# Desmoplastic Malignant Mediastinal Mesothelioma Presenting as Superior Vena Cava Syndrome: A Case Report and Literature Review

Kah-Mee Law, Yu-Feng Wei, Jiun-Ting Wu

Mediastinal mesothelioma is rare, accounting for less than 5% of all cases of mesothelioma. Primary pericardiac mesothelioma is also a rare type of mesothelioma, with a reported incidence of less than 0.0022% among 500,000 cases in a large necropsy study. Herein, we report the case of a 48-year-old man who presented to our outpatient department due to progressive cough with prominent body weight loss within 2 months. Chest computed tomography showed a right mediastinal mass encasing the superior vena cava with obliterated vessels. The pathology of the mass revealed desmoplastic mesothelioma, which was most likely pericardial in origin, based on the imaging findings. Echocardiography showed tumor thrombus in the superior vena cava, extending to the right atrium. The patient died of sepsis after chemotherapy 5 days later. ***(Thorac Med 2015; 30: 92-98)***

Key words: desmoplastic, malignant mediastinal mesothelioma, superior vena cava syndrome

## Introduction

Malignant mesotheliomas are derived from the mesothelial or submesothelial connective cells covering the tunica serosa. Mediastinal mesotheliomas account for less than 5% of all mesotheliomas [1]. Most malignant mediastinal mesotheliomas are considered to originate from the pericardium [2]. This type of mesothelioma is associated with exposure to asbestos, but only 14% of cases of malignant mesothelioma have a history of asbestos exposure. The mechanism of asbestoses in pericardial mesothelioma is still under investigation.

Desmoplastic mesothelioma is another rare mesothelioma subtype. More than 50% of the specimen consists of dense, hypocellular collagenous tissue in epithelial, sarcomatous and mixed or biphasic subtypes. Desmoplastic malignant mesothelioma was first described by Kannerstein and Churg in 1981, and accounts for 5% to 10% of all malignant mesotheliomas [3]. Although more than 350 cases of primary pericardial mesothelioma have been reported, no cases of primary pericardial mesothelioma with superior vena cava syndrome have been

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reported to date. Herein, we present a case of desmoplastic malignant pericardial mesothelioma with invasion to the adjacent superior vena cava and right atrium, causing superior vena cava syndrome and distant metastasis.

## Case Report

A 48-year-old man with no history of exposure to asbestos first came to our chest medicine outpatient department due to progressive cough with whitish sputum production accompanied with prominent body weight loss of 4 to 5 kg and progressive exertional dyspnea for the last 2 months. He had a smoking history of more than 30 pack/years. He presented in April 2013 with swelling of his upper extremities and a swollen face. A physical examination revealed superficial vein engorgement in the right anterior chest wall with a crackling sound in both lungs when breathing. No other symptoms such as fever, chest pain, dyspnea, or palpitation were noted. His vital signs showed only mild tachycardia. The significant laboratory findings included leukocytosis with a left shift and hyperuricemia, and tumor markers such as carcinoembryonic antigen and alpha-fetoprotein within a normal range, which suggested inflammation or an infection. Chest radiography (CXR) revealed increased soft tissue opacity at the right lower paratracheal region, with a left blunt C-P angle (Figure 1). Chest computed tomography (CT) (Figures 2a, 2b) showed a prominent right mediastinal mass 5×5 cm in size encasing the superior vena cava with obliterated vessels and suspected tracheal wall invasion.

Bronchoscopy was arranged and showed a bulging mass with mucosa swelling in the right main bronchus. We arranged video-assisted thoracic surgery (VATS) to obtain a tissue sample.

