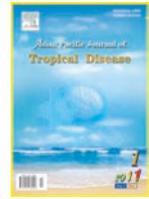


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Malign mesothelioma and gelatinous pleural fluid

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ABSTRACT

Gelatinous or viscous pleural fluid can be seen in malignant mesothelioma. We reported a 65-year-old patient with mesothelioma, also diagnosed as non-hodgkin lymphoma and chronic lymphocytic leukemia. Mini-thoracotomy was performed in order to get the fluid out, and to make pleurodesis. This patient had been followed up for four years then he died. Gelatinous fluid can be manageable well with surgery and pleurodesis and can be the messenger of long survival.

1. Introduction

Malignant mesothelioma is a tumor of the serous membranes and primarily related to asbestos exposure^[1]. Central Anatolia in Turkey has rich asbestos reserve and the disease was usually seen endemically with a high incidence rate at that region^[2,3]. Other malignancies may accompany with this entity (10%)^[4,5]. Herein, we presented a mesothelioma case with non-hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL) along with gelatinous pleural effusion and its prolonged survival as a very rare clinical entity.

2. Case report

A 65-year-old man was admitted to our oncology department with fatigue, dyspnea and chest pain history during last two years. He worked as a farmer and has been

living in the central Anatolia. He has 25 pack-years of smoking history. On physical examination, left axillary fixed lymph node was palpated and breath sounds diminished on the right lung base. Lymph node and bone marrow biopsies revealed non-hodgkin lymphoma and chronic lymphocytic leukemia infiltration, respectively. Chest x-ray showed a homogeneous opacification on the right hemithorax. Computed tomography (CT) scans also showed massive pleural effusion at the right side and patient was consulted to chest diseases department. Diagnostic thoracentesis revealed gelatinous honey-like exudative serologic fluid. Cytological examination of the fluid showed atypical mesothelial proliferation. Pathological examination of the pleural biopsy reflected malignant mesothelioma. The fluid was drained by a Pleurocan® catheter, and then intrapleural cisplatin and systemic gemcitabine was administered. His pleural fluid was resolved after treatment.

24 months later, he was admitted to our chest diseases department with nearly the same clinical condition. He had no complaints prior to this time so he did not come for follow-up before. His CT scans showed mediastinal and hilar lymph node enlargement and massive pleural effusion along with volume reduction at the right lung

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and possibly malignant pleural masses without chest wall invasion (Figure 1). Thoracentesis was reperformed and sero-hemorrhagic, black cherry colored and jelly-like fluid which was too dense to obtain by syringe was aspirated (Figure 2). It can only be examined by adding 250 micro liters of hyaluronidase to resolve. Biochemical analysis revealed exudative pattern with glucose 56 mg/dL, protein 8.4 mg/dL, and lactate dehydrogenase 5115 IU/L. Hyaluronan level was measured as 258 mg/L. Mini-thoracotomy was performed in order to get the thick and viscous fluid out and to make chemical pleurodesis. Histopathologic examination of the pleural biopsy revealed the infiltration of neoplastic cells. There was focal intracytoplasmic and extracellular mucin formation (Figure 3). By immunohistochemistry panel, the diagnosis of epithelioid mesothelioma was re-established. Pleurodesis was performed using 5gr talc slurry via chest tube after the operation. Due to obvious long survival and inactive diseases status, best supportive care was offered for him. This patient had survived for four years after the diagnosis without any obvious manifestation. It was learned that he passed away at home with cardio-respiratory insufficiency.



Figure 1. Computed tomography of the patient exhibits hilar lymph node enlargement and massive pleural effusion along with volume reduction at the right lung and possibly malignant pleural masses without chest wall invasion.



Figure 2. Black cherry jelly-like gelatinous fluid is shown while

creeping down into the aspirator jar and lying on the green fabric creeping with the syringe.

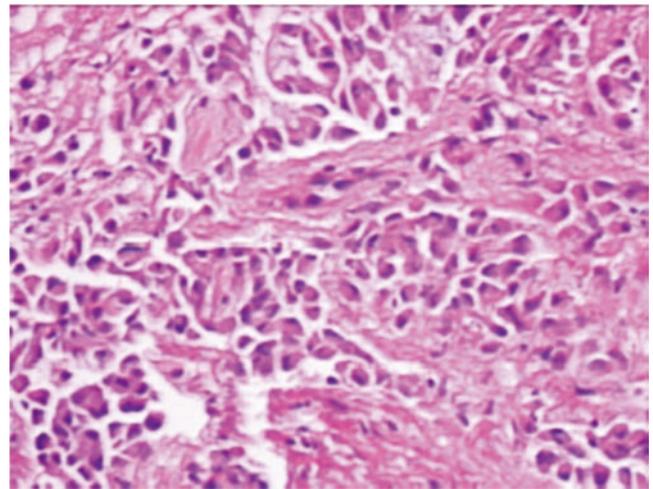


Figure 3. Tumor cells with tubule formation or solid growth pattern in a fibrous or hypocellular edematous stroma (H&E $\times 400$).

