Malignant pleural mesothelioma in young patient with recurrent pleural effusion

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ABSTRACT

Background: Malignant pleural mesothelioma (MPM) is a rare, aggressive, and hard-to-treat tumor whose worldwide incidence has been rising since mid-20th century. It that has been etiologically associated to asbestos exposure. Prognosis is poor with an overall survival rate of less than 1 year in untreated patients. Although considered a disease of the elderly, a subset of patients with mesothelioma are young. MPM is a rare cause of pleural effusion in the clinical practice among younger adults. Therefore, a high index of suspicion is required for its diagnosis.

Case presentation: We herein describe a 31-year-old male patient with a BRCA1-associated-protein-1 negative MPM who presented with recurrent pleural effusions. The patient had no history of asbestos exposure.

Conclusion: MPM is a rare cause of pleural effusion in the clinical practice among younger adults. Therefore, a high index of suspicion is required for its diagnosis.

Keywords: Malignant pleural mesothelioma, pleural effusion, pleurectomy/decortication, case report.

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Background

Malignant mesothelioma is an uncommon aggressive tumor with an estimated worldwide incidence of 2,000-3,000 new cases per year [1]. Although the tumor can grow in different organs such as pleura, peritoneum, and pericardium [2], the most common location is pleura, accounting for about 65% of all malignant mesotheliomas [3]. Malignant pleural mesothelioma (MPM) spread locally with distant metastasis being rare [2].

Asbestos exposure is the major cause of MPM and the link between asbestos and MPM goes back to a study performed in 1960 in South Africa [4]. Over the years, other less common etiologies have been proposed such as high-dose radiation exposure and irradiation with thorium dioxide, carbon nanotubes, and simian virus infection [2].

MPM has a peak incidence in the fifth and sixth decades of life with a male-to-female ratio of approximately 3:1 [5]. This tumor is rare among young adults, with less than 1% reported in patients under 35 years between 2008 and 2012 in the United States National Cancer Institute's Surveillance, Epidemiology, and End Results Program database [5].

MPM patients typically report respiratory symptoms such as shortness of breath, painful chest, and dry cough. Fatigue and unexplained weight loss are also common [6]. This tumor is usually managed by a combination of surgery, chemotherapy or radiation [6].

Case Presentation

A previously healthy 31-year-old man was admitted to the emergency room of our hospital with a sudden left-sided chest pain. Fever, dyspnea, and cough were denied. Patient had no history of exposure to asbestos and there was no family history of malignancies. After interrogation, patient told that for the last 4 years he had occasionally felt a less intense pain on that same site, that he associated with physical effort.

On physical examination, he had dullness to percussion on the left hemithorax. Lab evaluation showed an elevated reactive C protein (4.55 mg/dl) and chest X-ray revealed a left-sided pleural effusion (Figure 1A). Negative blood cultures were found. Thoracentesis yielded exudate with negative fluid cytology (Figure 1B). Patient was started on antibiotics and discharged from the hospital.

After 11 months asymptomatic, pleural effusion recurred. A computed tomography scan showed a large effusion and irregular pleural thickening.

A positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro-D-glucose integrated with computed tomography was performed, and two pleural sites with irregular morphology and up normal metabolism were identified on the left pulmonary base (Figure 2). The findings were compatible with pleural disease but unspecify regarding its etiology (benign inflammatory versus neoplastic). To proceed toward a diagnosis, patient was submitted to a thoracoscopic pleural biopsy. The anatomopathological specimen analysis of showed an epithelioid MPM with focal invasion and loss of expression of BRCA1-associated-protein-1 (BAP1).

Pleurectomy/decortication followed by adjuvant chemotherapy was proposed in a dedicated thoracic oncology group meeting. The patient was submitted to surgery with extubation at 24 hours (Figure 3A) and hospital discharged after 15 days. Four weeks post-surgery, the patient started a course of four cycles of cisplatin and pemetrexed. After adjuvant chemotherapy completion, he remained on maintenance treatment with pemetrexed.

At 4-month follow-up visit, patient denied dyspnea and reported a gradual increase in his physical capacity (Figure 3B). He nowadays exercises four times a week and follows a daily breathing exercise program.

Discussion

MPM seems to behave differently in younger comparing to older population. Distinctively from the elders, sex distribution among young patients is roughly the same (51% males and 49% females) [5]. Moreover, considering tumor's long latency period, MPM in the young is less likely to be due to asbestos exposure and increased genetic predisposition may probably play a role in tumor's development [5].

