Journal of BUON **14:** 123-125, 2009

Malignant pleural mesothelioma with brain metastasis

P. Hurmuz[1], F. Zorlu[1], C. Cansiz[2], S. Emri[3]

[1]Hacettepe University, Faculty of Medicine, Department of Radiation Oncology, Ankara; [2]Ankara University, Faculty of Medicine, Department of Pathology, Ankara; [3]Hacettepe University, Faculty of Medicine, Department of Chest Diseases, Ankara, Turkey

Summary

Malignant pleural mesothelioma (MPM) is a rare neoplasm associated with poor prognosis. Local disease progression is the major cause of death rather than distant metastasis. Intracranial metastases are seen very rarely. Herein, we report a case of MPM with brain metastasis treated with cranial irradiation.

Key words: brain metastasis, malignant pleural mesothelioma

Introduction

MPM is an uncommon neoplasm associated with poor prognosis. Without treatment, median survival is 4-12 months [1]. The majority of patients, treated or untreated, die of complications of local disease rather than distant metastasis. Distant metastases are uncommon with mostly involved organs being the liver, adrenal gland, kidney, and contralateral lung [2]. Intracranial metastases are seen very rarely (< 3%) and are predominantly of sarcomatous type [3]. Herein, we report a case of MPM with brain metastasis treated with cranial irradiation.

Case presentation

A 56-year-old female patient who had had a history of household exposure to asbestos for 28 years and smoked one pack of cigarettes per day for 25 years applied to the hospital in July 2006 complaining of dry cough and left chest pain. Chest radiographs and CT of the chest showed left pleural thickening and pleural effusion with no lymph node involvement. Bronchoscopy was normal. Pleural cytology and biopsy were suspicious for MPM. Subsequently, she underwent video-assisted thoracoscopic surgery (VATS) and biopsy was taken. On immunohistochemical analysis, the tumor was TTF-1, MOC-31, and CEA-negative and calretinin, mesothelin, cytokeratin 5/6 and WT-1-positive, confirming the diagnosis of MPM. The diagnostic work up showed disease limited to the left hemithorax. Extrapleural pneumonectomy was suggested to the patient but she refused the operation. She then received 6 courses of cisplatin (75 mg/m^2), and pemetrexed (500 mg/m^2) at 3-week intervals. Although after 4 cycles of chemotherapy chest CT showed stable disease, at the end of the 6th cycle there was progression of the pleural thickening along with newly appearing mediastinal lymphadenopathy. The pleural mass displayed mediastinal and abdominal invasion.

A month later, the patient developed headache, dizziness and slurred speech. Neurological examination demonstrated ataxia, right dysmetria and dysdiadochokinesia. Cranial MRI revealed multiple lesions located in brain (Figure 1). Radiologically they were consistent with the metastases of mesothelioma. The neurosurgery department evaluated the patient and didn't suggest surgical intervention. So the patient was referred to Radiation Oncology department and was put on steroids and palliative radiation therapy, receiving

Correspondence to: Pervin Hurmuz, MD. Hacettepe University, Faculty of Medicine, Department of Radiation Oncology, 06100 Sihhiye, Ankara, Turkey. Tel: +90 312 305 2900, Fax: +90 312 309 2914, E-mail: phurmuz@hotmail.com, phurmuz@yahoo.com

Received 07-04-2008; Accepted 26-05-2008

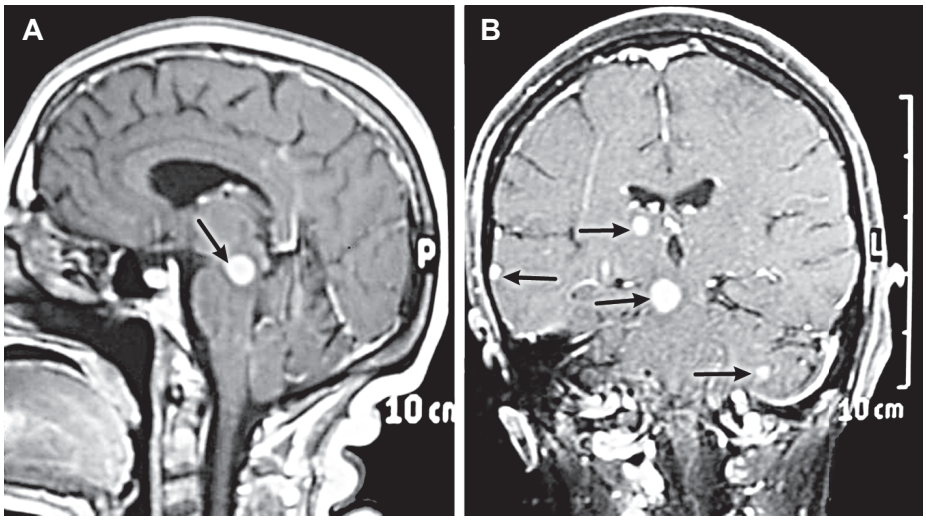

Figure 1. Sagittal (**A**) and coronal (**B**) sections of cranial MRI showing multiple brain lesions (arrows).