3. Discussion

Malignant mesothelioma is a rare and aggressive neoplasm. It is arising from mesothelial cells in the pleura frequently presenting with dyspnea and chest pain, and uncommonly with cough, fatigue and weight loss. Three primary pathologic types of mesothelioma (epithelioid, sarcomatoid, and biphasic) exist. Patients with epithelioid mesothelioma (55%–65%) have a slightly better median survival time. Massive pleural fluid at the time of the presentation is possible, but moderate fluid is also more likely. The incidence is 10–30 per million per year in unselected male populations, and approximately 2 per million per year in female subjects. Median survival ranges from 12 to 17 months in general and it does not last more than 2 years[6]. Histopathological examination of the pleural biopsy showed neoplastic cell infiltration with epithelioid morphology and tubulopapillary or solid growth pattern. These morphologic features required making differential diagnosis of mesothelioma and adenocarcinoma, therefore a broad immunohistochemical panel was performed. Tumor cells showed positive staining with mesothelin, CK 5/6, calretinin and WT-1 representing mesothelioma, while no other staining with TAG-72, CEA(m), TTF-1, eliminating the diagnosis of adenocarcinoma. Finally, the diagnosis of epithelioid mesothelioma was solidified[7,8].

NHL is the malignant disease of the lymph node. It can also be converted to CLL and invade the bone marrow during the disease progress. NHL survivors are at higher risk for developing both solid tumors and hematologic secondary malignancies than the general population. In the literature association of malignant lymphoma with mesothelioma has been reported. The co-existence of mesothelioma, mostly asbestos-related, and other primary malignancies has

repeatedly been reported (10%) suggesting that mesothelioma and associated malignancies might share some etiologic factors (asbestos and others). Several possible explanations were described for the combined diseases: coincidence; increased susceptibility to cancer due to malignant lymphoma; radiation or chemotherapy for the first neoplasm increasing the likelihood of the second; and a common etiology such as asbestos exposure^[9]. It was emphasized that the intense stimulation of B lymphocytes and decreased T lymphocyte activity seen in asbestos-exposed populations as possibly resulting in the development of B cell malignancies and chronic lymphocytic leukemia associated with malignant mesothelioma^[5]. In this particular case, this co-existence was most probably due to asbestos exposure.

Gelatinous pleural fluid can look similar to synovial fluid, or honey due to elevated levels of hyaluronic acid, a glycosaminoglycan, that is broadly distributed in extracellular spaces. High molecular weight hyaluronan forms a highly viscous network that is important for molecular exclusion, flow resistance, tissue osmosis, lubrication, and hydration^[10]. Increased amounts of hyaluronan in the pleural fluid from patients with malignant mesothelioma were first described by Meyer and Chaffee in 1939^[11]. Mesothelial cells are recognized as a source of secreted hyaluronic acid and chondroitin glycosaminoglycan. Perhaps, some mesotheliomas will be characterized also according to their hyaluronan production, in the near future^[12]. Cut-off value for high hyaluronan level was mentioned as >100 mg/L. If the level exceeded 225 mg/L, it turned out to be a good prognostic factor in malignant mesothelioma. It is also reported that an elevated concentration of hyaluronan in the pleural fluid also indicated longer survival in older patients and in patients receiving therapy other than supportive care^[13]. In this case, high hyaluronan level was detected and the patient had a reasonable prolonged survival time as mentioned even if existence of other comorbidities.

The ideal chemotherapeutic agent for pleurodesis, should be highly effective, easy to administer, inexpensive, virtually free of adverse effects, and not associated with serious adverse events. Talc fits all these criteria and especially in intra or post-operative period, talc slurry was highly preferable due to its low complication rate and high clinical success^[14,15]. We performed talc pleurodesis in our patient and he had been remained stable for a long time.

We presented an interesting malignant mesothelioma case with gelatinous pleural fluid which was previously honey-like then black cherry-like in two years period. He also had synchronic malignancies which were NHL and CLL. We observed that decompression of the accumulation and pleurodesis are appropriate treatments for such cases as viscous fluid is difficult to remove by thoracentesis and it can easily be accumulated again unless something fill or affix the pleural space. Hence, a physician should bear in mind that gelatinous fluid along with high hyaluronan levels in mesothelioma can be manageable well with surgery

and pleurodesis and has the feature of long survival even if alternated malignancies exist.

Conflict of interest statement

We declare that we have no conflict of interest.

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