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Original research article

Radiotherapy applications of patients with malignant mesothelioma: A single center experience

Muge Akmansu[a], *Ozge Petek Erpolat*[a,*], *Fatih Goksel*[b], *Evrim Tunc*[c], *Can Ozturk*[d]

[a] *Gazi University Medical Faculty, Department of Radiation Oncology, Ankara, Turkey*
[b] *Ankara Diskapi Yildirim Beyazit Educational and Research Hospital, Department of Radiation Oncology, Ankara, Turkey*
[c] *Ataturk Chest Disease and Chest Surgery Research Hospital, Department of Radiation Oncology, Ankara, Turkey*
[d] *Gazi University Medical Faculty, Department of Chest Disease, Ankara, Turkey*

ARTICLE INFO

Article history:
Received 10 January 2012
Received in revised form
21 May 2012
Accepted 19 July 2012

Keywords:
Malignant pleural mesothelioma
Prophylactic radiotherapy
Palliative radiation

ABSTRACT

Background: In the management of malignant pleural mesothelioma, radiotherapy has been used for the purpose of prophylaxis to reduce the incidence of recurrence at surgical insertion sites or palliate the symptoms.
Aim: The purpose of the study was to evaluate the techniques and effectiveness of radiotherapy in malignant pleural mesothelioma.
Materials and methods: Forty-four (18 female, 26 male) patients diagnosed with malignant pleural mesothelioma were retrospectively evaluated. All patients had surgery or thoracoscopic biopsy for diagnosis, staging or treatment and all received palliative or prophylactic radiotherapy. Fifty-seven percent of the patients received chemotherapy.
Results: Prophylactic radiation was applied to 27 patients with 4–15 MeV electron energies. The median radiotherapy dose was 30 Gy with 3 Gy daily fraction dose. During treatment, 12 patients had grade 1 erythema according to the RTOG scale. In 3 (12%) patients, a local failure at treatment field was observed. Palliative radiotherapy was applied to 17 patients for pain palliation. The median radiation dose was 40 Gy with 2 Gy daily fraction dose by using 6–18 MV photon and/or 4–12 MeV electron energies. Two patients had grade 1 erythema and one patient had grade 2 odynophagy according to the RTOG scale. For 10 (59%) patients, palliation of chest pain was delivered. No late toxicity was observed for all cases.
Conclusion: Our experience showed that prophylactic and palliative radiotherapy are effective and safe therapy modalities in malignant pleural mesothelioma in preventing seeding metastasis at intervention sites or relieving pain. Prospective randomized studies are still needed to determine the benefits of radiotherapy application and to indicate optimum dose schemes.

* *Corresponding author at*: Gazi Üniversitesi Tıp Fakültesi Radyasyon Onkolojisi AD, Beşevler, Ankara 06500, Turkey. Tel.: +90 533 348 59 50.
E-mail address: petektater@yahoo.com (O.P. Erpolat).
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http://dx.doi.org/10.1016/j.rpor.2012.07.015

1. Background

Malignant pleural mesothelioma (MPM) is a relatively rare thoracic tumor which is originates from the lining cells of the pleura.[1] The incidence of MPM is expected to increase over the next decade in most industrial countries and in the countries with poor regulations of asbestos mining, production and household use.[2,3] The domestic usage of soil mixed with asbestos causes a major health problem in Turkey, especially in Eastern and South Eastern Anatolia. A mineral other than asbestos named fibrous zeolyte (erionite) is accepted to be one of the most powerful carcinogens and was found in some rocks used in the construction of houses and in the walls of caves used as storerooms in the villages of the Cappadocia region in Turkey.[4] Asbestos and erionite are known factors in the etiology of MPM. Although it varies between series, there is a contact with asbestos in 70–80% of cases.[5–7]

MPM is considered as an aggressive disease with dismal prognosis. Median survival varies between 9 and 17 months.[8,9] Local disease progression is the main cause of death.[10,11] The major problem is poor control of local disease and the dissemination of MPM through the drain sites and tracks of chest wall instrumentation.[10] There is no definite standard of care, only a minority of patients are eligible for curative therapy. Single modality treatment [surgery, radiotherapy (RT) or chemotherapy] have generally failed to significantly improve survival.[12] Multimodality aggressive therapy seems to improve local control and survival, but the benefits of this approach have been questioned because of treatment related morbidity and mortality.[12,13] Although radical surgery has been advocated, most cases cannot be operated due to surgical or medical inoperability.[14] Many single and combined chemotherapeutic agents have been tried and reviews describe modest success with several agents.[15,16] As RT has never been compared to chemotherapy or surgery or best supportive care in prospective randomized trials, there exist no data to support one or the other therapies as a better option.[17]

