

Malignant mesothelioma presenting with unexplained recurrent pleurisy episodes

UĞUR GÖNLUGUR¹, İBRAHİM AKKURT¹, MELİH KAPTANOĞLU², SEMA ARICI³, TANSELİ EFEÖĞLU¹

Cumhuriyet University Medical School, Departments of ¹Chest Diseases, ²Thoracic Surgery and ³Pathology, Sivas-Turkey

ABSTRACT

Although it can remain stable for prolonged periods, malignant mesothelioma (MM) is an aggressive tumor usually associated with asbestos exposure. Herein we present a case of pleural MM characterized by recurrent exudative pleurisy. A 33-year-old male admitted to our department for four times due to recurrent right pleural effusion within 21 months. His pleurisies were subsided with or without any therapy. At his last admittance a diagnosis of malignant mesothelioma was obtained by open pleura biopsy. After six cycles of chemotherapy, he is still free of any symptoms and no recurrent pleurisy was detected. This is a rare case of malignant mesothelioma showing recurrent pleurisy episodes, and spontaneous regressions without any apparent radiological findings. Pleurisies with effusions may be due to anti-tumor immune response or a predisposing factor for the development of malignant mesothelioma. [Turk J Cancer 2006;36(3):142-145].

KEY WORDS:

Spontaneous regression, malignant mesothelioma, recurrent pleural effusion, recurrent pleurisy

INTRODUCTION

Recurrent exudative pleurisies can be seen in the course of collagen vascular diseases such as Systemic Lupus Erythematosus or Rheumatoid Arthritis, Familial Mediterranean Fever or associated with drugs or asbestos (1-4). Other causes of recurrent pleurisy are recurrent pulmonary emboli, bronchiectasis, tuberculosis, and pneumonia due to bronchial obstruction (5-8). Allergic bronchopulmonary aspergillosis and primary pulmonary lymphoma can rarely cause recurrent exudative effusions (9,10).

Malignant mesothelioma (MM) is a highly aggressive tumor of the serous membranes, which in humans results from exposure to asbestos and asbestiform fibers. Asbestos is an etiological factor both for benign asbestos pleurisy (BAP) and MM. It has been shown that environmental erionite and asbestos exposure exist in our region (11). There are a number of reports of the occurrence of BAP some years before the diagnosis of mesothelioma from our country but it is impossible to say whether this was the first symptom of the tumor or in fact a BAP that happened to occur at the same side as that on which a MM developed later (4). In below presented article, an interesting case of MM showing exacerbations and remissions is described.

CASE REPORT

A 33-year-old male patient admitted to our department with a fifteen days' history of right pleuritic chest pain. He had also cough, exertional dyspnoea, and night sweat. He had a smoking history of 5 pack-years but no alcohol consumption. He was previously healthy and no medication was noted. His physical examination was normal except diminished respiratory sounds at right lower lung fields. The white cell count was $7900/\text{mm}^3$, platelets $515,000/\text{mm}^3$, hemoglobin 14.1 g/dL, erythrocyte sedimentation rate 71 mm/h, SGPT 93 U/L, gamma-glutamyl transpeptidase 93 U/L, HBs Ag positive, and anti-HBs negative. LDH was 387 U/L, total protein was 8.9 g/dL and albumin was 3.6 g/dL. Chest X-ray revealed a homogenous opacity suggestive for pleural effusion. Pleural fluid total protein, albumin, and LDH levels were 6.3 g/dL, 2.8 g/dL, 543 U/L, respectively. Neither pathogen microorganism nor acid-fast bacillus was observed in pleural fluid. There was reactive mesothelial cell hyperplasia in pleural fluid and chronic non-specific pleuritis in closed pleura biopsy. He had not a history of a myocardial infarction or a cardiac operation that suggests Dressler's syndrome. Abdominal ultrasonography was normal but Doppler ultrasonography of lower extremities was positive and pulmonary perfusion scan indicated a segmental defect in superior segment of the right lower lobe. Then the diagnosis of pulmonary emboli was assumed and anticoagulant therapy was started for next six months. No pleural effusion was observed in this period.

