Table 1. Patients' characteristics

Characteristic	Treatment groups: Tube only	Tube + chemotherapy + radiotherapy
No. of patients (total 20)	10	10
Male : female	10 : 0	9 : 1
Median age (years)	53	55
Performance status (ECOG)		
1	5	5
2	5	5
Differentiation of tumour		
Well	—	2
Moderate	10	8
Location of primary tumour		
Upper thoracic	1	—
Middle thoracic	9	6
Lower thoracic	—	4
Tracheo-bronchial involvement or small mediastinal fistulae	4	4
Median length of tumour (cm)	7	8
Median survival (weeks)	19	11

An interim analysis showed that patients randomised to observation had a median survival of 19 weeks while patients treated with radiotherapy, 5-FU and cisplatin had a median survival of 11 weeks, ($P = 0.03$, Mantel–Cox test). This difference in survival was due to toxicity of the combined chemoradiotherapy and tube. This made early termination of the trial ethically necessary.

The documented haematological toxicity of the 10 patients on the chemoradiotherapy arm was mild to moderate (ECOG grade I–II) in 3 patients and severe (ECOG grade III) in 1 patient. Gastrointestinal toxicity was acceptable with mild to moderate nausea and vomiting in 4 patients (ECOG grade I–II). 3 patients developed pulmonary infection requiring antibiotic treatment. 2 patients developed ECOG grade III neuromotor complications which fully reversed.

A lethal perforation of the oesophagus developed in 1 patient outside the tumour area, shown at postmortem to be related to oesophagitis and mechanical stress of the tube. In this patient 80% tumour necrosis was also demonstrated with multiple representative sections of the tumour at necropsy. 3 patients on chemoradiotherapy died at home after 25, 25 and 36 days, with a clinical picture related to toxicity, and not progressive disease. Confirmation with necropsy could not be obtained as the patients lived in rural areas.

The chemoradiotherapy combination has considerable reported tumour activity [4]. It should, however, not be used (at least in Southern Africa) for patients with far advanced disease where intubation has been selected for palliation. The 4 deaths due to complications occurred despite the selection of cytostatic doses in the lower range as the radiation dose was high per fraction. Whether the combination of 5-FU and cisplatin plus radiotherapy will prolong survival of patients with advanced disease still needs to be confirmed in a prospective randomised trial. We are currently randomising patients after dilatation to observation vs. chemoradiotherapy. Furthermore, patients with mediastinal fistulae or involvement of tracheo-bronchial tree are now excluded.

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Palliation of Malignant Phaeochromocytoma with Combination Chemotherapy

Suresh Senan, Nicholas Reed and John Connell

RECENT REPORTS have highlighted the role of ^{131}I-labelled meta-iodobenzylguanidine (MIBG) in the diagnosis and treatment of malignant (metastatic) phaeochromocytoma and have dismissed any useful role for chemotherapy [1, 2]. However, only 60% of our patients with malignant phaeochromocytoma show MIBG uptake. This may be due to tumour dedifferentiation and occurs in cases initially showing uptake [2]. Here, we describe useful symptomatic and biochemical responses in 2 patients with this tumour whose lesions did not show MIBG uptake.

Patient 1, a 17-year-old-female, presented in September 1988 with palpitations and chest pain. She was hypertensive, had elevated plasma noradrenaline (radioenzymatic assay [3]) and a left extra-adrenal tumour with multiple bony metastases. Biopsy of a rib lesion revealed metastatic phaeochromocytoma and an ^{131}I MIBG scan showed no uptake. The hypertension was controlled with atenolol and phenoxybenzamine and a left-sided extra-adrenal tumour was excised in November 1988. Three postoperative noradrenaline levels remained high (61–113 nmol/l) and she started chemotherapy every 3 weeks with cyclophosphamide 750 mg/m^2 on day 1, vincristine 1.4 mg/m^2 day 1 and dacarbazine 600 mg/m^2 on days 1 and 2, receiving seven cycles of chemotherapy between December 1988 and April 1989.

