Gelatinous Pleural Effusion: A Diagnostic Challenge for Pleural Mesothelioma in an 80-Year-Old Man

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Patient: Male, 80-year-old
Final Diagnosis: Pleural epithelioid mesothelioma
Symptoms: Pleural effusion • shortness of breath
Clinical Procedure: Pleural aspiration
Specialty: Oncology • Pulmonology

Objective: Unusual clinical course
Background: Gelatinous pleural effusion, due to raised hyaluronic acid, can be associated with pleural infection and malignancies, such as tuberculosis, metastatic pleural disease, and mesothelioma. This report is of an 80-year-old man presenting with a gelatinous pleural effusion and diagnosis of pleural mesothelioma.

Case Report: An 80-year-old man with diabetes mellitus, ischemic heart disease, metastatic prostate cancer, 30-pack-year smoking history, and 5-year history of asbestos exposure (during his 30s), presented with a 4-week history of breathlessness and was found to have right-sided pleural effusion. Thoracic computed tomography (CT) showed mild right-sided pleural thickening. Pleural tap revealed exudative fluid, with a pH of 7.4, and unremarkable cytology and microbiology analyses. The patient was treated for pneumonia and para-pneumonic effusion and discharged home. He came back 5 weeks later with worsening of symptoms and re-accumulation of pleural fluid. Repeated thorax CT showed extensive right-sided pleural lobular thickening. Pleural tap again yielded an exudative fluid, with a pH of 7.37. Cytology and microbiology did not reveal any positive signs for malignancy or infection. This time the pleural fluid appeared gelatinous in consistency. Pleural biopsy showed atypical epithelioid mesothelial cells arranged in trabeculae, with a tubulo-papillary configuration. Also, immunohistochemistry panel showed tumor cells expressed calretinin, EMA, WT1, and D2-40, with negative TTF1, CEA, and BerEp4. Final diagnosis was epithelioid mesothelioma.

Conclusions: This report has shown that a gelatinous pleural effusion can be associated with malignant and inflammatory pleural diseases. In this case, imaging and pleural biopsy with histopathology confirmed a diagnosis of pleural mesothelioma.

Keywords: Crystallization • Gelatin • Mesothelioma, Malignant • Pleural Effusion, Malignant

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Background

Pleural effusion is a pathological accumulation of fluids in the pleural cavity. Many etiologies exist, which are widely classified as exudates or transudates, based on the modified Light’s Criteria and depending on the biochemical analysis of the aspirated fluid [1]. Infections, malignancies, and other inflammatory processes result in exudate effusions, while transudate effusions are usually caused by disorders that disrupt the orthostatic and oncotic pressures in the pleural cavity, such as congestive cardiac failure, nephrotic syndrome, and liver cirrhosis [1].

A higher pleural fluid viscosity might be linked to certain underlying pathologies, mainly infections, including tuberculosis, and malignancies, including adenocarcinoma of the lung, and pleural mesothelioma. This is caused by the rich hyaluronic acid content of the fluid, and can present as a gelatinous effusion [2-5].

Mesothelioma is the main type of primary pleural cancer and carries a poor prognosis. It is a disease related mostly to asbestos exposure. Pleural thickening and pleural effusions are both manifestations of mesothelioma [6]. Despite the widely available and advanced investigatory methods of pleural fluid, microscopic analysis gives false-negative results in approximately a quarter of cases of mesothelioma [7]. Clinical history and macroscopic features of pleural fluid are as highly important as the microscopic findings in considering the possible differential diagnoses.

Several cases have been reported in the literature with a presentation of gelatious pleural fluid and a final diagnosis of mesothelioma [8-11]. We report a case of an 80-year-old man who presented with a gelatious pleural effusion, which could not be poured out of the aspiration syringe, and received a diagnosis of pleural mesothelioma.

Case Report

An 80-year-old man presented with gradual worsening of breathlessness on the background of ischemic heart disease, diabetes mellitus, and prostate carcinoma with metastasis to the spine. Initial clinical evaluation and chest X-ray confirmed right-sided pleural effusion. A chest drain was inserted, which yielded a straw-colored pleural fluid, with exudative characteristics on biochemical analysis (pleural protein 37 g/L, albumin 22 g/L, LDH 873 U/L) and a pH of 7.4. Pleural fluid cytology revealed: “Abundant polymorphs mixed with inflammatory and reactive mesothelial cells. No malignant cells seen”. The fluid did not grow any microbes, including tuberculosis. Computed tomography (CT) of the thorax showed right-sided pleural effusion with mild pleural thickening (Figure 1A) and no new metastatic lesions of prostate cancer. The patient was treated as a case of para-pneumonic effusion.

Five weeks after his discharge from the hospital, he presented with worsening of the same symptoms and re-accumulation of the previously drained pleural effusion. A chest drain was placed again, and upon aspiration of a clear straw-colored fluid, it immediately gelatinized and was difficult to pour into sample tubes (Figure 2). The drain filled no more than 50 mL of fluid while being regularly flushed, despite a lung ultrasound showing a large pleural effusion. Fluid biochemistry, cytology, and microbiology analyses came back with results similar to those obtained on the initial presentation.