One year later, he readmitted because of right-sided pleural effusion. Biochemical analysis was consistent with exudates. Microbiological cultures for aerobic bacilli and *Mycobacterium tuberculosis* were negative in pleural fluid. There was reactive mesothelial cell hyperplasia but not malignant cells in pleural fluid. For ruling out recurrent emboli, pulmonary perfusion scan were performed and D-dimer were investigated. Both of them were normal. Anti-nuclear antibody, anti-DNA, romatoid factor, and cardiolipin antibodies were negative. In this period, both clinic and radiological findings completely regressed within two months with symptomatic (non-steroid anti-inflammatory drugs) therapy. The patient readmitted again after two months. He had recurrent aphtous stomatitis and arthralgias

but Pathergy test was negative. Microbiological and pathological analysis of pleural fluid and biopsy specimen showed no specific etiology. His eye examination and pulmonary angiography were normal. Tuberculin test was 20 mm (positive). Chest CT-scan demonstrated that pleural effusion repeated but two weeks later, it disappeared spontaneously. Despite of negativity of microbiological cultures antituberculous therapy was started. When exudative pleurisy recurred five months later, an exploratory thoracotomy was performed and multiple biopsies were taken from mediastinal, diaphragmatic, and thoracic pleura. There were calcific plaques in parietal pleura. Histopathologic examinations showed epithelial-type malignant mesothelioma (Figure 1). The tissue demonstrated malignant cells with large pleomorphic nuclei exhibiting very prominent nucleoli with abundant eosinophilic cytoplasm. Immunohistochemistry showed staining for high molecular weight cytokeratin, thrombomodulin but not calretinin. There were dense lymphoplasmocytary infiltrations in tumor stroma. Six cycles of postoperative chemotherapy consisting of cisplatin ($75 \text{ mg}/\text{m}^2$) and mitomycin C ($10 \text{ mg}/\text{m}^2$) were administered, and we have never seen a recurrence during the last eight months.

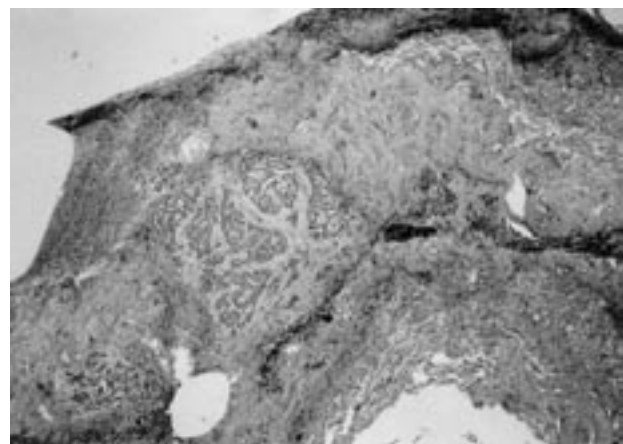


Fig 1. Pleural tissue showing malignant cells with large pleomorphic nuclei

DISCUSSION

MM presents infrequently periodical diseases such as recurrent laryngeal nerve paralysis, recurrent pneumothorax or recurrent pleurisy as in our patient (12,13). This periodicity indicates a dynamic competition between host and tumor for the appearance/disappearance of the disease. Current concepts of MM biology suggest that the tumor is, to some extent, immunogenic and in patients with MM, clinical trials utilising immunomodulatory agents have shown evidence of response in a proportion of patients (14). The presence of lymphoplasmocytary infiltrates in tumor stroma suggests that an immunologic mechanism may be responsible for spontaneous regressions in our patient. The accumulation of exudative effusions is probably due to this inflammatory response. When tumor-associated antigens are eliminated by inflammatory response, the effusion may regress spontaneously. However, the expression of a new antigen can cause another exacerbation of pleurisy. Effusions due to MM tend to disappear in the later stages but this process is associated with the obliteration

of pleural space by tumor tissue (15). In our patient, we did not see any residual lesions in multiple chest CT investigations.

