrexed 500 mg/m^2 on day 1 in case of non-squamous histologies, and 2 cycles of cisplatin 80 mg/m^2 on day 1 and etoposide 100 mg/m^2 days 1–3 q for 3 weeks. Radiotherapy was administered to a dose of 46–60 Gy, in fractions of 2 Gy, commencing on day 2 of the second cycle of chemotherapy for logistical reasons. Details of radiotherapy were reported previously.[11] Adequate supportive therapies, such as hydration, diuretics and anti-emetic medication, were provided during chemotherapy. Nutritional status was supervised by a dietician and nasogastric tube feeding commenced when weight loss in excess of 10% of baseline weight was observed. All patients were restaged after completion of induction therapy by means of a CT-scan of the chest and upper abdomen. Patients showing any disease progression during or after chemoradiotherapy were not operated upon, and are not included in this database. In patients with suspected or proven N2 disease, a mediastinoscopy was performed for restaging after induction therapy.

Since 2003, the institutional protocol underwent a number of changes:

1. In 2007, brain MRI was added to pre-induction staging in accordance with ACCP recommendations.[9]
2. In 2008, mediastinoscopy after induction therapy was discarded as mediastinal lymph node dissection was routinely performed, and persistent N2 disease was excised as it was felt that a failure to achieve local control of an SST would have resulted in a risk of severe morbidity.

Surgery and histopathological evaluation

Patients without any local or distant progression of disease underwent surgery at 4–6 weeks after completion of induction therapy. All patients were operated by the same surgical team, led by two senior surgeons. At thoracotomy, an upper lobe resection was performed with en-bloc resection of the involved chest wall. In addition, the T1 branch of the brachial plexus was resected. A hilar and mediastinal lymph node dissection was performed and the bronchial stump was covered by a vascularized intercostal muscle flap. All patients received epidural analgesia for postoperative pain control and subcutaneous fraxiparin injections for prophylaxis of thromboembolic complications.

Resection specimens were fixed in neutral buffered formalin. During gross pathological examination of the resection specimen at least two blocks are taken from the tumour area and two from the adjacent lung. If no viable tumour cells were seen in these blocks with histological examination, the remaining of the lesion was embedded in paraffin. Pulmonary lymph nodes are cut at 3 mm slices and embedded. The histopathological response in the resection specimens was scored by estimating the percentage of vital tumour cells within the macroscopical tumour rest in relation to areas of fibrosis, necrosis and inflammatory changes. A 4-tier scoring system was used: (1) complete pathological response; (2) less than 10% vital tumour cells; (3) more than 10% vital tumour cells; (4) no pathological response.

Data collection

Data on patient characteristics, diagnostic work-up and treatment, pathological results and recurrence and survival were collected. Follow-up data were derived from medical records, clinical charts, imaging reports and by contacting patients' general practitioner, referring physicians and the patient or his/her family. Survival data were obtained up to December 2011.

Statistical analysis

All statistical analyses were performed using the statistical software package SPSS, version 17.0 (SPSS, Inc., Chicago, IL, USA). Survival was calculated with the Kaplan–Meier method from the date of operation. For the analysis of disease free survival, events were defined as local recurrence, progressive disease (i.e. distant metastasis) or death of any cause. In addition, survival was compared with pathological response, N2 lymph node status and radical resection using the log-rank test. Values in text and tables are presented as medians unless stated otherwise. To identify prognostic factors for survival at 2 years, all possible prognostic factors were entered in stepwise backward logistic regression analysis using a cut-off value of $P = 0.05$. Odds ratios (OR) were presented with 95% confidence intervals. Statistical significance was defined as $P < 0.05$.