if given in 2 Gy fractions (LQED2) for different values of α/β and the percentage increase in dose above mpd. Firstly, this shows that the calculations of Dardoufas and colleagues are misleading. For $\alpha/\beta = 1$, the LQED2 for $8.5\ Gy \times 2$ is less than 55 Gy and for $\alpha/\beta = 1.5$ less than 50 Gy. Secondly, if as is reasonable to assume, the cord dose will on average be 5% greater than mpd and $\alpha/\beta = 2$, then LQED2 will be approximately 48–49 Gy. In their review of the radiation response of the spinal cord, Schultheiss and Stephens considered the risk of RM with 45 Gy in 2 Gy fractions to be 0.2% [1].

As a result of this, we believe that there is a small and clinically significant risk of RM to the normal population if the regimen is used without taking precautions over the dose to the spinal cord. It is not necessary to invoke intrinsic idiosyncratic hypersensitivity to explain these cases as was suggested by Dardoufas and colleagues.

Oncologists who often treat patients with this regimen will see RM from time to time. If it is felt that the undoubted efficacy and convenience of the regimen justify its use, then the dose to the cord should be reduced. Our practice in Glasgow has been to shield the cord from the posterior field with a 2 cm midline block for the second fraction. This reduces the dose to the cord to about 16 Gy. There is a theoretical risk that the palliative efficacy will also be reduced, but the symptomatic disease is usually away from the midline. We have employed this technique for the past 4 years in over 400 patients and have seen no further cases of RM.

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Breast Metastases of Merkel Cell Carcinoma

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THERE IS increasing interest in Merkel cell tumours. This rare but very aggressive neuroendocrine carcinoma of the skin, which mainly occurs in elderly patients, was first described by Toker [1]. Some 100 cases have been reported in the literature over the past 30 years. The Merkel cell carcinoma has distinct ultrastructural and immunohistochemical characteristics. Demonstration of membrane-bound dense-core neurosecretory granules by electron microscopy, or immunohistochemical proof of neuron-specific enolase are required for diagnosis [2, 3].

The tumour has a very aggressive behaviour with frequent local recurrences, regional lymph node metastases and distant metastases, eventually leading to death. Merkel cell carcinomas mainly occur in the head and neck region of elderly patients, but also in other sites. Despite the chemo- and radiosensitivity of the tumour, optimal management has not yet been defined. Distant metastases may occur in lymph nodes, CNS, lung, liver and the skin [3–5]. We report here on 2 female patients with metastases of the breast. Clinical behaviour and treatment options will be outlined.

Case 1

An 85-year-old woman presented with a symptomless tumour on her right eyebrow. The radically excised mass measured 1.8 cm in diameter. After one month, a local recurrence appeared which was re-excised. Five months later three regional cutaneous metastases were removed and the patient was referred for radiotherapy. She had locoregional ^{60}Co external beam irradiation with 50 Gy including the right cervical lymph nodes and additional 10 Gy boost to the scars. Six months later multiple metastases appeared on her left cheek which were excised and the same postoperative radiotherapy was delivered. After several months, a painless mass in her right breast was detected at follow-up examination. Mammography revealed a round tumour measuring 1.5 cm. This lesion was excised under the assumption of a primary breast cancer but histopathological examination showed metastases of Merkel cell carcinoma. Postoperative radiotherapy of the whole breast was delivered with 50 Gy using CT-based individual treatment planning. The patient died one year later from intercurrent disease without local recurrence in the breast, but with recurrence on her left cheek.

Case 2

An 84-year-old woman presented with an axillary mass without detectable breast cancer. After axillary clearing, the histopathological diagnosis was metastases of a Merkel cell tumour. The patient subsequently reported that a tumour of 1.5 cm on her forearm had been removed 4 months previously. A review of the pathological specimen showed that this was the primary. An axillary recurrence occurred 3 weeks before radiotherapy was initiated. This recurrence was irradiated including the axillary, supra- and infraclavicular nodes with a dose of 60 Gy. The tumour regressed completely. CT and MRI did not show a lesion in the breast. Four months later the patient developed metastases in the oropharynx and cervical lymph nodes which again were irradiated with 60 Gy. The patient was then seen for regular follow-up in 4 week intervals. Three months after radiotherapy of the oropharynx, she presented with a lump in the right breast of 12×10 cm and two local skin metastases. She underwent radical mastectomy but during wound healing several locoregional metastases appeared which were subsequently excised. The patient died from abdominal dissemination 23 months after the diagnosis of the primary tumour.

