Case report

Sudden cardiac death due to primary malignant pericardial mesothelioma: Brief report and literature review

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Abstract

Sudden cardiac death is an unexpected clinical condition that typically occurs due to a cardiac cause, generally within 1 h of symptom onset, in people with known or unknown cardiac disease. Primary malignant pericardial mesothelioma, as a cause of sudden death, is an uncommon consequence of a rare disease. Herein, we present a case of cardiac tamponade due to a primary pericardial mesothelioma. Cytological, histopathology and gross post-mortem findings, in a previously asymptomatic 46-old-year man, are reported. The medical literature regarding this topic is also reviewed.

1. Introduction

Sudden cardiac death (SCD) is an unexpected clinical condition typically due to cardiac causes that manifest in a short time period, generally within 1 h of symptom onset, in people with known or unknown cardiac disease. Approximately 50% of all cardiac deaths are sudden [1]. Cardiac tamponade (CT) is among the causes of SCD. CT results from an accumulation of pericardial fluid under pressure, leading to impaired cardiac filling and haemodynamic compromise. Although CT is a clinical diagnosis, this condition can be diagnosed through imaging techniques, electrocardiography and laboratory studies (e.g. presence of abnormal cellularity in pericardial fluid samples) [2].

A variety of diseases may be responsible for CT (e.g hemopericardium). Malignant disease of the pericardium, either primary or metastatic, is an infrequent cause of CT. Among primary malignant tumours, mesothelioma of the pericardium is the main tumour encountered [3–5]. A more frequent finding is metastatic adenocarcinoma from lung, breast, and gastric/esophageal cancer, in this order of frequency [6].

SCD due to CT in the context of primary malignant mesothelioma of the pericardium (PMPM) is a very uncommon condition [7,8]. Not surprisingly, the cyto-histologic findings in such cases have not been well elucidated.

Herein, we present and discussed the cytomorphological findings of a case of fatal CT due to PMPM.

2. Case report

A 46-year-old unconscious man, who was a worker in a building demolition company, was admitted to the emergency room because of suspected cardiac arrest. Significant occupational exposure to asbestos was unknown. Adverse hemodynamic signs such as tachycardia, hypotension, jugular venous distension, cyanosis, and pulsus paradoxus were noticed. His ECG revealed sinus tachycardia with electrical alternans and a chest x-ray showed an enlarged heart. Echocardiography showed a large pericardial effusion with CT. A pericardiocentesis yielded 800 ml of haemorrhagic fluid. Despite vital emergency support measures that were carried out, this patient died suddenly. An autopsy was performed. On the basis of the pathologic results, a diagnosis of PMPM was made.

2.1. Autopsy findings

At post-mortem, there was uncoagulated blood in the pericardial sac and both the parietal and visceral layers of the pericardium appeared thickened showing irregular and granular surfaces with necrotic foci (Fig. 1). In some areas the pericardium was adhered to the heart surface due to superficial infiltration of mesothelioma into the cardiac muscle. Mesothelioma had no spread to adjacent structures. The great vessels had no anomalies. The patient's lungs and pleura were healthy. The other body cavities showed no gross abnormal findings. Both tissue and fluid samples were removed for histopathological and cytological
2.2. Histopathological findings

Histological sections showed diffuse infiltration of the pericardium by epithelioid malignant mesothelial cells. These cells had sharply defined cell borders, abundant glassy eosinophilic cytoplasm and large nuclei with a prominent nucleolus (Fig. 2A). Occasional mitotic figures were also observed. No asbestos bodies were observed. The tumour cells demonstrated positivity for pan-cytokeratin, EMA (clone E29), and calretinin (Fig. 2B). Immunostains for CEA and TTF-1 were negative. This immunoprofile supports the diagnosis of mesothelioma.

2.3. Cytomorphological findings

Pericardial fluid was hypercellular and showed abundant malignant mesothelial cells forming many large irregular clusters (Fig. 3A). The malignant cells demonstrated increased N:C ratios, pleomorphism, coarse chromatin, and prominent nucleoli (Fig. 3B).
Immunocytochemistry confirmed calretinin positivity of these malignant mesothelial cells (Fig. 3C).

