

Case Reports

Triplet Chemotherapy for Malignant Pericardial Mesothelioma: A Case Report

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Malignant pericardial mesothelioma (MPM) is a relatively rare neoplasm in Japan, and no standard treatment regimens have been established for this disease. A 47-year-old woman with MPM presenting with cardiac tamponade was treated using four cycles of chemotherapy consisting of cisplatin (CDDP) 40 mg/m², gemcitabine (GEM) 800 mg/m² and vinorelbine (VNR) 20 mg/m² on days 1 and 8 every 4 weeks after pericardial drainage alone. The diagnosis of MPM was confirmed by an immunohistochemical procedure using either positive or negative markers of malignant mesothelioma in addition to conventional cytological examinations using pericardial effusion. The patient experienced no severe non-hematological or hematological toxicities except for grade 3 neutropenia. The patient has returned to her usual activities and has remained well for 24 months after the last chemotherapy without any evidence of disease progression.

Key words: malignant pericardial mesothelioma – triplet chemotherapy – long-term survival

INTRODUCTION

Malignant mesothelioma is a relatively rare neoplasm in Japan. The number of deaths and the proportional mortality rate from this disease in 2001 were 722 and 0.26%, respectively (1). Overall, malignant mesothelioma of the pericardium accounted for ~6% of all mesotheliomas in a large study of registered autopsy cases in Japan (2). No satisfactory treatment is available, because malignant pericardial mesothelioma (MPM) tends to be diagnosed at a late presentation. As a result, the prognosis is poor. We previously reported that combination chemotherapy consisting of cisplatin (CDDP), gemcitabine (GEM) and vinorelbine (VNR) was effective for the treatment of malignant pleural mesothelioma (3). We herein report on a patient with MPM in whom triplet chemotherapy was found to result in long-term survival without any evidence of disease progression.

CASE REPORT

A 47-year-old woman, complaining of breathlessness on effort and of systemic edema, was admitted to our department.

The patient was found to have a cardiac enlargement on chest X-ray and computed tomography (CT). The patient had no history of exposure to asbestos. A cytological examination of pericardial effusion revealed the findings typical of malignant mesothelioma. The malignant mesothelial cells proliferated mainly in a papillary pattern, as shown in Fig. 1A. In addition, immunohistochemical studies were performed using antibodies to CEA (prediluted, Nichirei), MOC-31 (1:50, DAKO), BerEP4 (1:100, DAKO), calretinin (1:50, Zymed), D2-40 (prediluted, Nichirei), HBME-1 (1:50, DAKO), thrombomodulin (1:50, DAKO), EMA (1:100, DAKO), CK 7 (1:100, DAKO) and CK 20 (1:25, DAKO) (4). Malignant cells stained in this case for four mesothelioma markers, namely calretinin (Fig. 1B), D2-40, HBME-1 and thrombomodulin, and other markers of EMA and CK 7. However, three adenocarcinomatous markers, namely CEA, MOC-31 (Fig. 1C) and BerEP4, and other markers of CK 20 were negative. The patient was diagnosed to have malignant mesothelioma originating from the pericardium because of the absence of effusion or any lesions in the bilateral pleural spaces. The clinical stage at diagnosis was T1N0M0, stage I according to the International Mesothelioma Interest Group (IMIG) staging system (5). After treating the cardiac tamponade by pericardial drainage, the patient received four cycles of chemotherapy consisting of CDDP 40 mg/m², GEM 800 mg/m² and VNR 20 mg/m²

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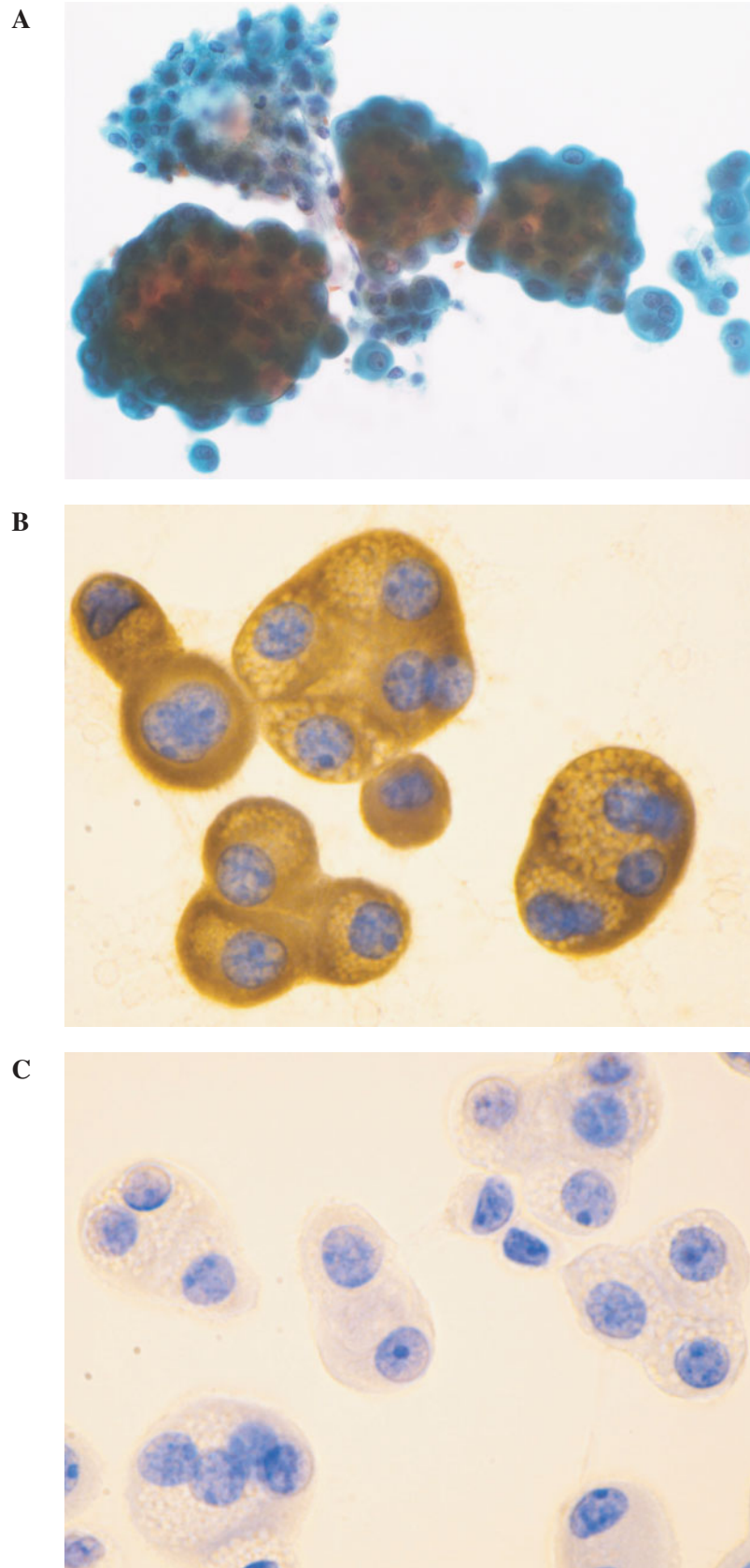


