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Acute Blindness During Treatment of Recurrent or Metastatic Nasopharyngeal Carcinoma with Doxorubicin and CCNU

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NASOPHARNYNGEAL cancer (NPC) is almost exclusively treated by radiation therapy, which provides local complete regression of tumour and lymph nodes in 85% of the cases. Five-year survival rates, however, range from 44 to 59% after such therapy, and the high rate of distant metastasis precludes cure of most patients [1]. There is no standard chemotherapy for recurrent or metastatic NPC, although doxorubicin (response rate 39%), cyclophosphamide (31%), bleomycin (28%) and methotrexate (17%) are active on their own [2]. Because of good results with a combination of doxorubicin and CCNU in five patients [3] (three out of five patients achieved complete remission, two of which have been sustained for over 104 and 115 months, respectively, and one partial remission) we started a phase II study to assess the antitumour activity and toxicity of doxorubicin–CCNU in recurrent or metastastic NPC.

Inclusion criteria were histologically confirmed poorly differentiated or anaplastic NPC, documented progressive measurable or evaluable disease, age 75 or less, WHO performance status 0–2, adequate renal function, normal liver function tests and hamatological indices. No patient had received previous chemotherapy. Doxorubicin was given by intravenous bolus injection at a dose of 50 mg/m^2 every 3 weeks; CCNU 120 mg/m^2 was given orally every 6 weeks. Standard WHO criteria were used for the assessment of response and toxicity [4].

Fifteen patients entered this study (Table 1). Median performance status was 1. The patients received a median of four courses. Five responses (one complete response and four partial responses) were achieved (33%), three patients had no change (three to six cycles) and six patients had progressive disease: one patient was not evaluable for response (one cycle only).

Toxicity was considerable. Eight patients (53%) had grade 3 or 4 leucopenia; four of these had treatment-related infections. One patient had acute blindness in his right eye after two cycles. This was followed by blindness in the left eye. Since no other cause for the blindness could be found by physical examination and computed tomography, it was assumed to be a toxic neuropathy of the optic nerves. The patient was subsequently lost to follow-up. Other toxic effects are listed in Table 1.

Table 1. Patients' details

No. of patients	15
Male/female	10/5
Median age (range)	60 (27–72)
WHO performance status	
0	3
1	10
2	2
Previous radiotherapy	14
Previous surgery	2
No previous treatment	1
Median No. of cycles (range)	4 (1–11)
Non-haematological side-effects	
nausea/vomiting	13 (87%)
hair loss	12 (80%)
infection	4 (27%)
diarrhoea	3 (20%)
increased creatinine	1 (7%)
optic neuritis	1 (7%)

The treatment was stopped in six patients (40%) because of excessive toxicity, and in seven patients because of progressive disease. One patient refused to continue and one patient left the country and was lost to follow-up after three cycles. The duration of the complete response was 2 months and the duration of the partial responses were: 4, more than 8 (lost to follow-up), 9 and 12 months.

This combination of doxorubicin and CCNU proved to be an active but toxic regimen for the treatment of recurrent or metastatic NPC. The most severe event was sudden blindness after two courses. Sudden blindness has been described in three patients who were treated with CCNU, two of whom had also received cranial irradiation [5]. Although it was not possible to prove a relation between the chemotherapy and the blindness in our patient, the absence of any other cause suggested that the blindness was drug-related. Since this regimen had to be stopped because of excessive toxicity in 40% of the patients, we decided to discontinue the trial. Despite the observed 33% response rate, this combination cannot be recommended for the treatment of patients with advanced NPC.

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