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A case of carcinomatous meningitis despite prophylactic cranial irradiation in small cell lung cancer during treatment with amrubicin

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Abstract. A 47-year-old man was diagnosed with limited-disease small cell lung cancer. Treatment was initiated with concurrent chemotherapy and radiotherapy. A partial response was achieved, and prophylactic cranial irradiation (PCI) was administered. Local recurrence was identified on follow-up and treated with amrubicin (AMR). After two courses of AMR, a state of stable disease was achieved and AMR treatment was continued. After the third course of AMR, the patient was urgently hospitalized suffering from a headache and disturbance of consciousness, and a diagnosis of carcinomatous meningitis was made. This case report concerns a case of carcinomatous meningitis despite PCI during treatment with AMR.

Introduction

Patients with small cell lung cancer (SCLC) are surviving for longer with the aid of more effective contemporary anticancer treatments (1,2). For this reason, metastases of the central nervous system (CNS) are becoming increasingly common. Prophylactic cranial irradiation (PCI) significantly reduces the rate of brain metastases and improves survival in both limited disease (LD)- and extensive disease (ED)-SCLC patients who respond to first-line treatment, and should therefore be part of the standard treatment for responders with both disease types (4,5). Carcinomatous meningitis is clinically less common than brain metastasis, but has a poor outcome in terms of both quality of life and overall survival (6). We report a case of carcinomatous meningitis despite PCI during treatment with amrubicin (AMR).

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Case report

A 47-year-old man was admitted to our hospital with a cough and hoarseness in September 2009. Chest roentgenography and computed tomography (CT) revealed a tumor in the right upper lobe extending to the mediastinum, from which CT-guided biopsy identified SCLC. No metastases were detected in any other organs and thus a diagnosis of LD was made. Treatment was initiated with 4 courses of carboplatin (CBDCA; AUC 6 on day 1) and etoposide (VP-16, 100 mg/m^2 on days 1-3) with 54 Gy of concurrent radiotherapy, achieving partial response (PR). Levels of the tumor marker pro-gastrin-releasing peptide (ProGRP) decreased to within the normal range following chemoradiotherapy. We then administered 25 Gy of PCI in January 2010. In October 2010, enlargement of the mediastinal lymph nodes was detected on the chest CT. This was considered to represent sensitive relapse; thus, retreatment with 4 courses of CBDCA and VP-16 was performed, and again PR was achieved.

In July 2011, enlargement of the mediastinal lymph nodes was detected on chest CT. As AMR has recently been shown to exhibit significant activity against SCLC as a second-line treatment, with predictable and manageable toxicities (2), we used AMR (40 mg/m^2 on days 1-3) as a second-line treatment. After two courses of AMR, chest CT revealed stable disease. Follow-up of brain metastasis with magnetic resonance imaging (MRI) revealed no significant lesions on August 16 (Fig. 1A), therefore the administration of the third course was commenced on September 21.

On October 3, the patient was urgently hospitalized suffering from a headache and disturbance of consciousness with neck stiffness. As blood testing revealed grade 3 neutropenia, yet ProGRP remained within the normal range, we first suspected septic meningitis. Cytological examination of the cerebrospinal fluid revealed SCLC cells, and abnormal leptomeningeal enhancement (cerebral cortex, cerebral ventricles and cerebellum) was detected on gadolinium-enhanced MRI (Fig. 1B). Carcinomatous meningitis without

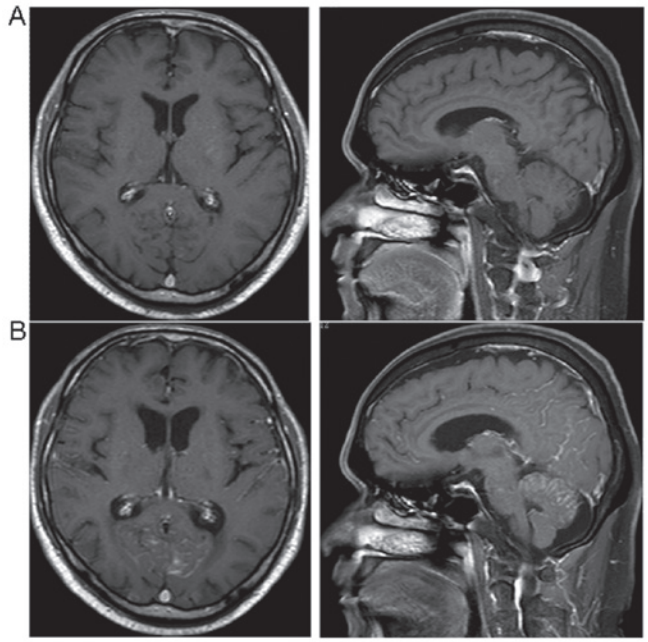

Figure 1. T1-weighted MRI of the brain with gadolinium enhancement. (A) August 16, 2011. (B) October 3, 2011, showing signal hyperintensity in the leptomeninges.