Dietary or hormonal factors may have a role on the progression of MM but the patient did not make any changes in his nutritional habits and we did not observe a specific finding suggestive for hormonal disturbances (16,17).

The procedure of chemotherapy can alter anti-tumor immune response but it is important to note that spontaneous regression of a cancer is rare and transient (18). On the other side, miliary dissemination can occur in the absence of clinically identifiable pleural-based tumor in MM (19).

CONCLUSIONS

Unexplained recurrent pleurisy may be a rare feature of MM. Despite the aggressiveness of tumor, MM-associated pleural effusions can spontaneously regress without any identifiable lesion and the radiological appearance may change markedly within a short time.

References

- Halla JT, Schronhenloher RE, Volanakis JE. Immune complexes and other laboratory features of pleural effusions. A comparison of rheumatoid arthritis, systemic lupus erythematosus, and other disease. *Ann Intern Med* 1980;92:748-52
- Lidar M, Pras M, Langevitz P, et al. Thoracic and lung involvement in familial Mediterranean fever (FMF). *Clin Chest Med* 2002;23:505-11
- Kuwahara T, Hamada M, Inoue Y, et al. Warfarin-induced eosinophilic pleurisy. *Intern Med* 1995;34:794-6
- Baris YI, Artvinli M, Sahin AA. Environmental mesothelioma in Turkey. *Ann N Y Acad Sci* 1979;330:423-32.
- Fedullo PF, Auger WR, Channick RN, et al. Chronic thromboembolic pulmonary hypertension. *Clin Chest Med* 1995;16:353-74.
- Nicotra MB, Rivera M, Dale AM, et al. Clinical, pathophysiologic, and microbiologic characterization of bronchiectasis in an aging cohort. *Chest* 1995;108:955-61.
- Wallis RS, Ellner JJ. Cytokines and tuberculosis. *J Leukoc Biol* 1994;55:676-81.
- Kirtland SH, Winterbauer RH, Dreis DF, et al. A clinical profile of chronic bacterial pneumonia – A report of 115 cases. *Chest* 1994;106:15-22.
- O'Connor TM, O'Donnell A, Hurley M, et al. Allergic bronchopulmonary aspergillosis: a rare cause of pleural effusion. *Respirology* 2001;6:361-3.
- Jego A, Paillot D, Cuvelier A, et al. Recurrent pleural pericarditis. *Rev Mal Respir* 1996;13:430-2.
- Rohl AN, Langer AM, Moncure G, et al. Endemic pleural disease associated with exposure to mixed fibrous dust in Turkey. *Science* 1982;216:518-20.
- Porter JM, Cheek JM. Pleural mesothelioma. Review of histogenesis and report of 12 cases. *J Thorac Cardiovasc Surg* 1968;55:882-90.
- Situnayake RD, Middleton WG. Recurrent pneumothorax and malignant pleural mesothelioma. *Respir Med* 1991;85:255-6.
- Robinson BW, Robinson C, Lake RA. Localised spontaneous regression in mesothelioma – possible immunological mechanism. *Lung Cancer* 2001;32:197-201.

- 15- Hillerdal G. Malignant mesothelioma 1982: Review of 4710 published cases. *Br J Dis Chest* 1983;77:321-43.
- 16- Maesen F, Willighagen R. Regression of a malignant tumor of the pleura. *Eur J Respir Dis* 1987;71:135-8.
- 17- Horita K, Inase N, Miyake S, et al. Progesterone induces apoptosis in malignant mesothelioma cells. *Anticancer Res* 2001;21:3871-4.
- 18- Charlton RC. Spontaneous regression of cancer or misdiagnosis? Four case reports. *Int J Clin Pract* 1997;51:248-50.
- 19- Musk AW, Dewar J, Shilkin KB, et al. Miliary spread of malignant pleural mesothelioma without a clinically identifiable pleural tumor. *Aust N Z J Med* 1991;21:460-2.