Onur TURAN¹
Ahu YALABIK²
Emine OSMA³
Aydanan KARGI⁴
Atila AKKOÇLU¹

MALIGN MEZOTELYOMA TANILI YAŞLI BİR HASTADA PEMETREKSET TEDAVİSİ İLE DRAMATİK TÜMÖR YANITI

ÖZ

Anahtar Sözcükler: Mezotelyoma/iłaç tedavisi; Pemetrexed; Cisplatin; Yaşlı; Tedavi çıktısı.
INTRODUCTION

Malignant mesothelioma is a rare and highly aggressive kind of tumor with a poor prognosis which primarily arises from the surface serosal cells of the pleural, peritoneal, and pericardial cavities (1). The most important risk factor for mesothelioma is known to be asbestos exposure (2). Characteristic thoracic computed tomography (TCT) findings are pulmonary nodules, pleural plaques, thickening, masses and lymphadenopathy; however the definitive diagnosis of mesothelioma requires histopathological evidence obtained from biopsy samples.

Currently, there is no gold standard treatment for mesothelioma, the treatment options being surgery, chemotherapy and radiotherapy. Surgical resection is possible only in a minority of patients and approximately 15% of them live beyond 5 years (3,4). Radiotherapy has limited benefits in decreasing the tumour volume, and is also toxic to the surrounding normal tissue (5). However, chemotherapy may improve the symptoms and may decrease the size of the tumour. Various chemotherapy regimens (either as a single agent or in combination) are used for treatment of malignant mesothelioma and although they are not curative, they may prolong survival in selected patients (6).

Effectiveness of chemotherapy with single agents is limited (7,8). Although response rates up to 48% (9,10) were observed with combination chemotherapy regimens, neither single agents nor combination chemotherapy regimens were shown to improve survival. In addition, the toxicity profile of chemotherapeutic agents may be a major problem especially in older patients, and may increase mortality and morbidity.

Pemetrexed disodium (Alimta), a multi-targeted antime- tabolite agent inhibiting the folate pathway, has demonstrated promising clinical activity in a wide variety of solid tumors. In recent years, pemetrexed disodium is being used for chemotherapy treatment in unresectable malignant pleural mesothelioma.

We present a case with a perfect response to pemetrexed disodium chemotherapy showing that pemetrexed may be an effective chemotherapeutic agent in malignant mesothelioma treatment.

CASE PRESENTATION

A 81-year old female patient was admitted to our hospital because of cough and dyspnea. She was a housewife and she had a history of direct exposure to asbestos. She had a smoking history of 5 packs a year. She had no medical history of comorbid diseases or operations.

Posterior-anterior chest X-ray revealed a right-sided pleural effusion with loss of volume and possible pleural thickening (Figure 1A). A massive unilateral pleural effusion and multiple pleural nodules were determined by a TCT (Figure 1B). Pleural effusion aspirated by thorascopy contained mostly lymphocytes, and was not diagnostic. A pleural biopsy
was performed by video-assisted thoracoscopic surgery for diagnosis. Histopathological analysis showed malignant neoplasms with a tumour lesion with irregular tubuloglandular structures, irregular solid areas settled in desmoplastic stroma, and cells with nuclear pleomorphism and atypical mitosis. Immunohistochemical analysis revealed positive staining of tumour cells for D-PAS, vimentin and calretinin; and was negative for carcinoembryonic antigen (CEA), transcription termination factor (TTF-1) and mucicarmin.

The patient was diagnosed with malignant epithelial mesothelioma using this histopathological analysis and we decided to apply radiotherapy for her primary tumour considering her age, as chemotherapy could be more toxic for elderly patients. After radiotherapy, she was followed up without any symptoms for 18 months until she had a new complaint of effort dyspnea. In the new TCT, there were multiple pleural nodules, massive pleural effusion in the right hemithorax, mediastinal lymph nodes with pathological sizes and a subcutaneous mass localized at the previous biopsy region; which was interpreted as progression of the primary tumour (Figure 2A,B). We decided to apply chemotherapy containing pemetrexed (Alimta) and cisplatin. After the first two cycles, a clinical improvement was observed and chemotherapy was well tolerated without any toxicity, therefore four cycles were completed. Following the last cycle, the patient was evaluated with a TCT which showed that her subcutaneous mass had disappeared and her mediastinal lymph nodes and pleural nodules had dramatically regressed (Figure 3A,B). Also, she had no complaints in this period, with an increase in her Karnofsky Performance Status.

**CONCLUSION**

Malignant pleural mesothelioma (MPM) is a disease with a poor prognosis and limited response to chemotherapy (7,8). The survival time without any treatment is approximately 4-12 months (11), therefore, a number of treatment options may be tried to extend it. Although most cytotoxic agents have been evaluated for treatment of mesothelioma, response rates observed were above 20% with only a few single agents (12). In general, chemotherapy regimens (single agent/combination) are not curative but they may prolong survival in selected patients (6).

A few chemotherapeutic agents have been used for treatment of mesothelioma. Antimetabolites, like metotrexate, are known to be the most active drugs against mesothelioma; and one of the most effective members of this group is antifolate drugs (12). Pemetrexed (Alimta) is a multitargeted and newer antifolate drug and has been used both as a single agent and as a part of a combination regimen with a tolerable toxicity profile and high activity in a variety of solid tumours, including MPM (13,14). In addition, it is considered as a favorab-
le treatment option in exclusively selected elderly patients and in patients unfit for a platinum based chemotherapy (15).

Pemetrexed cisplatin combination was shown to prolong survival significantly when compared to cisplatin alone and the combination was also found to be superior in terms of quality of life, response rates, pulmonary functions and clinical benefit (12,13,16). In an analysis of 456 patients randomized to combination therapy or single-agent cisplatin, median survival times were found to be 12.1 and 9.3 months, and the response rates were found to be 41.3% and 16.7% respectively (1). As the most common adverse events like dehydratation, nausea and vomiting were clinically manageable and tolerable, pemetrexed was considered to have a good safety profile (15). Vogelzang et al. recommended that pemetrexed-cisplatin combination should be regarded as the standard therapy for the first-line treatment of MPM (17).

Age is generally considered as a risk factor for increased toxicity and poor tolerance to chemotherapy. An age-dependent increase in toxicity due to chemotherapy was observed in elderly cancer patients (18), however, pemetrexed was demonstrated to be a good alternative in this age group. Kulkarni et al. found similar response rates in older and younger patients with pemetrexed therapy, as a single-agent or in combination and pemetrexed was also well tolerated in the elderly population (19).

Pemetrexed (Alimta) seems to be a useful treatment option with a good efficacy and a favourable toxicity profile in malign mesothelioma, however further studies with larger samples are required to confirm this result. Due to observation of a dramatrical tumour response to pemetrexed-cisplatin combination in our case, we would like to affirm that pemetrexed should be considered as an effective chemotherapeutic agent in MPM, even in elderly patients.

REFERENCES


