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Chemotherapy-Induced Recall of Cetuximab and Radiation Skin Reaction

Sir — We would like to report the first case to our knowledge of recall of a cetuximab radiation reaction. A 70-year-old man presented in April 2007 with a right-sided neck lump. Biopsy of the tonsil confirmed squamous cell carcinoma and computed tomography showed an enlarged tumour in the right tonsil with extension into the base of the tongue and enlarged nodes were seen in the right level 2 and 3 nodes.

The patient underwent a right radical neck dissection followed by radiotherapy to the primary and adjuvant radiotherapy to the nodal areas on both sides. In view of a history of previous cerebrovascular accident (CVA) it was decided to give concomitant cetuximab with the radiotherapy (rather than cisplatin) as it has been shown to have superior results to radiotherapy alone [1]. The synergistic effect of cetuximab is thought to be due to mediating cell growth, differentiation and survival [2].

The patient received 68 Gy in 34 fractions over 7 weeks to the primary tumour using a two-phase technique coming off cord at 44 Gy and matching on electron fields to the posterior neck and a matched anterior neck field. During the treatment he received standard weekly cetuximab [1]. He had a marked skin reaction with grade 3 toxicity and there were areas that took 6 months to heal (Fig. 1).

In March 2008, he developed skin nodules on his chest outside the previous radiation field and biopsies of these confirmed a squamous cell carcinoma with similar appearances to his primary tonsillar cancer. Computed tomography showed bilateral pulmonary metastases and pleural effusions.

The patient was given palliative chemotherapy with carboplatin and gemcitabine rather than cisplatin/5-fluorouracil-based chemotherapy because of his previous CVA. After the first cycle his skin nodules had disappeared and the response to chemotherapy was confirmed on chest X-ray, with significant reductions in the size of pleural effusion and pulmonary metastases.

At the fourth and final cycle of chemotherapy, an area of ulceration was noted at the site of a previous skin reaction during radiotherapy (Fig. 2). He had no other skin lesions and it was consistent with a recall reaction after his chemotherapy. A biopsy was not undertaken due to the risk of non-healing.

Similar radiation recall reactions have been reported after chemotherapy, but to our knowledge this is the first case of recall of a skin reaction with cetuximab-based radiotherapy. The area of ulceration subsequently improved when his chemotherapy was completed. Radiation recall reaction is thought to be an acute inflammatory reaction in previously irradiated areas after the administration of certain inciting systemic agents [3]. Gemcitabine has been implicated in several cases [4] and was possibly a precipitant in this case. Radiation recall reactions are usually characterised by erthyema, but in this case it was more marked and similar to the pronounced skin reaction seen during the primary chemoradiation. If replicated in other patients, this will give further information on the pathology of both cetuximab skin reactions and also the radiation recall phenomenon.

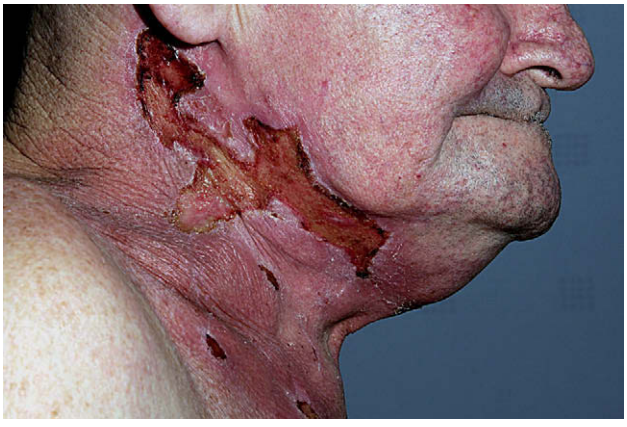

Fig. 1 — Photograph showing the skin reaction that occurred during radiotherapy with concomitant cetuximab.