In the literature, case reports of mesothelioma in young adults are rare. In 1990, Kane et al. [7] published a review of 10 cases of MPM in patients under 40 years with a median survival of 13.0 months. In 2010, Bitchatchi et al. [8] reported a case of a 27-year-old woman diagnosed with MPM with only 8 years of age, that was submitted

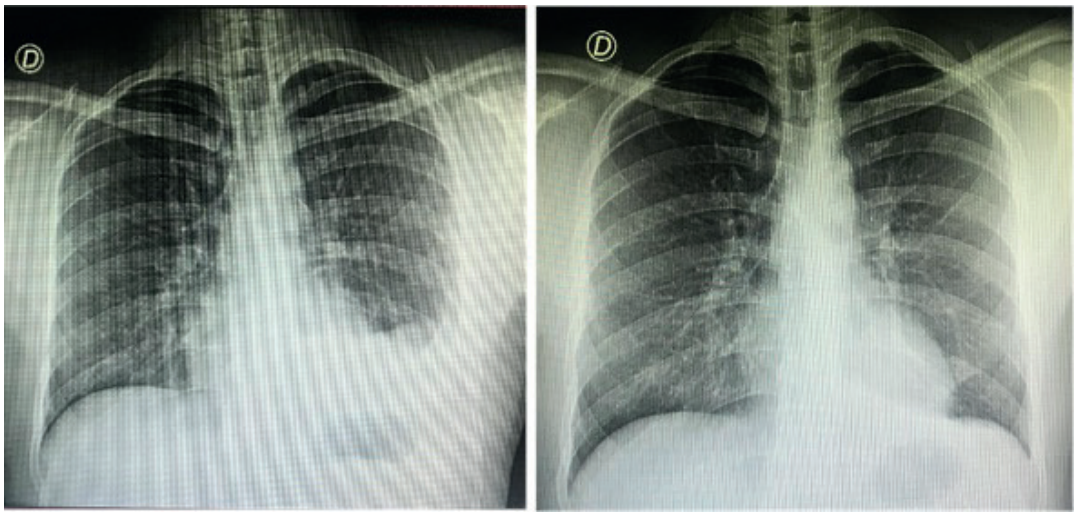

Figure 1. *(A) Chest radiograph at hospital admission showing a left-sided pleural effusion. (B) Chest radiograph after performing a thoracentesis that yielded 650cc of an exudate liquid, showing significant improvement of the pleural effusion.*

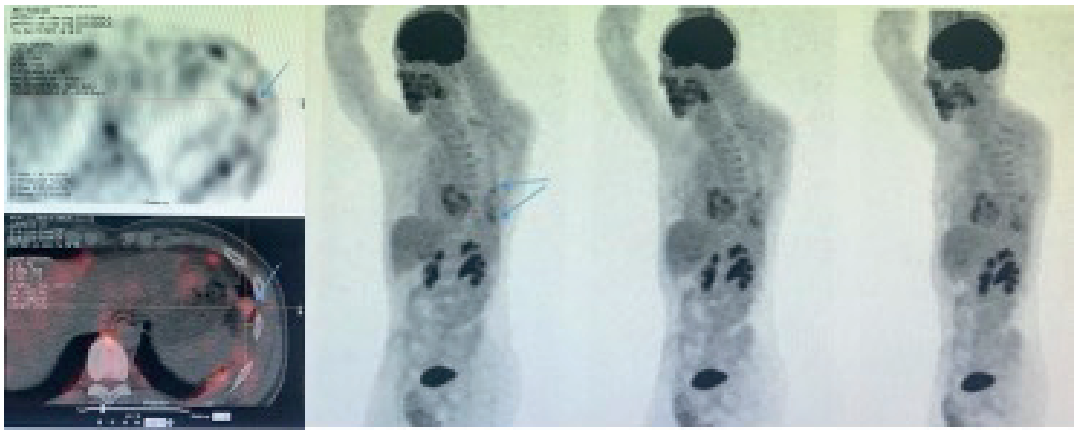

Figure 2. *Fluorodeoxyglucose positron emission tomography fusion CT scan showing moderately increased uptake in the left-sided pleura (blue arrows) consistent with two focal pleural thickening sites.*