Merkel cell carcinoma is seen in age groups ranging 7–96 years, but most of the patients tend to be elderly. The initial lesion is usually a small prominent nodule with pink or bluish

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colour and indistinct margins which shows rapid growth. Routine light microscopy detects primitive small malignant cells growing in diffuse, organoid or ribbon-like fashion. Immunohistochemically, neuron-specific enolase and cytokeratin are important diagnostic markers [2]. Most of the tumours occur in the head and neck region and subsequently in the extremities and trunk. The reported incidence of local recurrence varies between 30 and 45%. The risk of regional lymph node involvement is >50% and for distant metastases 20–40%, respectively. Approximately 30% of the patients die of metastatic disease [3–7].

Treatment of the primary lesions should be wide excision, which especially in the head and neck region, is difficult to achieve. After less extensive surgery, tumours >2 cm should be irradiated with generous margins up to 50–60 Gy. This dose has also been recommended by other authors [7, 8]. There is no consensus about adjuvant treatment of regional lymph nodes, nor for prophylactic dissection or radiotherapy. Short-term follow-up is mandatory due to the rapid growth of recurrence and metastases. Metastatic disease can be treated either with radio- or chemotherapy regimens which are normally used for small cell lung cancer. Merkel cell carcinoma is known to be highly radiosensitive, confirmed in Case 2 with a complete regression of gross disease after 60 Gy. Complete clinical remissions have also been reported with various cytotoxic drugs, i.e. doxorubicin, etoposide, cyclophosphamide and vincristine [8–10].

Dissemination usually appears within 2 years after diagnosis of the primary. Most commonly involved are soft tissues, liver, lymph nodes, bone, lung, spine and bone marrow whereas the brain, kidney, pancreas, parathyroid gland and pleura are less frequently affected [5]. Metastases of Merkel cell carcinoma in the breast, to our knowledge, have not been reported before. We therefore recommend careful review of the pathological specimen if a rapidly growing tumour in the breast of an elderly patient has been excised and primary histopathological diagnosis indicates metastases of small cell lung cancer or lymphoma. Immunohistopathological staining with neuron-specific enolase and cytokeratin should be performed to exclude or confirm Merkel cell carcinoma. In this case, axillary clearing might be unnecessary, but postoperative radiotherapy of the breast with at least 50 Gy should be initiated without delay.

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Myocardial Infarction Associated with Vinorelbine (Navelbine^{R})

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VINORELBINE (NAVELBINE^{R}) is a unique semisynthetic vinca alkaloid. The drug is effective as a single agent in inoperable/advanced non-small cell lung cancer (NSCLC), producing objective response rates of approximately 15–30% [1]. Myelosuppression is the most frequent side-effect, while neurotoxicity, nausea, emesis, alopecia and mucositis occur less often.

In this letter, we report on the case of a 87-year-old Caucasian man who developed acute myocardial infarction that was probably related to the administration of vinorelbine. He had a history of coronary heart disease with a posterior Q-wave infarction 35 years ago. However, over the last 30 years, the patient had not experienced any cardiac problems. He was in excellent physical condition, when locally advanced NSCLC was diagnosed. At that time, levels of electrolytes, haemoglobin and thrombocytes, and liver and kidney function and coagulation tests were all in the normal range. An electrocardiogram (ECG) and two-dimensional echocardiography confirmed the old myocadial scar. Vinorelbine monotherapy was initiated (30 mg/m^2) and 10 h later the patient developed long-term angina pectoris. Repeated ECG controls revealed an acute anteroseptal infarction that was stuttering in nature, with only slightly elevated levels of creatinine kinase (100 U/ml) and troponin-T. Treatment with aspirin, low-dose heparin and mononitrate was initiated. Repeated echocardiography confirmed the diagnosis of an anteroseptal myocardial infarction and showed a marked depression in left ventricular function.

To the best of our knowledge, this is the third report of a vinorelbine-related myocardial infarction [2, 3]. We conclude

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