Diagnostic challenges of pericardial mesothelioma: A case report and review of literature

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Abstract

Primary pericardial malignant mesothelioma (PPMM) is a rare malignancy arising from the serous mesothelial lining of the pericardium. These neoplasms are aggressive, pose diagnostic difficulties, and have a poor prognosis. The median survival is less than six months. Presenting symptoms are non-specific and include fatigue, dyspnea, and low-grade fever. Given the nature of presenting symptoms, it is imperative that appropriate imaging, tissue sampling, and histological analysis are undertaken to establish a clinical diagnosis. In cases of localised disease, surgical resection remains the primary treatment. In advanced disease, chemotherapy or palliative procedures may be beneficial. We describe two cases of PPMM and provide an update and guidance on the contemporaneous management of this challenging condition.

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Declarations

Consent for publication

Both patients in this case report provided written informed consent to report their case. Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Ethics approval

Ethical approval was not needed for compiling this case report.

Availability of data and materials

Not applicable

Permission to reproduce material from other sources

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Authors contribution

YT, SS, DM and NK were all involved in the conception, critical revision, and final approval of this article. YT drafted the initial version of the article.

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Abstract

Primary pericardial malignant mesothelioma (PPMM) is a rare malignancy arising from the serous mesothelial lining of the pericardium. These neoplasms are aggressive, pose diagnostic difficulties, and have a poor prognosis. The median survival is less than six months. Presenting symptoms are non-specific and include fatigue, dyspnea, and low-grade fever. Given the nature of presenting symptoms, it is imperative that appropriate imaging, tissue sampling, and histological analysis are undertaken to establish a clinical diagnosis. In cases of localised disease, surgical resection remains the primary treatment. In advanced disease, chemotherapy or palliative procedures may be beneficial. We describe two cases of PPMM and provide an update and guidance on the contemporaneous management of this challenging condition.

Background

Malignant mesotheliomas are aggressive neoplasms arising from the mesothelial cells that line the pleura, peritoneum, pericardium, and tunica vaginalis. Most cases reported in the literature involve the pleura. PPMM is a rare malignancy with an incidence of 0.002% of all primary cancers and accounts for less than 1% of malignant mesotheliomas.[1] Patients with PPMM present with non-specific symptoms, which include fatigue, general weakness, and dyspnea.[2] Being a rare malignancy with non-specific presenting symptoms, most cases of PPMM are typically diagnosed at an advanced stage or during autopsy. Currently, there is no consensus on optimal treatment for PPMM.[3] While surgical resection may be curative in the early stages of the disease, there is a lack of therapeutic options for more advanced disease. Accordingly, there is an associated poor prognosis with high mid-term mortality. We herein present two cases of PPMM from a tertiary hospital that demonstrates the diagnostic and therapeutic complexity.

Case 1

A 75-year-old woman presented with a 4-month history of progressively worsening dyspnoea, 6kg of unintentional weight loss, intermittent fevers and chest pain. She had a left breast lumpectomy for medullary carcinoma with adjunct radiotherapy in thirty years previously. Follow-up mammograms were negative for recurrence. She stopped smoking 50 years ago and had no exposure to tuberculosis or asbestos. A computed tomography (CT) chest scan revealed a markedly thickened pericardium (predominantly parietal) with dense pericardial fluid. Two large pericardial masses measuring 18mm in diameter were noted anterior

to the right ventricle, protruding into the intra-pericardial fat (Figure 1). There was no significant mediastinal lymphadenopathy. A transthoracic echocardiogram (TTE) confirmed these findings. Percutaneous ultrasound-guided biopsy was non-diagnostic. The pericardial masses were excised through a lower mini-sternotomy. Histopathology of the pericardial masses revealed malignant mesothelioma with homozygous deletion of CDKN2A (9p21) (Fig 2 and 3). Following discussion at the thoracic multidisciplinary meeting, she was referred to medical oncology for palliative chemotherapy. Unfortunately, her dyspnoea and exercise tolerance deteriorated, and she died two months following her formal diagnosis.

