Eur J Cancer Clin Oncol, Vol. 21, No. 5, pp. 585–586, 1985.
Printed in Great Britain.

0277-5379/85$3.00+0.00

Pulmonary Embolism in Patients Receiving Chemotherapy for Advanced Ovarian Cancer

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Abstract—*The incidence of pulmonary embolism was examined in a series of 83 patients who had received chemotherapy for advanced ovarian cancer and ten embolic episodes occurred. The incidence of pulmonary emboli was highest in those patients who had gross bulk disease (>10 cm diameter) before chemotherapy and occurred in 9/49 cases, with all six fatalities being in this group. Five of the six fatal emboli occurred within 1 week of the first course of chemotherapy. As the mortality rate from pulmonary emboli in patients with gross bulk tumour was 12% in this series, anticoagulation before initiating chemotherapy is suggested for this group of patients.*

INTRODUCTION

EPISODIC thrombosis and thrombo-embolism can be a major problem for patients suffering from generalised malignancy, including patients with ovarian cancer, but this is normally a feature of the disease prior to treatment and not a commonly recognised complication of therapy. The outlook for patients with advanced ovarian malignancy has improved considerably since the introduction of combination chemotherapy, and during a prospective study of the efficacy of *cis*-platinum and doxorubicin in patients with stage III and IV disease we noted a high incidence of pulmonary emboli during treatment. The implications of this observation are presented and discussed.

MATERIALS AND METHODS

Eighty-three consecutive patients presenting with ovarian carcinoma (Figo stages 3 and 4) who received chemotherapy with *cis*-platinum and doxorubicin were examined retrospectively to determine the incidence of pulmonary embolism. For those patients who developed features of an embolus whilst in hospital the diagnosis was confirmed by ECG, chest X-ray and lung perfusion studies or, if fatal, post-mortem examination. If death occurred at home, where no post-mortem examination was possible, a presumptive diagnosis was made in view of the nature of the clinical features associated with the death.

RESULTS

Results are summarised in Table 1. None of 13 patients with minimal residual disease developed a pulmonary embolus. Of 21 patients with moderate bulk disease one patient sustained an embolus that was successfully treated with anticoagulants. However, of 49 patients who had gross bulk disease nine (18%) developed pulmonary emboli immediately following the first course of chemotherapy, of which six (12%) were fatal. Of the six patients who died five did so within 1 week of the first course of chemotherapy. None of these patients had any clinical evidence of thrombotic phenomena prior to treatment. Thus the mortality rate is 7% overall and 12% for patients with bulk disease in this series.

Table 1. Incidence of pulmonary embolism by bulk of disease prior to chemotherapy

Bulk of disease prior to chemotherapy	Pulmonary emboli No.	Overall	Fatal
Minimal residual disease (<2 cm)	13	0	0
Moderate bulk disease	21	1	0
Gross bulk disease (>10 cm)	49	9	6
Total	83	10	6

Accepted 12 November 1984.
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DISCUSSION

The high incidence of pulmonary embolism in patients with ovarian malignancy may be attributed to several factors. Local invasive disease may involve pelvic veins, particularly in the mucinous-producing carcinomas, which are often associated with intravascular extensions and are frequently complicated by thrombosis. An increased thrombotic tendency has previously been noted in patients with malignant ovarian tumours; Astedt *et al.* [1] found that of 32 patients with malignant ovarian tumours 23 had pre-operative elevations of fibrin degradation products (FDP) compared to only six of 131 patients with benign tumours. The largest group of patients with an elevated FDP occurred in those with serous cyst adenocarcinoma. Planner *et al.* [2] demonstrated peaks of thrombocytosis occurring in 43 of 59 patients during treatment with chemotherapy for ovarian carcinoma, and that these peaks were associated with thrombotic or embolic episodes, although no relationship to disease bulk or temporal association between embolic episodes and the institution of chemotherapy was noted. The fact that the majority of fatalities occurred very shortly after the first course of chemotherapy must imply an effect of treatment on the tumour or upon an altered coagulation state associated with the tumour, but the precise explanation for the release of thrombus can only be a matter for conjecture.

However, the mortality in this group is unacceptably high, particularly in the face of continued development of drug regimens which offer a better prognosis. We therefore suggest that patients with bulk disease who require combination chemotherapy are routinely anticoagulated prior to treatment. The courmarins are compatible with any regimen in current use, with the exception of methotrexate, and this relatively simple measure may be of benefit and help improve the prognosis.

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