MPM is tradionally thoght to be radioresistant, however, tumor cells derived from MPM were found to be more sensitive to radiation than non-small cell lung carcinoma.[18] In the management of MPM, RT is used in three ways: as prophylaxis to reduce the incidence of recurrence at sites of diagnosis or therapeutic instrument insertion, or in a multimodal treatment to improve locoregional control after resection of early-stage disease and to palliate symptoms for patients with advanced disease.[7] Mesothelial tumor cells seeding through the instrument tracts after pleural intervention occurs in around 20%, but may be as high as 50%.[19–21] In the presence of seeding metastasis, the lesion can be extremely painful and difficult to palliate with RT,[21] and surgery is the only effective procedure if applicable.[10] For this reason, prophylactic RT to drain sites or incision scars is the main preventing option.[7,21] However, no clear consensus on the benefit of prophylactic RT can be reached, because the trials have conflicting results.[7,12] Moreover, RT has been applied to relieve symptoms associated with MPM. Althogh previous studies had confimed that RT can palliate chest pain in nearly 60% of patients,[22–24] no optimal RT dose and fractionation scheme has been specified from these studies.

2. Aim

Rarity of this disease and few available retrospective and prospective data led us to review our experience. The purpose of this study was to evaluate the tecniques and effectiveness of RT when given on a prophylactic and palliative basis either alone or combined with chemotherapy in MPM patients.

3. Materials and methods

We retrospectively evaluated the files of cases with MPM, treated at Gazi University Faculty of Medicine, Department of Radiation Oncology between 1996 and 2010. The informed consent form was obtained from all patients. Forty-four patients (18 female, 26 male) with a median age of 55 (range 36–84) years at diagnosis were assessed. Dyspnea (87%), chest pain (75%) and cough (65%) were the most common presenting symptoms. All patients' Karnofsky Performance Statuses were $\geq$70. These patients underwent detailed investigations before therapy. Routine blood tests, chest X-ray, chest and abdomen computed tomography, pulmonary function testing, and, more recently, positron emission tomography were performed. The MPM diagnoses were histopathologically proven for all cases. Epitheloid subtype was reported in 38 (86.4%) patients while biphasic subtype in 6 (13.6%) patients. Video-assisted thorascopic surgery (VATS) and pleural biopsy were applied to 9 (20.5%) patients, 9 (20.5%) patients had pleural decortications, 2 (4.5%) patients had thoracotomy and wedge resection, 2 (4.5%) patients had thoracotomy and pleurodesis, 5 (11.4%) patients had biopsy and pleurodesis and 17 (38.6%) patients had only biopsy. Twenty-five (57%) patients received chemotherapy and different drug regimens were used. Most patients received gemcitabin and cisplatin or cisplatin and pemetrexed and remaining patients received different protocols including ifosfamide, epirubicin and adriamicin. Chemotherapy was usually applied in 4–6 cycles. All patients received RT. Six weeks after completion of RT and within 3 months' interval thereafter, patients were followed-up with physical examination, routine blood chemistry, chest X-ray and/or computed tomography. If any suspicious lesions were observed, biopsies were taken for histopathological confirmation. For the evaluation of pain response, patients were revised at 1 month after completion of RT. Evaluation of pain relief (patient reported) or other symptomatic response was based on patient records. Pain was evaluated by using a visual analog scale.

The statistical analysis was performed by using the Statistical Package for Social Sciences software package, version 13 (SPSS Inc., Chicago, IL, USA). Patients and treatment characteristics were described using median, mean, standard deviation and range (minimum–maximum) for continuous variables. The follow-up time was estimated from initial date of RT to date of death or last follow-up. The survival time was estimated from date of the histopathologic diagnosis to date of death or last follow-up. The survival analysis was performed by using the Kaplan–Meier method.