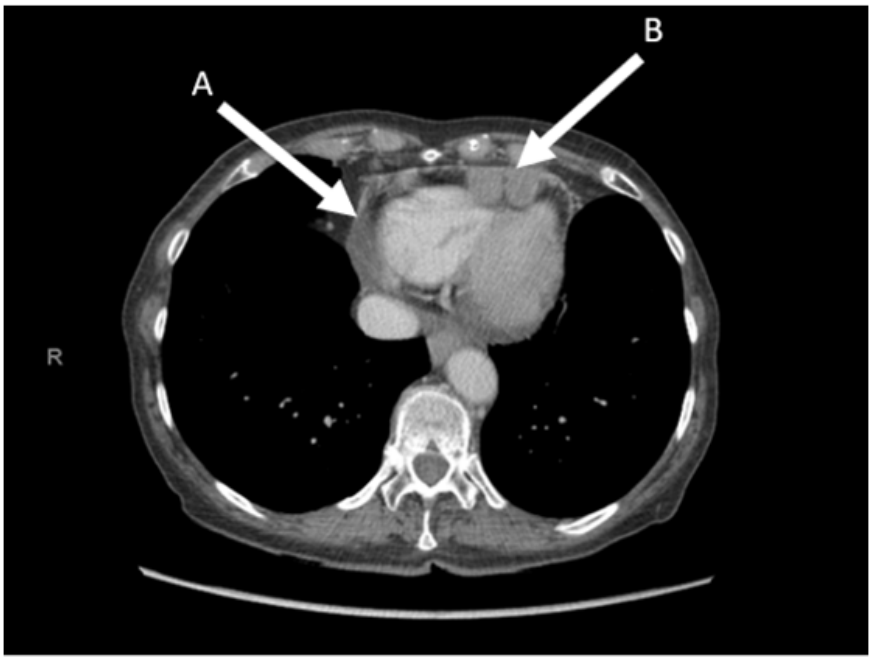

Figure 1: Axial CT scan showing thickened pericardium (A) and two large pericardial masses anterior to the right ventricle (B).

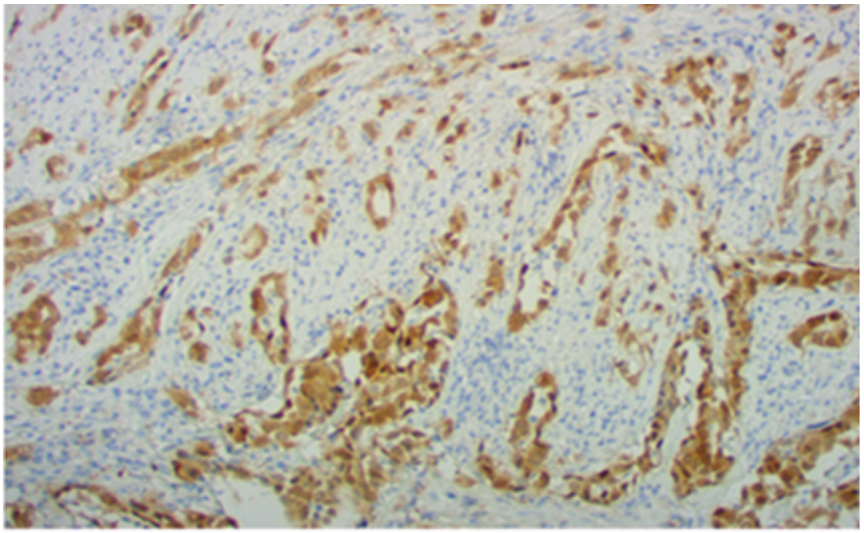

Figure 2: Histology demonstrating calretinin positive staining, characteristic for mesothelial cell proliferation.

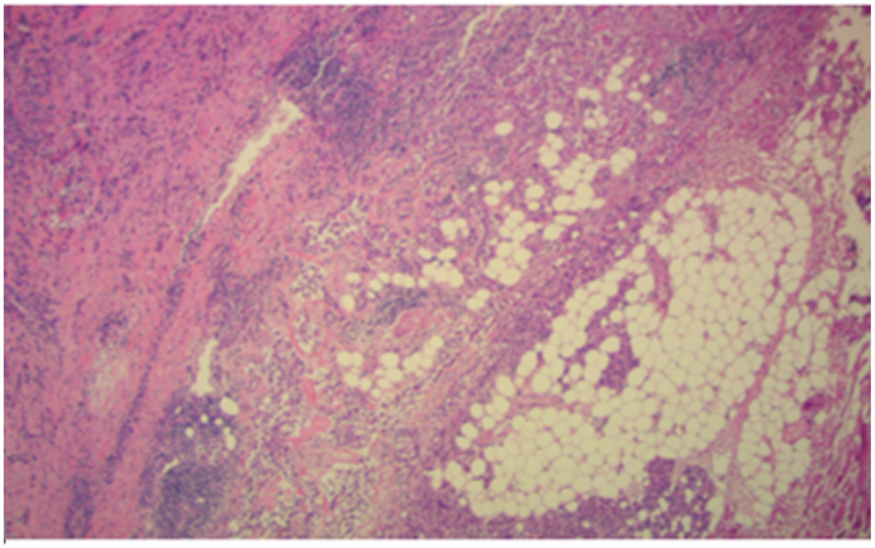

Figure 3: Haematoxylin and eosin staining demonstrating infiltration by epithelioid cells into adipose tissue.