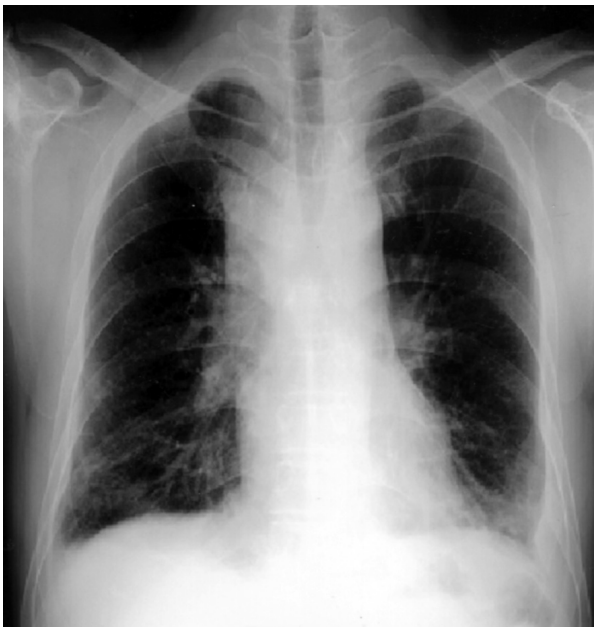

**Fig. 1.** CXR showed increased soft tissue opacity at the right lower paratracheal region, with bilateral costophrenic angle blunting.

During the operation, the mediastinal mass was found to be adherent to the right upper lobe of the right lung with active oozing. The pathology report of the mediastinal mass showed mesothelioma, and immunohistological staining was positive for calretinin (Figure 3a) and cytokeratin (CK) (Figure 3b), and negative for various tumor cell markers, including CD5 (T-cell neoplasma), CD34 (Ewing's sarcoma/primitive neuro-ectodermal tumor (PNET)), CD56 (small cell lung carcinoma), CD68 (histiocytic lymphoma), CD117 (gastrointestinal stromal tumors (GISTs)), CK5/6 (pulmonary squamous carcinoma), S-100 (melanomas, schwannomas, neurofibromas), WT-1 (Wilms' tumor), and TTF-1 (pulmonary adenocarcinomas). Histoimmunology confirmed desmoplastic mesothelioma (Figure 3c, 3d). For staging purposes, brain magnetic resonance imaging showed an 8-mm enhanced nodule with perifocal edema at the right parasagittal occipital region, favor-

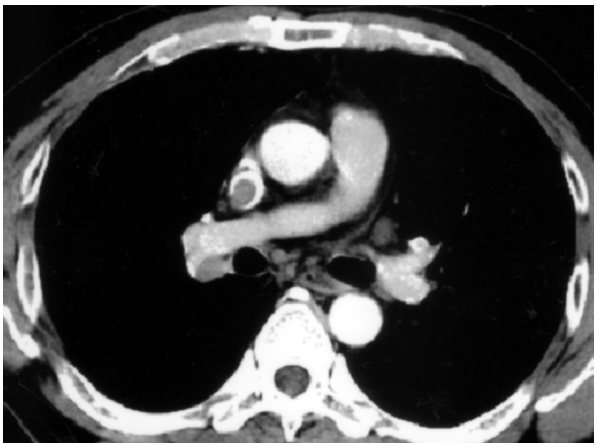

**Fig. 2 (a).** Thrombus within the superior vena cava with left aortopulmonary lymphadenopathy in the chest CT.

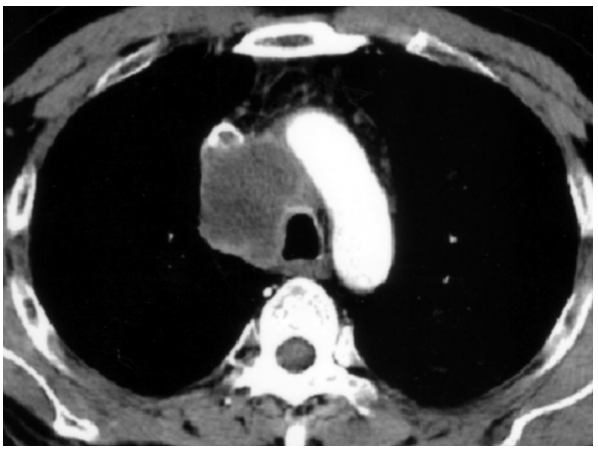

**Fig. 2 (b).** Middle mediastinal mass causing nearly total occlusion of the superior vena cava with suspected tracheal wall invasion in the chest CT.

ing a metastatic lesion. A bone scan was also performed which showed a reaction in the right 5-6th ribs, also suggesting metastasis.