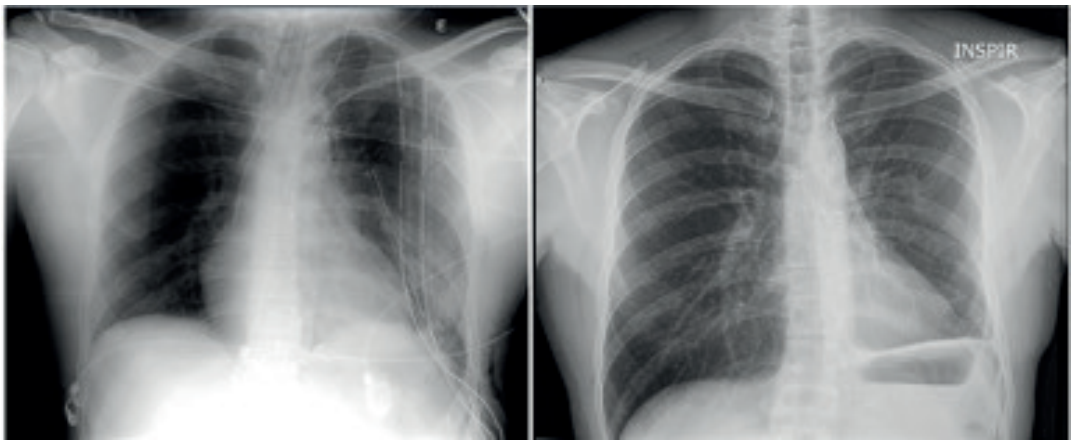

Figure 3. *(A) Chest radiograph at 24 hours post-pleurectomy/decortication surgery. (B) Chest radiograph at 4 months post-pleurectomy/decortication surgery.*

to extrapleural pneumectomy and intrapleural infusion of cisplatin post-operatively. This case relates an uncommonly short disease latency with a long survival superior to 12 years. In 2014, a Turkish group led by Kanbay et al. [2] reported a case of a 26-year-old patient diagnosed with MPM with no previous known exposure to asbestos or erionite, which is another main cause of MPM in Turkey. He was referred to the oncology department for six cycles of cisplatin and pemetrexed chemotherapy treatment and died 28 months after diagnosis. In 2018, Vivero et al. [5] compared the clinicopathologic and genetic characteristics of MPM of patients under 35 years and older than 48 years old. They concluded that young patients were more frequently women, reported less asbestos exposure and had live approximately 16 months longer than patients in the older group.

Recent studies have identified germline mutations in the gene encoding BAP1 which can predispose to several malignancies [9-11]. In fact, germline BAP1 mutation carriers are thought to be susceptible to develop mesothelioma even at non-tumorigenic levels of asbestos exposure less to the general population [10]. Nevertheless, mesothelioma associated with germline BAP1 mutations have been reported to be linked with longer tumor survival compared with sporadic mesothelioma [11]. Further studies are needed to shed light on the real burden of genetics in the arousal of MPM among the young population.

With the sustained worldwide increase in MPM, an aggressive search for its cure is needed. The treatment of MPM is still controversial with no common agreement on best treatment. Screening the literature for surgical and non-surgical therapeutic approaches in patients with MPM yields limited results: two randomized clinical trial mesothelioma and radical surgery (MARS and MARS2 trials) [12,13] and two observational studies [14,15]. MARS trial was a multicenter-randomized controlled trial that took place in 12 UK hospitals between October 2005 and November 2008. Its results suggested that radical surgery in the form of extrapleural pneumonectomy within tri-modal therapy offered no benefit and possibly harmed patients [13]. Nevertheless, results from retrospective cohort studies performed over the last decade diverge those of MARS trial showing a survival benefit tendency toward surgery [14,15]. The MARS 2 trial, which is now in its phase 3, aims to test the hypothesis that (extended) pleurectomy decortication associated with platinum and pemetrexed chemotherapy is superior to chemotherapy as single treatment in overall survival for MPM patients. Patient recruitment ended past November 2020 and to our knowledge no results have yet been publicly disclosed [14].

Conclusion

The case herein reported is a paradigm of the cooperation between several medical specialties, namely, internal medicine, pneumology, radiology, anatomopathology, oncology, and thoracic surgery. As a result of this teamwork, patient underwent treatment and remains asymptomatic.
We wish to alert physicians to the importance of the early recognition of MPM, which is essential in reducing complications and mortality. MPM can be a cause of pleural effusion even in young patients without exposure to asbestos, and it should therefore be considered in the differential diagnosis of pleural effusion.

What is new?

Although considered a disease of the elderly, a subset of patients with mesothelioma are young. We herein describe a 31-year-old male patient with a BAP-1 negative malignant pleural mesothelioma who presented with recurrent pleural effusions. The patient had no history of asbestos exposure. MPM is a rare cause of pleural effusion in the clinical practice among younger adults.

List of Abbreviations

BAP1	BRCA1-associated-protein-1
MARS	Mesothelioma and radical surgery
MPM	Malignant pleural mesothelioma

Conflict of interests
The authors declare that there is no conflict of interest regarding the publication of this article.

Funding
No financial support has been obtained for this study.

Consent for publication
A written informed consent to publish this case was obtained from the patient.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 31 year old
2	**Final diagnosis**	MPM
3	**Symptoms**	Sudden left-sided chest pain
4	**Medications**	Cisplatin and pemetrexed
5	**Clinical procedure**	Thoracentesis, thoracoscopic pleural biopsy, pleurectomy/decortication
6	**Specialty**	Internal medicine, thoracic surgery