Figure 1. (A) A cytological examination of the pericardial effusion indicating the typical findings of malignant mesothelioma. (B) Immunohistochemistry using calretinin as a mesothelioma marker. Calretinin was expressed in malignant cells. (C) Immunohistochemistry using MOC-31 as an adenocarcinomatous marker. Malignant cells did not stain for MOC-31.

on days 1 and 8 every 4 weeks according to the treatment schedule described in a previous report (3). During the four cycles of chemotherapy, the patient did not experience any severe non-hematological or hematological toxicities, except grade 3 neutropenia. The patient has since returned to her usual activities and has remained well for 24 months after the last chemotherapy without any evidence of disease progression.

DISCUSSION

The onset of symptoms of MPM is usually insidious. The most common clinical manifestations of MPM are constrictive pericarditis, pericardial effusion, cardiac tamponade, and heart failure caused by myocardial infiltration. No satisfactory treatment has yet been established because MPM is commonly diagnosed at a very late stage. Fortunately, this case was diagnosed at an early stage while demonstrating cardiac tamponade due to pericardial effusion, and using a cytological and immunohistochemical examination of such effusion. Malignant cells stained in this case for four mesothelioma markers, namely calretinin, D2-40, HBME-1 and thrombomodulin, and not for three adenocarcinomatous markers, namely CEA, MOC-31 and BerEP4 (4). For distinguishing malignant mesothelioma from adenocarcinoma of the lung it is very useful to perform the immunohistochemical procedure using these markers in addition to conventional cytological examinations using the effusion.

Occupational asbestos exposure has been reported, and in a prospective study was found to be definite in 3 out of 15 cases (20%) and possible in 4 out of 15 cases (27%). In further support of this association, asbestos bodies have occasionally been identified within MPM. Treatment is usually purely palliative, and 50–60% of patients die within 6 months. The prognosis of MPM appears to be clearly worse than that of pleural or peritoneal mesotheliomas (6). Although no standard treatment has yet been established, surgery, radiotherapy, chemotherapy or the combination therapies are most frequently used in practice, and the average survival of the 140 cases reviewed by Kaul et al. was 10 months regardless of the treatment. The 2-year survival rate of the surgically treated cases, which we calculated from the literature in their review, was 14% (7). As a result, no optimal surgical therapy has yet been established regarding the extent of a pericardial resection. In addition, radiotherapy with a curative intent cannot be delivered to control the local disease, because the side effects of such radiation tend to cause primarily pericarditis or myocarditis. There is also no standard chemotherapy regimen. However, one report did describe the use of cyclical combination chemotherapy with doxorubicin, vincristine and cyclophosphamide as resulting in a 1-year event-free survival (8). We herein report, for the first time, that the triplet chemotherapy consisting of CDDP, GEM and VNR was effective for MPM. Objective response rates of 16–48% and median survivals of 9.6–11.2 months have

been reported with the combination of CDDP and GEM in malignant mesothelioma (9–11). Recently, an objective response rate of 24% has been reported with the single agent of VNR in a single institution study (12). We have previously reported that triplet chemotherapy consisting of CDDP, GEM and VNR is feasible and effective for the treatment of malignant pleural mesothelioma. This regimen produced a 58% objective response rate in patients with malignant pleural mesothelioma (3). Therefore, this triplet chemotherapy seems to have potential anti-tumor activity against MPM. Recently, antifolate-based doublet chemotherapy consisting of pemetrexed and CDDP has demonstrated a high efficacy in the treatment of malignant pleural mesothelioma (13). The same regimen may be applied for the treatment of MPM. A phase I/II trial using this doublet regimen is now under way in Japan; therefore, the effectiveness and toxicity for Japanese patients is still uncertain.

In conclusion, CDDP–GEM–VNR combination chemotherapy may also be effective in patients with MPM.

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