After VATS, empyema developed and antibiotics were prescribed for the infection. Radiotherapy was performed for progressive orthopnea related to superior vena cava syndrome. Chest CT with contrast was done 2 months later, and showed progressive superior vena cava thrombus with occlusion and tumor invasion to

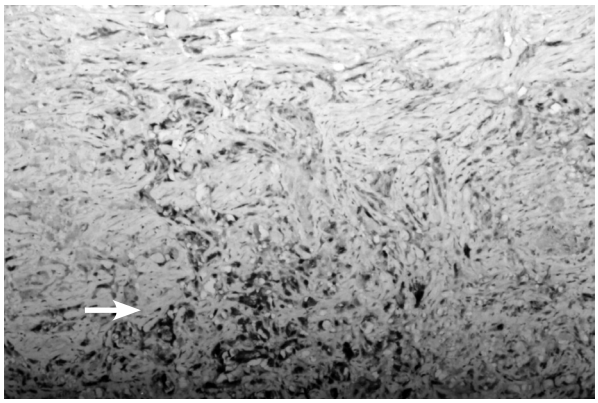

**Fig. 3 (a).** Positive staining for calretinin. (brown color stain) (as arrow)

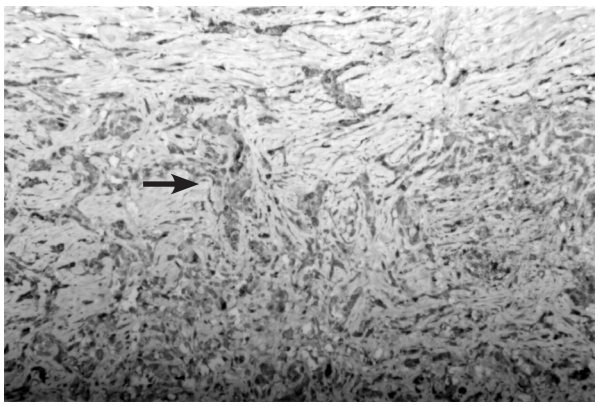

**Fig. 3 (b).** Positive staining for CK (brown color stain) (as arrow)

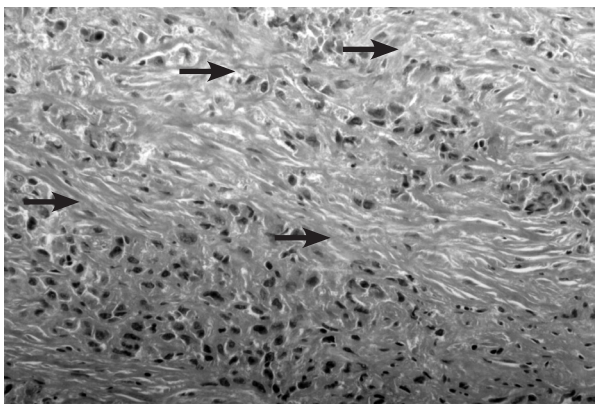

**Fig. 3 (c).** HE under 200 magnification power showed a collagen fiber bundle (as arrow)

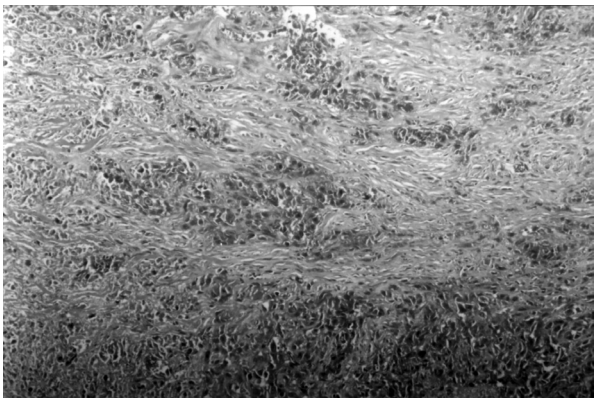

**Fig. 3 (d).** HE under 100 magnification power showed positive staining for Masson's Trichrome (blue color stain indicates collagen fiber, red color stain indicates muscle fibrin)