Case 2

A 77-year-old man presented with a two-month history of worsening dyspnea, fatigue, and decreased exercise tolerance. He had a percutaneous coronary intervention to the left anterior descending and circumflex arteries ten years earlier. He was a non-smoker with no previous asbestos exposure. A TTE demonstrated global pericardial effusion with an echo dense structure attached to the basal posterior wall of the pericardium. A chest CT scan revealed an irregular soft tissue mass posterior to the left atrium measuring 75x47mm in axial dimensions (Figure 4). Bilateral pleural effusions were evident in the absence of pulmonary nodules, mediastinal or hilar lymphadenopathy. Pericardial biopsy was taken through a left anterior thoracotomy, and a pericardial window was created to prevent pericardial tamponade. Histopathology demonstrated

sarcomatous mesothelioma with homozygous deletion of CDKN2A (Fig 5). This patient was discussed in the thoracic multidisciplinary meeting, and was referred to medical oncology for palliative management due to the presence of extensive disease. He was readmitted to hospital a month later with pulmonary embolism and died shortly after admission.

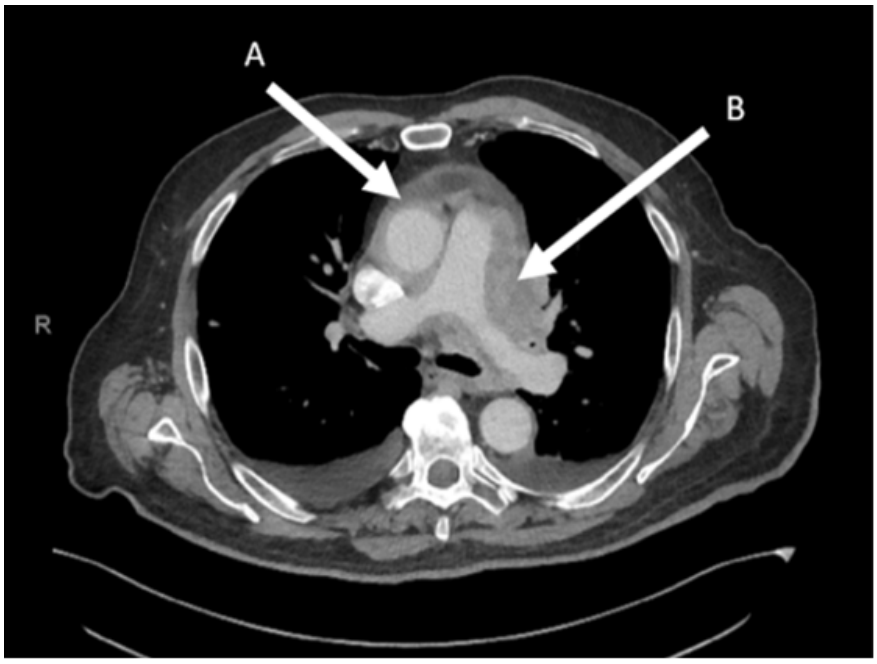

Figure 4: Axial CT scan showing global pericardial effusion (A) and an irregular soft tissue mass (B).

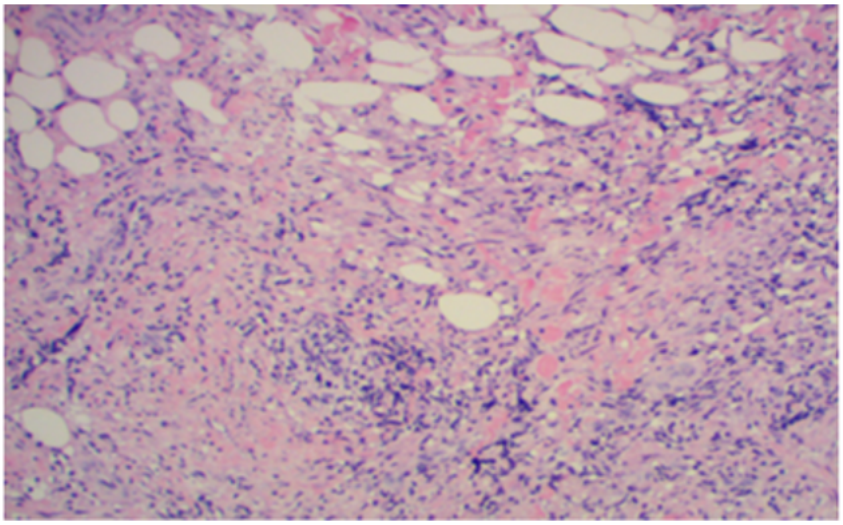

Figure 5: Histology demonstrating irregular proliferation of spindle cells with pleomorphic nuclei extending into adipose tissue

Discussion

PPMM is a rare malignancy that is more frequent in males in their fifth to seventh decades .[4] As outlined in our 2 cases, the combination of an aggressive malignancy, non-specific presenting symptoms, diagnostic complexities, and ineffective treatment options results in a poor prognosis with high mortality. Once the diagnosis is established, one-year survival is 22%, with a median survival rate of two months.[4,5] The most common cause of death is cardiac tamponade, heart failure, or pulmonary embolism. One of our patients died two months after diagnosis due to progressive disease.[6] The other patient also died two months after diagnosis due to pulmonary embolism, most likely due to the hypercoagulable state caused by the underlying malignancy.