After we discussed his case with microbiologists, we started him on treatment for the provisional diagnosis of partially treated empyema with a prolonged course of antibiotics; however, the inflammatory markers did not improve, which, along with his persistent symptoms and hypoxia, mandated a CT of the chest be performed; this interestingly showed lobular thickening of the pleura on the right side, with significant progression compared with the previous study (Figure 1B). In addition, the uncommonly encountered gelatinization of the pleural fluid raised the suspicion of malignancy.

CT-guided biopsy was the next step and showed “Cores of fibrous tissue infiltrated by an epithelioid cell lesion. These cells are arranged in trabeculae along with a tubulo-papillary configuration; in addition, there is a surface proliferation of similar atypical cells” (Figure 3A). Immunohistochemistry confirmed the diagnosis of primary epithelioid malignant pleural mesothelioma when the mesothelial markers calretinin (Figure 3B), EMA, Wilms Tumor 1, and D-240, came back positive, while the adenocarcinoma markers TTF1, CEA, +desmin, and BerEp4 were all negative (Figure 3C).

Given the poor performance status (PS) of the patient (PS=3) and his comorbidities, including prostate cancer, and after the case was discussed in the mesothelioma multidisciplinary team meeting, he was deemed not fit enough for first-line chemotherapy. In addition, it was agreed that any pleural intervention, such as an indwelling pleural catheter insertion or talc pleurodesis, would cause more harm than benefit. Therefore, he was discharged and eventually died a couple of weeks later.

It is worth mentioning that the patient had a brief history of asbestos exposure, as he worked in the docks for 5 years in his 30s, and he was a smoker (30 pack-years).

Discussion

Macroscopic characteristics of pleural fluid, such as gelatinous consistency, can provide good clues when analyzed in the correct context, along with the clinical presentation and other laboratory and radiological information. The diagnosis of
Figure 1. Thoracic computed tomography (CT) illustrating the rapid progression of pleural thickening over a period of 8 weeks, with new pleural nodularity. Both of the CT scans were taken after draining most of the pleural effusion. (A) Minimal right-sided diffuse pleural thickening on the initial CT Scan (→, ↓), with presence of pleural effusion. (B) Lobular thickening of the pleura on the right side with significant progression (↑, ←), along with pleural effusion.

Figure 2. Gelatinized, ie, jelly-like pleural fluid was noted immediately after aspiration.
Mesothelioma can be challenging, and although pleural effusion is a common presentation [6], it usually mandates more investigations to reach the diagnosis when compared with other causes of malignant pleural effusion [6]. Therefore, negative or equivocal initial pleural fluid investigations should not be taken for granted, and more extensive investigations should be considered to prove or decline the presumed diagnosis.

In relation to the findings described here, we came across a few cases that have been reported with similar pleural fluid macroscopic characteristics: rapid gelatinization of pleural fluid or jelly-like pleural fluid, with a final diagnosis of mesothelioma [8-12]. Nonetheless, gelatinous pleural fluid has been also linked to other types of malignancies and infectious pleural conditions, such as tuberculosis [3-5].

Gelatinization of pleural fluid is suggestive of higher viscosity, mostly attributable to a rich cellular and protein content, in particular mucin, which is produced in large amounts by malignant cells [13]. Hyaluronic acid is another component of malignant pleural effusion that is related to the higher viscosity and was found to be present in higher concentrations in mesothelioma than in other malignancies [11,12]. Successful attempts to facilitate the drainage of difficult to drain effusions have been reported by the means of intrapleural injection of hyaluronidase, which works by reducing the viscosity of the pleural fluid, making it amenable to drainage [3].

Immunohistochemistry using cytology or biopsy specimens is recommended for the diagnosis of malignant pleural mesothelioma [14]. While cytological examination of our patient revealed a mixture of different inflammatory cells, with no evidence of malignant cells, similar to some previous cases [9,10], others reported a cytological evidence of malignant pleural mesothelioma [11]. In fact, it is recommended to not rely on cytology alone to diagnose malignant pleural mesothelioma [14]. Pleural biopsy confirmed the diagnosis of epithelioid malignant pleural mesothelioma in most of the reported cases, as well as in ours [9-11].

The management of malignant pleural mesothelioma depends largely on the PS of the patient as well as the prognostic score; for instance, chemotherapy (cisplatin/pemetrexed) is offered to patients with a PS of 0-1 [10,14]. Symptomatic pleural effusion would benefit from talc pleurodesis or an indwelling pleural catheter being decided for each patient individually [14]. In one reported case, a middle-aged woman who presented with gelatinous pleural effusion and a diagnosis of malignant pleural mesothelioma received chemotherapy and an indwelling pleural catheter insertion, with regular drainage [10]. On the other hand, the cases of most older patients with poorer performance status were managed symptomatically, including that of our patient [9,11,12].
Conclusions

This report has shown that a gelatinous pleural effusion can be associated with pleural disease, including malignant pleural mesothelioma. In this case, imaging and pleural biopsy with histopathology confirmed a diagnosis of malignant pleural mesothelioma.

Department and Institution Where Work Was Performed

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Declaration of Figures’ Authenticity

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