3. Discussion

Both ante-mortem and post-mortem findings in this case confirm that SCD in this man was due to a PMPM. PMPM is a very rare condition with an incidence of less than 0.002% according to the largest reported retrospective series, which represent less than 5% of all mesotheliomas [9]. Nonetheless, PMPM is still the most common primary malignancy of the pericardium [10]. On the basis of histologic growth patterns, PMPM can be classified into three types: epithelioid (most frequent), mixed (biphasic), and sarcomatous (least frequent). Moreover, different pathologic subtypes can be found such as tubulopapillary, deciduoid, desmoplastic, among others.

A literature search using PubMed and EMBASE for PMPM revealed a total of 269 cases. In PMPM cases associated with CT, only 37 cases have been reported. Of these published cases, only three other patients also resulted in SCD [7,11,12]. A brief comparison between these published cases and ours is showed in Table 1.

Various risk factors have been reported for PMPM including exposure to asbestos [13,14], post-irradiation [15], and speculative infection with Simian virus 40 [16].

The diagnosis of PMPM has typically been made at the time of post-mortem examination. There are only limited reports that describe the histological and cytological findings of PMPM [17–21].

Pericardial effusion fluid cytology may help to determine tumour origin, prognosis and modality of therapy [22]. The cytological diagnosis requires a constellation of cytomorphology, immunocytochemistry and correlation with the relevant clinical history of the patient [23]. Cytological sensitivity for detecting malignant cells by pericardiocentesis is variable across different series, ranging from 30% to more than 90%; these differences are due partly to the amount of fluid obtained (minimum of 60 ml is necessary) and the expertise of the cytologist [24].

CT as the initial manifestation of primary malignant tumours with no pericardial origin such as lung, urinary bladder, kidney, vagina, ovarian, fallopian tube, endometrium, uterine cervix, colon, stomach, thyroid, thymus, breast, lymphoma, and melanoma have all been reported [25–39]. Furthermore, sudden death due to CT caused by metastatic lung cancer has been mentioned [40,41]. Metastases are therefore an important consideration in the differential diagnosis. Misdiagnosing PMPM as pericardial metastatic cancer is another possibility [42,43].

In summary, we present a fourth case where PMPM contributed to SCD showing cytopathological, histopathological and post-mortem autopsy findings.

Cardiac manifestations due to neoplastic involvement of the pericardium are uncommon, and the presence of CT as the initial presentation is very rare with a poor prognosis. Although the interval between cancer diagnosis and malignant CT onset and the prognosis after pericardiocentesis may differ regarding to cancer type [44], performing cytological analysis in all patients who present with CT is recommended, even if malignancy is not suspected initially.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.01.011.
| Clinical findings                        | Mesotheloma extent                  | Histopathology                       | Cytopathology   |
|-----------------------------------------|-------------------------------------|--------------------------------------|-----------------|
| Pulmonary paradoxic, respiratory distress, distended jugular veins, diaphoretic heart sounds, thickening of the pericardium | Limited to pericardium and encased to heart (two cases) | Epithelioid malignant mesothelioma (three cases) | Positive for malignancy (one case) |
| Post-irradiation (two cases)            |                                    | Deciduoid-like malignant mesothelioma (one case) | Negative for malignancy (two cases) |

Table 2: Comparison between patients with PMPM with and without SCD

| PMPM with tamponade | Without SCD (N = 34) |
|---------------------|----------------------|
| Gender (M:F)         | 3:1                  |
| Age (average, range) | 40.5 (27–46)         |
| Risk factors         | Asbestos exposure (two cases). |
| Clinical findings    | Asbestos exposure (12 cases). |
| Mesotheloma extent   | Limited to pericardium and encased to heart (11 cases). |
| Histopathology       | Epithelioid malignant mesothelioma (23 cases). |
| Cytopathology        | Deciduoid malignant mesothelioma (one case). |

*Our case included.*

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