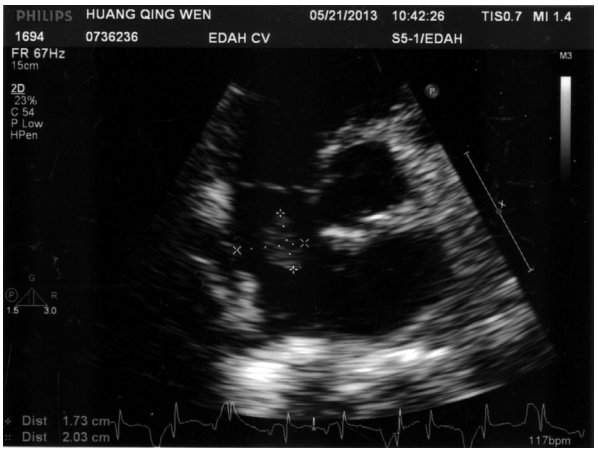


**Fig. 4.** Tumor thrombus within the right atrium in echocardiography.

the right atrium. Cardiac sonography (Figure 4) was also performed later and showed diastolic dysfunction with a small amount of pericardial effusion. A 2.0×1.7 cm mass at the tricuspid valve atrial site, suspected to be vegetation or thrombus, was also found.

We started pemetrexed and cisplatin treatment for the mesothelioma in combination with antibiotics after discussing the situation (the high risk of infection deterioration after chemotherapy) with the patient. Five days after initiation of chemotherapy, he developed an irritable mood with dyspnea. He expired the same day due to suspected sepsis progression. The patient had a "do not resuscitate" will.

## Discussion

Malignant mesothelioma is not rare, with a reported average of more than 3000 cases annually in the United States [4-5]. Up to 80% of malignant mesotheliomas are associated with exposure to asbestos [6]. Mesotheliomas have a long latency period of 30 to 40 years from first exposure to asbestos to developing the disease [7]. Besides the pleural cavity (80%), mesotheliomas also occur in the peritoneum, tunica vaginalis testis and pericardium (10%, <5%, and <5%, respectively) [8]. The mean age of patients with malignant mesothelioma is 60 years, and the mean average survival time is 6 months [9].

Pericardial mesothelioma is extremely rare, although it is the most common primary malignant pericardial tumor. The reported incidence was less than 0.0022% among 500,000 cases in a large necropsy study [10-11]. Many case reports of malignant pericardial mesothelioma have been published, in which some presented with diffuse pericardial nodules, diffuse pericardial thickening, or a solitary nodule in the parietal and visceral pericardium, causing obliteration of the pericardial space or cardiac chamber encasement [12]. In our case, the tumor initially appeared as a solitary mediastinal tumor without direct invasion to the pericardium, and only encasing of the superior vena cava caused partial obliteration. The tumor was found to have invaded the right atrium chamber 2 months later.

Most primary pericardial malignant me-

sotheliomas present clinically as constrictive pericarditis, cardiac tamponade and congestive heart failure either by serous effusion or by direct tumor invasion causing heart constriction [13]. In our case, the patient presented as superior vena cava syndrome due to invasion of the mediastinal mass into the superior vena cava, with symptoms of progressive orthopnea and exertional dyspnea and swelling of the bilateral upper extremities.

Localized pericardial mesothelioma is considered to be a distinct, rare variant of malignant mesothelioma [2]. Although localized, this type of mesothelioma can still cause direct invasion to adjacent organs [14-15]. Most localized primary pericardial mesotheliomas can be resected by surgery, with good overall survival. Allen *et al* suggested differentiating localized mesothelioma from the diffuse type due to the superior prognosis of the former compared to diffuse malignant mesothelioma [16].