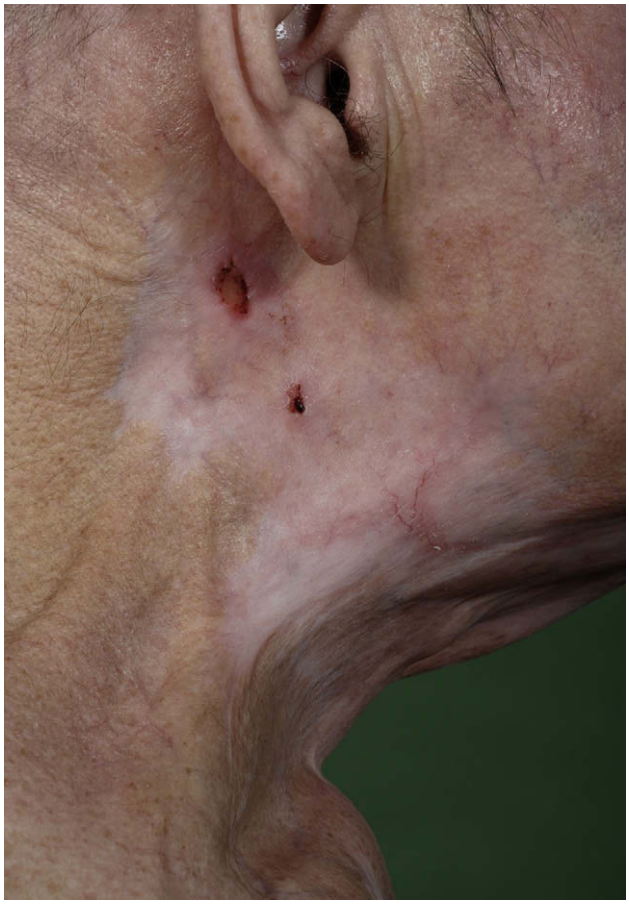

Fig. 2 — Photograph showing radiation recall reaction after administration of carboplatin and gemcitabine.

A. B. LAW *Edinburgh Cancer Centre, Edinburgh, UK*
E. J. JUNOR

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Radiotherapy in Extensive-disease Small Cell Lung Cancer. A Survey of Current UK Practice

Sir — Following the results of the European Organization for Research and Treatment of Cancer (EORTC) 08993—22993 study, which showed a survival benefit at 1 year for extensive-disease small cell lung cancer (ED-SCLC) patients who received prophylactic cranial irradiation (PCI) [1], we conducted a survey of radiotherapy practice for ED-SCLC in the UK. In December 2007, a 10-item questionnaire was sent electronically to a clinical oncologist in 52 radiotherapy centres in the UK involved in the treatment of ED-SCLC.

Completed questionnaires were returned from 39 (75%) centres. Almost half the responding centres (48.7%) were involved in recruiting patients to the EORTC 08993—22993 trial. Since the results of the EORTC trial were presented at the American Society of Clinical Oncology meeting in June 2007 and published in the New England Journal of Medicine in August 2007, radiotherapy centres in the UK have been quick to adopt PCI in this setting. Before the presentation of the data, 12.8% of responding centres were routinely offering PCI for patients with ED-SCLC who had responded to systemic therapy. This figure had risen to 89.7% just 4 months after the publication of the trial. Previous experience has shown a delay between the publication of clinically important radiotherapy trial data and a change in clinical practice [2—5]. In 2003, only eight of 23 UK radiotherapy centres responding to a survey of treatment for limited-disease small cell lung cancer (LD-SCLC) were using concomitant chemoradiotherapy, despite previous publications of several phase III trials showing its improved efficacy over sequential treatment [6]. The rapid change in clinical practice for PCI in ED-SCLC reflects familiarity with PCI as a routine for patients with LD-SCLC, the participation of a large number of UK centres in the study, and the flexibility in radiotherapy dose and fractionation ('according to local practice') permitted by the trial design.

Most centres were following the EORTC trial inclusion criteria regarding patient selection (World Health Organization performance status score of 0—2, age $\leq$75 years). No centre had treated patients with a performance status score $\geq$ 3. However, 10 centres had treated a patient over 75 years old. These patients were excluded from the EORTC trial. The most widely used dose/fractionation regimen in the UK was 20 Gy in five fractions (60%), reflecting the 66.4% of patients treated with this regimen in the EORTC trial. Of the responding centres with a policy regarding the timing of PCI, 80% aimed to start treatment within 4 weeks of completing systemic treatment, with the remaining 20% giving PCI 4—6 weeks after chemotherapy. The EORTC trial stipulated that PCI should start 4—6 weeks after the completion of systemic therapy.

Consolidation thoracic irradiation was routinely being delivered after a response to systemic chemotherapy in 35.9% of responding centres. The Dutch Lung Cancer Study Group have proposed a randomised trial of consolidation thoracic irradiation (CREST trial; 30 Gy in 10 fractions consolidation thoracic radiotherapy and PCI vs PCI alone). There is considerable interest in such a trial in the UK, with 79.5% of centres expressing an interest to take part. It is hoped that with active participation in the UK, the question surrounding the role of consolidation thoracic irradiation in these patients can be answered as succinctly as it has been for PCI.

N. BAYMAN *Department of Clinical Oncology,*
P. LORIGAN *The Christie NHS Foundation Trust,*
F. BLACKHALL *Manchester M20 4BX, UK*
C. FAIVRE-FINN

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