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Small Cell Anaplastic Carcinoma of the Oesophagus Following Mantle Field Radiotherapy for Mediastinal Hodgkin's Lymphoma: First Case Report

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We would like to report what we believe is the first documented case of a small cell anaplastic carcinoma of the oesophagus following mantle field radiotherapy for mediastinal Hodgkin's lymphoma. In 1987, a 33-year-old female, with no relevant previous medical, social or family history of note, and specifically no history of tobacco use or excessive use of alcohol, was diagnosed as having nodular sclerosis Hodgkin's lymphoma of the mediastinum. Mediastinotomy and staging laparotomy at that time established that disease was limited to the mediastinum (stage IA; Ann Arbor staging). At the start of mantle field radiotherapy, an involved lymph node was present in the neck on the left side (stage IIA); a dose of 40 Gy, in accordance with the European Organisation for Research and Treatment of Cancer (EORTC) guidelines, was administered followed by complete remission. No chemotherapy was given. Subsequent regular follow-up did not detect any recurrence.

In April 1997 the patient complained she was having difficulty with swallowing but clinical and radiographic examination did not detect any abnormalities. By August she was having increased difficulty with swallowing and had lost approximately 2.5 kg in weight. Endoscopy identified a mucosal ulceration in the oesophagus extending from 29 to 25 cm. Bronchoscopy was normal. Computerised tomography demonstrated a thickening of the wall of the oesophagus, free from any contiguous structures. No other abnormalities were seen. Biopsies were taken and histology showed a classical small cell anaplastic carcinoma with a typical neuroendocrine immunohistochemical profile (keratin weakly positive, neuron-specific enolase positive, synaptophysin weakly positive). Considering the radiological features, the lesion was regarded as having its origin in the oesophagus and not the result of local extension from elsewhere in the mediastinum.

Over the last two decades it has become clear that there is a significantly increased risk of a second malignancy following the treatment of Hodgkin's lymphoma [1]. Three groups of second malignancies have been seen: the acute leukaemias, non-Hodgkin's lymphomas (NHL) and solid tumours [1]. The vast majority of acute leukaemias (88%) and most NHL (70%) appear within the first decade following treatment [1]. The median time for developing solid tumours (epithelial, mesenchymal, melanoma) is greater than for the acute leukaemias and NHL; recent work suggests that less than half of all solid tumours arise within the first 10 years following the original treatment [1]. No neuroendocrine lesions arising after radiotherapy for a first cancer, appear to have been documented to date.

Our case is interesting in that it appears to be the first reported case of a small cell anaplastic carcinoma following mantle field radiotherapy and represents a relatively early onset for a second malignancy of the solid tumour group. Previously described cases of cancers of the oesophagus following radiotherapy appear to be squamous cell carcinomas with a later time of onset [2]. Patients with cancer of the oesophagus following radiotherapy present special problems: growth is usually extensive and palliative measures are not very successful. Additionally, the few reported cases of primary small cell anaplastic carcinomas of the oesophagus have had a very poor prognosis [3].

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Pre-operative CYFRA 21-1 Levels in Patients with Lung Cancer: Correlation with Mediastinal Lymph Node Involvement

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MEASUREMENT OF CYFRA 21-1, a novel tumour marker derived from cytokeratin 19 fragment (CYFRA 21-1), has recently been clinically introduced, and has proven to be suitable for monitoring results of therapy for lung cancer [1–4]. We examined the correlation between serum levels of CYFRA 21-1 and lymph node involvement in lung cancer patients. 81 patients with untreated lung cancer were included in this study. They were pathologically staged [5] as stage IA–IIIA after undergoing curative tumour resection and lymph node dissection. Pre-operative sera from these patients were tested for levels of CYFRA 21-1, using an enzyme immunoassay (Enzymun-Test CYFRA 21-1, Boehringer-Mannheim, Tokyo, Japan).

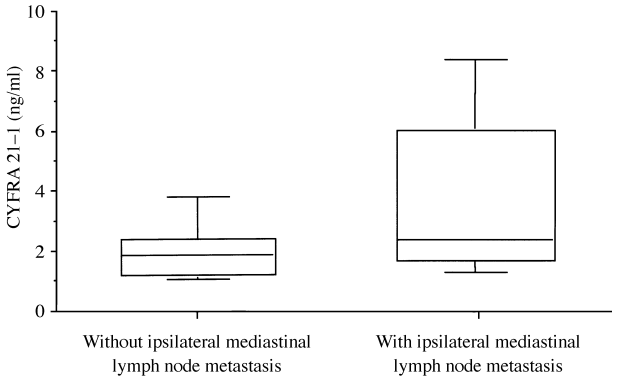

Figure 1. Percentile distribution of serum levels of CYFRA 21-1 in untreated patients with or without mediastinal lymph node metastasis. Each box indicates the 25th and 75th percentiles, with the median values indicated by the lines within the boxes. The bars extending above and below the box indicate the 90th and 10th percentiles, respectively.

For the 42 N0 patients, there was no significant correlation between the serum level of CYFRA 21-1 and the size of the primary lesion (Spearman's coefficient correlation, $P = 0.3950$). Serum levels of CYFRA 21-1 differed significantly by nodal status between N0 and N2 patients (Kruskal–Wallis test, $P = 0.0104$). More interestingly, serum levels of CYFRA 21-1 in N2 patients (median 2.33 ng/ml, interquartile range 1.54–5.85 ng/ml) were higher than those in N0-1 patients (median 1.80 ng/ml, interquartile range 1.10–2.40 ng/ml) (Mann–Whitney U test, $P = 0.0434$) (Figure 1). There were no significant differences between these two groups of patients in terms of age ($P = 0.7382$), gender ($P = 0.7819$) or histologic type ($P = 0.7904$). On receiver characteristic curve analysis, the recommended cut-off level of CYFRA 21-1 between N0-1 and N2 patients was 2.30 ng/ml. The measurement of serum CYFRA 21-1 is useful for non-invasive prediction of extent of disease, especially in candidates for surgical treatment, since increased levels of this marker suggest the presence of N2 disease.

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