The current standard treatment for malignant mesothelioma is combination therapy with a folic acid antagonist such as pemetrexed plus a platinum-based anticancer drug such as cisplatin [17]. Treatment for primary pericardial mesothelioma is mainly palliative due to its poor response to radiotherapy and chemotherapy, as well as being surgically unresectable. However, studies on new regimens for pericardial mesothelioma have been published [18-19].

Three types of pathology are found in mesotheliomas: epithelial, sarcomatous, and mixed or biphasic. These patterns are found in roughly 55%, 15%, and 30% of cases, respectively [3]. Desmoplastic malignant mesothelioma has since been described in a number of reports with documented exposure to asbestos [3]. Our case did not have a history of exposure to asbestos. Mangano *et al* proposed the following histological criteria for desmoplastic malignant mesothelioma: a paucicellular fibrotic pleural lesion with a storiform or patternless pattern, plus 1 or more of the following; invasion of the chest wall or lung, bland necrosis, a frank sarcomatoid area, and distant metastasis [19]. In our case, the pathology was desmoplastic epithelial mesothelioma, and histo-immunological staining was positive for calretinin and CK, and negative for CD5, CD34, CD56, CD68, CD117, CK5/6, S-100, WT-1, and TTF-1. The report by Nicolini *et al* showed findings similar to our case, including a huge white tumor mass surrounding and encasing the heart and large vessels (aortic arch, pulmonary artery, and veins and vena cava) with strong pleuropulmonary adherence and macroscopically invaded myocardial tissue, and the pathology showed desmoplastic mesothelioma in primary pericardial mesothelioma [10]. We also found the same characteristics of encased great vessels with invasion into the right atrium, as well as distant metastasis. The prognosis of desmoplastic variant mesothelioma depends on whether it is derived from the epithelial, sarcomatous, or biphasic type, with a reported survival of 5-8 months for the sarcomatous variant and 6-8 months for the biphasic variant [3]. The recommended treatment is the same as for primary pericardial mesothelioma, which is mainly palliative care.

There are many differential diagnoses for an invasive mediastinal mass, including metastatic lesions from other primary sites such as primary non-small cell lung cancer, lymphoma, leukemia, angioimmunoblastic lymphadenopathy and solitary fibrous tumors of the pleura. We considered the possibility of metastatic lesions of other primary origins or lymphoma; however, after consultation with a pathologist,

mesothelioma was determined to be the most likely diagnosis for this case. Pathological proof and the histo-immunological diagnosis are very important to establish a final diagnosis.

In conclusion, desmoplastic malignant mediastinal mesothelioma is a rare type of mesothelioma. It presents with rapidly invasive metastasis and has much less of a superior vena cava syndrome. We reported this rare case to remind clinicians to be aware of this important differential diagnosis of mediastinal tumor.

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# 纖維惡性縱膈腔間皮癌以上腔靜脈症候群爲臨床表現：病例報告及文獻回顧

劉嘉美　魏裕峰　吳俊廷

惡性縱膈腔間皮瘤是一種很稀少的間皮瘤，大約佔了所有間皮瘤的 5% 以下，而心包膜間皮瘤是屬於更稀少的間皮瘤。根據一項驗屍解剖個案統計，在 500,000 個案裡面，其發生率小於 0.0022%。我們報告的病例是一位 48 歲男性病患，第一次出現在門診的主訴是咳嗽合併白色痰液及體重減輕已有 2 個月的時間。胸腔電腦斷層之下表現為右側獨立性縱隔腔腫瘤，且侵犯到上腔靜脈以及氣管。病理報告顯示為纖維性間皮瘤 ,並從影像學上判斷應是從心包膜長出來的間皮瘤。這病人在進行化學治療後 5 天因敗血症病逝。
*( 胸腔醫學* ***2015; 30: 92-98)***

關鍵詞：纖維性，惡性縱膈腔間皮瘤，上腔靜脈症候群

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