3 Gy/day to a total dose of 30 Gy to the whole brain. The patient tolerated the treatment well without any toxicity. Unfortunately, she died one month after the radiation therapy due to respiratory failure that didn't respond to the supportive treatment given.

Discussion

MPM is a highly lethal disease with median survival time of 4-12 months. The annual incidence in the United States is estimated at 2200 cases per year and in England 2700-3000 deaths per year from MPM are expected in 2020 [4]. After that the rates are likely to drop in the developed countries due to legislation to reduce asbestos exposure but the incidence rates are predicted to increase in the non-developed countries due to lack of these regulations.

Though 54-82% of patients had extrathoracic metastasis in an autopsy series, they usually die from local disease complications rather than distant metastasis [2]. Intracranial metastases are seen very rarely, but the rate may increase due to increase in the number of MPM cases and the use of multimodality approaches that improve survival.

No single treatment modality alone seems to be effective in dealing with the disease, while pemetrexed and cisplatin combination chemotherapy displayed a 4-month survival advantage over cisplatin alone in unresectable patients [5]. Patients who can go through aggressive multimodal treatment including extrapleural pneumonectomy, radiotherapy and chemotherapy for localized disease have improved survival and local control [6,7]. In a subgroup of patients with epithelioid histology, clean surgical margins and negative lymph nodes, 5-year survival rate of 46% was found [7]. These treatments will change the natural history of the disease and in the future we may come across with more cases with distant metastases, including involvement of the central nervous system.

Previously, the pathological diagnosis of MPM used to be confused with adenocarcinoma of the lung. It is known that adenocarcinoma of the lung is one of the most common tumors that metastasize to the brain. When the patient applied to our department with brain metastases we first thought that the diagnosis might be lung adenocarcinoma. We reviewed the pathological material and found out that the diagnosis was epithelioid type of MPM. Our patient's immunohistochemical analysis of VATS- biopsy confirmed the diagnosis of mesothelioma. Immunohistochemistry has proven valuable in the differentiation of epithelioid mesothelioma from pulmonary or metastatic adenocarcinoma. Calretinin, cytokeratin 5/6 and WT1 are the best positive markers while CEA and MOC-31 are the best negative markers for the diagnosis [4].

Although we didn't have pathological specimen from the brain, the clinical evolution of the condition with progression of the thoracic disease, radiological findings in the brain MRI and the previous immunohistochemistry results support the diagnosis of metastasis of the MPM to the brain.

Our patient refused to have surgery but she was administered chemotherapy that showed to improve survival.

In the literature few cases with symptomatic brain metastases are found while there are cases discovered at autopsy [3,8,9]. On histology they are usually of sarcomatoid or biphasic type, which are known to be associated with frequent hematogenous dissemination.

Our patient had epithelioid type MPM, which is known to be less aggressive.

We conclude that, irrespective of histological type, how localized the tumor is at diagnosis or how efficient agents we have against it, MPM is still a problematic field in the oncology practice. Though it seems that multimodality approaches improve local control and survival, clinicians must be ready to see cases with more distant metastases in the future.

References

1. Sugarbaker DJ, Jaklitsch MT, Liptay MJ. Mesothelioma and radical multimodality therapy: Who benefits? Chest 1995; 107: 345S-350S.
2. Pass HI, Hahn SM, Vogelzang NJ, Carbone M. Benign and malignant mesothelioma. In: De Vita VT Jr, Hellman S, Rosenberg SA (Eds): Cancer: Principles and Practice of Oncology (7th edn). Lippincott, Williams & Wilkins, Philadelphia, 2001, pp 1937-1964.
3. Falconieri G, Grandi G, DiBonito L et al. Intracranial metastases from malignant pleural mesothelioma. Report of three autopsy cases and review of the literature. Arch Pathol Lab Med 1991; 115: 591-595.
4. Sterman DH, Albelda SM. Advances in the diagnosis, evaluation, management of malignant pleural mesothelioma. Respirology 2005; 10: 266-283.
5. Vogelzang NJ, Rusthoven JJ, Symanowski J et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 2003; 21: 2636-2644.
6. Baldini EH, Recht A, Strauss GM et al. Patterns of failure after trimodality therapy for malignant pleural mesothelioma. Ann Thorac Surg 1997; 63: 334-338.
7. Sugarbaker DJ, Flores RM, Jaklitsch MT et al. Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. J Thorac Cardiovasc Surg 1999; 117: 54-65.
8. Huncharek M, Bseiso A, Huctchins L, Warner J. Presentation of malignant pleural mesothelioma with symptomatic brain metastasis: report of a case. Tumori 2004; 90: 424-427.
9. Kitai R, Kabuto M, Kawano H et al. Brain metastasis from malignant mesothelioma-case report. Neurol Med Chir (Tokyo) 1995; 35: 172-174.