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Short Communication

High-dose Etoposide for Meningeal Carcinomatosis in Patients with Small Cell Lung Cancer

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INTRODUCTION

In a high percentage of SCLC patients, central nervous system (CNS) metastases are found and this usually results in considerable morbidity and mortality [1]. This is especially the case in patients with meningeal carcinomatosis (MC). The incidence of MC in SCLC has been reported to be between 5 and 18%. With prolongation of survival , the chance of MC becoming symptomatic is rapidly increasing [1]. The results of therapy for this devastating form of metastatic disease have been rather poor.

After high-dose cyclophosphamide and etoposide with autologous bone marrow transplantation [2] and in a phase I study of etoposide [3], favourable responses of brain metastases from SCLC were found. In this report we describe the effect of high-dose etoposide (HDE) in five patients with MC from SCLC.

CASE REPORTS

Patient characteristics and therapy are described in Table 1. In all patients myelography was normal. In patient 4 the total protein of the CSF was elevated and the CSF-IgG index indicated an evident disturbance of the BBB.

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Abbreviations used: CDE = cyclophosphamide 1 g/m² i.v., d 1, doxorubicin 45 mg/m² i.v., d 1, q 3 weeks, etoposide 100 mg/m² i.v., d 1, 3, 5; CSF = cerebrospinal fluid; BBB = blood–brain barrier; HDE = high-dose etoposide, total dose 1 g/m² in 6 1 h infusions with 12 h interval, q 4 weeks.

DISCUSSION

Theoretically, intraventricular intrathecal therapy seems to be the best approach for patients with MC, but the results are very disappointing with regard to response and survival in SCLC patients. In combination with radiation of the neuraxis and/or the brain, the results are slightly better concerning clinical improvement [4]. In most patients MC is not the only site of tumour relapse; progression of the primary tumour and/or other metastatic sites is often seen and this will have considerable impact on the survival of these patients [4].

In our patients improvement of the neurological symptoms was seen although in three of the treated patients cytology still showed malignant cells. The length of the survival varied from 11 to 41 weeks after the start of HDE. Compared to other studies this is rather long [4].

It is conceivable that HDE penetrates the BBB sufficiently to establish the clinical effects just described [5]. Furthermore, the BBB may be considerably disturbed in the setting of extensive metastatic disease of the CNS. This is supported by the observed responses of brain metastases of SCLC in patients treated with standard dose combination chemotherapy [6].

A third possible factor might be the lipophilic character of etoposide in combination with the temporary disruption of the BBB by the solvent of etoposide [7].

These case reports demonstrate that HDE is an effective treatment for palliation of patients with MC of SCLC. Since HDE gives grade 3–4 myelotoxicity [3] it is necessary to study whether standard doses of etoposide will be sufficient to give the same effect.

Table 1. Patient characteristics and therapy

	Patient 1	2	3	4	5
Age	69	63	60	69	58
Previous therapy	12 CDE	12 CDE	5 CDE	6 CDE	–
Previous brain metastases	+	+	+	–	–
Cranial irradiation (10 × 3 Gy)	+	+	+	+*	–
Symptoms					
back pain	+	+	+	+	+
pareses arm and/or leg	–	+	+	+	–
urinary retention	–	–	+	+	+
Time MC after cranial irradiation (months)	3	2	1	8	–
CSF cytology before HDE	+	+	+	–	+
after 1× HDE	–	+	+	–	+
Clinical improvement† after HDE	+++	+++	+	++	+++
No. cycles HDE	4	8	3	3	6
Survival from start HDE (weeks)	22	41	11	33	27

*Prophylactic cranial irradiation.
†+++ = neurological symptomatology cleared completely; ++ = clear improvement but still some neurological symptoms present; + = some improvement of neurological symptoms.

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