The presenting symptoms are largely insidious and include dry cough, dyspnea, fatigue, and low-grade fevers. A review of 103 cases published in 2018 reported that 92% of all patients were symptomatic upon presentation.[7] The reported median time for a diagnosis was three months.[7] The frequent delay in diagnosis is due to the non-specific constellation of symptoms and the challenges of tissue sampling in this anatomic site.

PPMM may arise as a localized or diffuse mass. The three histological types are epithelioid (60%), sarcomatoid (20%), and biphasic (20%), with epithelioid tumours conferring a better prognosis.[8] While one of our patient's had an epithelioid subtype and the other had a sarcomatoid subtype, both died around the same duration after diagnosis was established. As opposed to pleural and peritoneal mesotheliomas which are generally associated with asbestos exposure, PPMM has not been directly associated with asbestos exposure. Instead, genetics, infection, recurrent serosal inflammation, radiation, and chemical exposure have been proposed to play a part. None of our patients had exposure to asbestos.[1,2,4]

A recent review of PPMM cases identified that 12.6% of patients were diagnosed through autopsy, which is a significant improvement from the 75% postmortem diagnosis cited in prior studies.[7]While cytological analysis from pericardiocentesis may be performed, the procedure yields malignant cells in only 20% of cases.[9] Imaging modalities may help identify functional cardiac evaluation, involvement of adjacent structures, degree of constriction, extent of metastasis, and involvement of neoplasm of the pleura. Evidence from the literature confirms that the most accurate diagnostic procedure is the histopathological analysis of tissue obtained through biopsy or surgical resection.[3]Fluorescence in situ hybridization (FISH) of our patients showed that both had 9p21 deletions. Several studies have stated that homozygous deletion of the 9p21 gene locus is linked to a poor prognosis and higher mortality rate.[10] Given the diagnostic challenges, perhaps genomic profiling may facilitate early detection, and there may be avenues for targeted gene therapy in the future.

There is no consensus on treatment strategies for patients with PPMM. In the early stages of malignancy, where the tumor is localized, surgical resection confers a survival benefit. McGehee et al. reported that mass resection resulted in median survival of 27 months compared to a median survival of 3 months in patients who did not undergo resection.[7] However, surgery is challenging as there is a risk of damage to local neurovascular structures, epicardium, and myocardium. With palliative intent, surgical drainage of large pericardial effusions may improve their quality of life[2].

As the response to radiotherapy is poor, chemotherapy has been utilized as an adjuvant to surgery or used solely in extensive malignancy. Both of our patients received chemotherapy, as surgical resection was deemed not to be beneficial to their prognosis. However, they died soon after the commencement of chemotherapy. Studies have shown that a combination of doxorubicin, vincristine, and cyclophosphamide reduces tumour progression prolonging survival up to 17.5 months.[11]Similarly, a study conducted by Kim et al. reported that combining cisplatin, gemcitabine, and vinorelbine in 4 cycles enabled the patient to remain disease-free for 24 months after completion of chemotherapy.[2]

Newer therapies for PPMM including anti-angiogenesis drugs, photodynamic therapy, gene therapy, biologic response modifiers, and more targeted chemotherapy regimens are currently undergoing clinical trials. These therapies provide hope for better treatment options in the future.[2,6,11] Presently it appears multimodal therapy confers the most notable median survival rate in patients diagnosed with PPMM.

Conclusion

PPM remains a rare and poorly understood malignancy of undetermined aetiology. This case report highlights the challenges in the diagnosis and management of PPMM. Given its non-specific symptoms, diagnosis is usually delayed leading to extensive unresectable disease. It is unlikely there will be a consensus soon on managing these patients. Thus, the clinical judgment of the treating surgeon will continue to play a significant role in deciding optimal treatment for the patient. Overall, a multimodal approach of combining surgery and chemotherapy seems to be the best treatment option, with more upcoming treatment modalities currently under clinical trials.

List of abbreviations

Abbreviation	Explanation
PPMM	Primary pericardial malignant mesothelioma
CT	Computed tomography
TTE	Transthoracic echocardiogram
FISH	Fluorescence in situ hybridization

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