brain metastasis was therefore diagnosed. As the symptoms progressed rapidly, supportive care was selected. The patient succumbed 3 weeks after the diagnosis of carcinomatous meningitis.

Discussion

Despite the development of systemic treatment, the majority of patients with SCLC relapse, and CNS is a frequent site of relapse. Approximately 10% of patients with SCLC initially present with brain metastases. The 2-year cumulative risk rises to ≥50% (6). As a result, the role of PCI has been studied in several trials. A published meta-analysis of PCI for SCLC in patients with complete remission following chemotherapy analyzed data from 7 randomized studies (3). The relative risk of mortality in the treatment group was significantly lower than that in the control group. PCI also decreased the cumulative incidence of brain metastases. Furthermore, ED-SCLC patients with response to first-line chemotherapy in the irradiation group exhibited a lower risk of symptomatic brain metastases and an increase in median survival from 5.4 to 6.7 months (4). These results suggest that PCI reduces the incidence of symptomatic brain metastases and prolongs survival in SCLC patients. However, whether PCI reduces the incidence of carcinomatous meningitis remains unclear. In many cases of SCLC, carcinomatous meningitis develops with brain metastasis (5). Further study is required to clarify whether SCLC cases demonstrating carcinomatous meningitis without brain metastasis also show an increased frequency of relapse involving the CNS following PCI.

Due to the lack of randomized studies, in particular studies referring to one specific primary tumor, no standard treatment for carcinomatous meningitis can yet be recommended. However, it is clear that treatment provides effective palliation and in certain cases achieves longer survival (7). Intrathecal chemotherapy may be administered either by lumbar puncture or intraventricularly through an Ommaya reservoir. Radiotherapy is also used in the treatment of carcinomatous meningitis for palliation of symptoms (8). Since our patient received 25 Gy of PCI as the standard dose for SCLC (9), the addition of sufficient whole-brain irradiation was difficult. In addition, the rapid progression of symptoms meant that our patient was unable to receive intrathecal chemotherapy.

This case demonstrated the difficulty of treating carcinomatous meningitis, particularly in treatment following PCI for SCLC.

References

1. Noda K, Nishiwaki Y, Kawahara M, *et al*: Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer. N Engl J Med 346: 85-91, 2002.
2. Onoda S, Masuda N, Seto T, *et al*: Phase II trial of amrubicin for treatment of refractory or relapsed small-cell lung cancer: Thoracic Oncology Research Group Study 0301. J Clin Oncol 24: 5448-5453, 2006.
3. Aupérin A, Arriagada R, Pignon JP, *et al*: Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. N Engl J Med 341: 476-484, 1999.
4. Slotman B, Faivre-Finn C, Kramer G, *et al*: Prophylactic cranial irradiation in extensive small-cell lung cancer. N Engl J Med 357: 664-672, 2007.
5. Sculier JP, Feld R, Evans WK, *et al*: Neurologic disorders in patients with small cell lung cancer. Cancer 60: 2275-2283, 1987.
6. Komaki R, Cox JD and Whitson W: Risk of brain metastases from small-cell carcinoma of the lung related to the length of survival and prophylactic irradiation. Cancer Treat Rep 65: 811-814, 1981.
7. Strady C, Ricciarelli A, Nasca S, *et al*: Carcinomatous meningitis and solid tumours. Oncol Rep 7: 203-207, 2000.
8. Chamberlain MC: Neoplastic meningitis. Oncologist 13: 967-977, 2008.
9. Le Péchoux C, Dunant A, Senan S, *et al*: Standard-dose versus higher-dose prophylactic cranial irradiation (PCI) in patients with limited-stage small-cell lung cancer in complete remission after chemotherapy and thoracic radiotherapy (PCI 99-01, EORTC 22003-08004, RTOG 0212, and IFCT 99-01): a randomised clinical trial. Lancet Oncol 10: 467-474, 2009.