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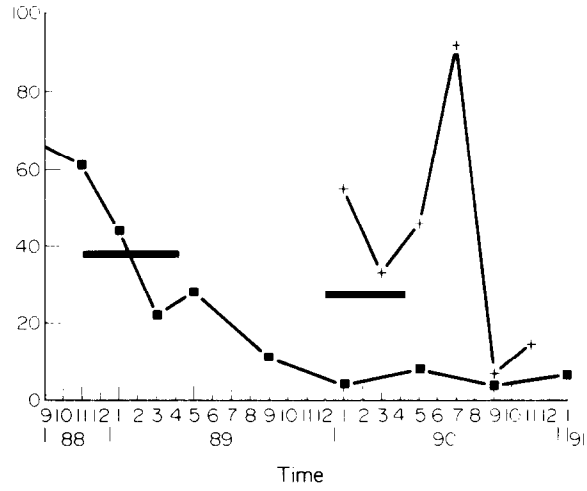

Fig. 1. Noradrenaline vs. time. Normal range < 5 μmol/l. —•— Patient 1, —|— patient 2, ▬ chemotherapy.

The serum noradrenaline levels (Fig. 1) declined slowly towards the second part of chemotherapy and normalised in February 1990, 10 months after treatment completion. Antihypertensives were discontinued in February 1990 and she remains asymptomatic. Her radiological abnormalities remain unchanged.

Patient 2, a 52-year-old man, presented with symptoms of episodic dizziness and had a left-sided intra-abdominal (extra-adrenal) phaeochromocytoma resected in 1987. His symptoms recurred in May 1988, when serum noradrenaline was rising. Treatment with atenolol and phenoxybenzamine provided symptomatic relief. In January 1990 his condition worsened with palpitations, 6 kg weight loss and poorly controlled hypertension. A repeat MIBG scan was again normal but computed tomography revealed intra-abdominal tumour recurrence and multiple skeletal metastases were shown on an isotope bone scan.

Chemotherapy (as for patient 1) was started and between February and June 1990, he received five cycles. Treatment was stopped when thrombocytopenia worsened with no change in tumour size. Following chemotherapy his noradrenaline decreased to 7 nmol/l and is now stable at 15 nmol/l (Fig. 1). His blood pressure remains controlled on atenolol; he is asymptomatic although the measurable tumour mass is unchanged.

Although the natural history for patients with these tumours is variable (with a 5-year survival of 44% [4]), improved pharmacological control of catecholamine secretion does not appear to influence mortality [5, 6]. Complete or partial biochemical responses were seen in nearly 80% of the 14 patients previously treated with this regime [7] (mean duration of response of 21 months) whilst only 8 had other evidence of tumour response (2 complete and 6 partial remissions). Treatment, however, was continued in this series until either disease progression or biochemical complete remission.

Both our patients had widely metastatic disease and the second had clear symptomatic deterioration associated with biochemical progression. Neither experienced the serious cardiovascular complications seen in patients with occult phaeochromocytoma who receive chemotherapy [8, 9]. There was a clear (delayed) fall in plasma noradrenaline associated with symptomatic improvement.

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Toxicity of Laevo-leucovorin and Dose-lowering

Federico Lonardi, Antonio Jirillo, Giorgio Bonciarelli, Giovanni Pavanato and Mario Balli

LEUCOVORIN IS widely used as a biomodulator in cancer chemotherapy. The D and L diastereoisomers have different metabolism and pharmacokinetics. L-leucovorin is the biologically active form and has recently become available. Therefore a 50% dosage reduction seemed a resonable step clinically, but the high level of toxicity we observed using L-leucovorin in otherwise well-tolerated schedules made such an approach questionable. Here we report our preliminary experience of 4 consecutive patients treated with L-leucovorin (Lederfolin, Lederle).

Two patients had advanced colorectal cancer and were scheduled for leucovorin as a 200 mg/m^2 push and 5-fluorouracil (5-FU) 400 mg/m^2 as a 15 min infusion on days 1–5 every 4

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