Advanced epithelioid pleural mesothelioma, long lasting disease stabilization and long term survival with cisplatin-pemetrexed chemotherapy re-challenge: a case report

C. Cirino, E. Veltri

UOC Oncologia Centro Oncologico G. Porfiri Ospedale Santa Maria Goretti, Latina, Italia

Abstract

In this paper we report the case of a seventy-year old man affected by epithelioid malignant mesothelioma with prolonged disease control after chemotherapy with cisplatin pemetrexed, followed by single drug chemotherapy with pemetrexed. Clin Ter 2016; 167(1):10-12. doi: 10.7417/CT.2016.1908

Key words: mesothelioma, cisplatin, pemetrexed, pleural effusion, PET scan, CT scan, survival

Introduction

Malignant mesothelioma (MM) is a rare and rapidly fatal tumour closely related to inhalation of asbestos fibres. The incidence of mesothelioma in people exposed to asbestos is 300 times higher than in the general population. It arises from the serous membranes of the pleura and, less frequently, from the peritoneal and pericardial cavities and the tunica vaginalis testis. Many western countries are currently suffering an MM epidemic, reflecting the widespread use of asbestos between the 1950’s and 80’s in many industrial applications. Mesothelioma is recognized as an occupational disease. Median overall survival is approximately 1 year. MPM occurs mainly in older men (median age 72 years) who have been exposed to asbestos. The time between exposure and diagnosis of MPM often exceeds several decades.

Diagnostic imaging includes CT, MRI and PET. The best method for a final diagnosis seems to be videothoracoscopy (1).

In cases where is not possible to perform a macroscopic complete resection (T4: multifocal masses, extension to peritoneal contralateral pleura or pericardium, N3: contralateral mediastinal lymph nodes, M1: distant metastases) 1 malignant pleural mesothelioma generally has an unfavourable prognosis, due to the poor sensitivity to chemotherapy and radiotherapy treatments. Treatment of advanced diseases relies primarily on chemotherapy with a combination of platinum and pemetrexed (2, 3) until the results of ongoing clinical trials provide information that may change our practice (association with bevacizumab, new targeted therapies or immunotherapy). Drugs to be used in second line are not well-defined: rechallenge with the initial combination in case of response, or vinorelbine, or inclusion in clinical trials. Response to rechallenge appears to be correlated with response to first line pemetrexed-based chemotherapy (4).

Case report

The clinical history of the discussed 70 yr old male patient started in August 2008 with the appearance of an exercise-induced grade 2 NYHA dyspnea. Because of the persistence of such symptom the patient was admitted to the medicine ward of our hospital. A CT scan showed a pleural effusion and mediastinal shift while the cytologic examination of pleural fluid was negative for neoplastic cells the discharge diagnosis was exudative pleuritis. The patient, who had been exposed to asbestos over the years, was referred to our service in January 2009, after a brief hospitalization in another institution where he had undergone a biopsy of the parietal pleura and talc pleurodesis for recurrent pleural effusion. The histological examination of biopsy specimens had highlighted a malignant epithelioid mesothelioma (Fig. 1) with the following immunohistochemical features: EMA negative, TTF-1 negative, CEA negative (Fig. 2), Calretinine positivity (Fig. 3), pancitokeratin negative, citokeratin 5/6 negative. The cytological examination of pleural fluid had shown the presence of numerous mesothelial cells, atypical and with a papillary arrangement.

The basal total body CT scan showed pleural effusion with mediastinal shift and extensive thickening of the parietal pleura, an inch deep, at the level of the phrenic cost. In February 2009 the patient started chemotherapy with cisplatin 75 mg/m² - pemetrexed 500 mg/m² both on day 1 q 21 and the revaluation with total body CT scan performed six months later, showed a marked reduction (>50%) of the
pleural effusion and the complete disappearance of pleural thickening. The patient was followed-up from January to May 2010. CT and PET examinations in January and May showed a stable pleural effusion. In September 2010, a CT scan highlighted the disease progression with a marked increase of pleural effusion and pleural scissural thickening. For this reason, a new thoracentesis was performed, which confirmed the diagnosis of epithelioid mesothelioma. Considering the significant progression free interval, the low toxicity and the poor patient’s compliance to perform a two-drug chemotherapy with cisplatin, it was decided to start chemotherapy again with single agent pemetrexed 500 mg/m² on day 1 q 212. After three cycles of treatment the total body CT scan evidenced stationarity of pleural effusion, therefore the treatment was continued, at the same dosage, for further three cycles until April. The follow-up control carried out in July and in September 2011 showed stationarity of the pleural effusion (maximum thickness 3.5 cm). The patient remained asymptomatic until January 2012 when, following the reappearance of exercise-induced grade 2 NYHA dyspnea and cough a CT scan was performed again. The latter showed an increase in the thickness of the pleural effusion - 8.7 cm- compared to 3.5 cm of the previous CT. The patient accepted to prosecute the treatment with the two different medications cisplatin and pemetrexed. From February 2012 to August 2012 six cycles of chemotherapy were administered, the first to 100% of the maximum dosage, the following cycles to the 75% because of the thrombocytopenia G2-G3 of the previous cycle. At the end of chemotherapy, the patient returned to be asymptomatic, with no cough and no dyspnea. The TC revaluation performed in August 2012 (Fig 4) showed the stationarity of the pleural effusion (7 cm), PET scan (Fig 5) highlighted complete metabolic response. In December 2012 a new CT and PET scan revealed progressive disease with multiple pleural metastases.
less than 1.5 cm maximum diameter with a PET SUV of 9.2. From January 2013 to May 2013 six cycles of Pemetrexed 500 mg/m² were administered. The CT (Fig 6) and PET scan performed on September 2013 revealed stable disease and the absence of pleural effusion. Nine months later a new CT scan revealed pleural effusion maximum diameter 4 cm. From July 2014 to March 2015 nine cycles of pemetrexed 500 mg/m² were administered, the last three with a 25% of dose reduction due to G2 thrombocitopenia. The CT scan performed in April 2015 revealed progressive disease again, for this reason it was given third-line chemotherapy with vinorelbine 25 mg/ m² day 1,8 q21 for 8 cycles until October 2015 when a CT scan revealed progressive disease with multiple pleural masses in right emithorax maximum diameter 43 mm and massive pleural effusion. Because of the good performance status of the patient (ECOG 1), since November 2015 it was given fourth line chemotherapy with gemcitabine 1000 mg/ m² on days 1,8 q 21 which is still ongoing at the time of the report.

Discussion

Long lasting survival and disease stability of malignant mesothelioma with chemotherapy alone is an event rarely described in literature; few cases of long-surviving patients are usually obtained with multi-modal treatments, combining surgery and chemotherapy5,6. In our case we obtained the patient’s survival of more than seven years, together with an optimal control of symptoms at the date of the report.

Aknowlegments

Italian-English translation by Prof. Gina Reale

References