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PERICARDIAL DISEASE (AL KLEIN AND CL JELLIS, SECTION EDITORS)

Pericardial Cysts: a Contemporary Comprehensive Review

Mohamed Khayata[1] · Saqer Alkharabsheh[2] · Nishant P. Shah[2] · Allan L. Klein[2]

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Abstract

Purpose of Review This is an in-depth review on the etiology, clinical manifestation, differential diagnosis, diagnostic modalities, complications, and management of pericardial cysts (PCs).

Recent Findings PCs are the third most common type of mediastinal masses and are usually identified incidentally by chest x-ray (CXR) or transthoracic echocardiography (TTE). Although most PCs are asymptomatic, they might lead to serious complications such as cardiac tamponade. Diagnosis is confirmed by cardiac computed tomography or cardiac magnetic resonance. Cysts need to be followed by imaging every 1 to 2 years; however, a recent report suggested less frequent follow-up. Most cases resolve spontaneously, but if needed, aspiration or surgical resection can be done.

Summary PCs are rare entities and are usually detected incidentally after CXR or TTE. Providers should be aware of this condition since it could potentially lead to serious complications.

Keywords Mediastinal masses · Pericardium abnormalities · Pericardial cysts · Pericardial imaging

Introduction

Cystic mediastinal lesions are uncommon entities in adults [1•]. They can arise from pericardial, bronchogenic, or enteric origins [1•]. The pericardium is anatomically structured as an outer fibrous layer and inner serous sac containing a visceral and parietal layer composed of mesothelial cells [2]. The normal thickness of the pericardial sac is less than 2 mm, and it contains approximately 25 to 50 ml of fluid [2].

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✉ Allan L. Klein
kleina@ccf.org

Mohamed Khayata
khayatm@ccf.org

Saqer Alkharabsheh
alkhars@ccf.org

Nishant P. Shah
shahn2@ccf.org

[1] Department of Internal Medicine, Cleveland Clinic, Cleveland, OH, USA

[2] Center for the Diagnosis and Treatment of Pericardial Disease, Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH, USA

Pericardial cysts (PCs) account for 6% of mediastinal masses (third most common type) and 33% of mediastinal cysts with an estimated incidence of 1 per 100,000 [3–5]. Nevertheless, this prevalence is believed to be underestimated since most patients remain asymptomatic [6].

PCs were previously thought to be equally common in men and women [7], although a recent review showed female predominance (67%) [8••]. They are more likely to be detected between the third and fifth decade of life [6, 8••]; however, one case was detected at the age of 102 years [6].

PCs can be simple or complex. Simple cysts contain fluid only. Complex cysts, on the other hand, are defined as the presence of solid elements within the cyst or the presence of internal septations [8••]. Simple cysts are more prevalent and typically uniloculated and smooth in contour, containing clear water-like fluid with occasional addition of blood and necrotic content [9]. Their size ranges between 2 and 28 cm [10], but usually measures less than 5 cm [6]. The cyst wall is formed of connective tissue lined by mesothelial cells [9]. Traditionally, they are more likely to be located at the right cardiophrenic angle (51% to 70%) followed by the left cardiophrenic angle (28% to 38%) and unlikely in other mediastinal sites [4]. A pericardial cyst fused to the right ventricle has also been described [1•]. Cysts typically occur in isolation, with multiple cysts being rare [8••].

Despite PCs being increasingly identified in the general population, limited data remain regarding the clinical course and the appropriate follow-up for these patients [8••].

How Often Is the Diagnosis Missed?

Mr. Smith is a 27-year-old male with no previous medical history who has been complaining of intermittent, non-exertional chest pain for approximately 10 years. For a few weeks, he has been complaining of exertional shortness of breath, and exercise-related dizziness and nausea. The night before he was seen by his primary care physician, he woke up in the middle of the night complaining of bilateral hand numbness, diaphoresis, and midsternal stabbing chest pain. When evaluated, he had elevated blood pressure and was sent to the emergency department. Physical examination was unremarkable except for elevated blood pressure. Electrocardiogram (EKG) showed normal sinus rhythm and chest x-ray (CXR) showed asymmetric prominence in the right cardiophrenic region. Chest computed tomography (CT) with contrast showed fluid containing a sharply circumscribed lesion measuring 7.5 × 3 cm. Outpatient transthoracic echocardiography (TTE) subsequently showed an echolucent space adjacent to the right atrium (RA), and cardiac magnetic resonance (CMR) confirmed a 7.6 × 2.5 cm simple pericardial cyst adjacent to the RA.

At follow-up, he complained of more exertional chest pressure and infrequent palpitations. Mr. Smith had a robotic-assisted cyst resection 9 months after his presentation with resolution of his symptoms. Follow-up imaging showed no evidence of recurrence.

Was the diagnosis delayed for Mr. Smith given his chronic complaint? Should providers think about pericardial cysts as differential for recurrent chest pain? Was Mr. Smith at risk of serious complication had his diagnosis delayed further?

Etiology

The etiology of PCs can be classified into two categories: congenital and acquired, with the congenital or idiopathic type being more common [11, 12]. Embryologically, the pericardium arises from lacunas that gradually merge and form the pericardial cavity. When the lacunas fail to unite, they metamorphosize into a cyst wall composed of a thin layer of fibrous tissue lined with a single layer of mesothelial cells, leading to pericardial cyst formation [11]. "Pinching off" of ventral pericardial recess and congenital localized weakness of the pericardium are other possible congenital etiologies [11].

Acquired PCs might occur as a result of inflammatory cysts, which comprise pseudocysts as well as encapsulated and loculated pericardial effusions [13••]. These encapsulated or loculated pericardial effusions are likely to be caused by inflammation, which might be due to rheumatic pericarditis, trauma or cardiac surgery concomitant pericarditis, post-myocardial infarction pericarditis, latent viral infectious pericarditis, or underlying infection after aspiration [10, 13••, 14]. Infections such as echinococcosis hydatid cysts and tuberculosis have been described as causes of PCs [15, 16]. Malignant metastasis is another acquired etiology [17].

Clinical Manifestation and Differential Diagnosis

The majority of PCs are asymptomatic and usually are detected incidentally [18]. The clinical manifestations of pericardial cysts vary depending on the location of the cyst. Overall, symptoms are pleuritic chest pain, dyspnea, palpitations [18], cough, dysphagia [6], fever, weight loss [2], and paroxysmal tachycardia [19]. Dizziness and syncope were also reported [1•]. Alkharabsheh and colleagues reported 103 cases of pericardial cysts, and chest pain was the most common complaint, followed by dyspnea and palpitations [8••]. Pain is explained by stretching, pulling, or touching the visceral innervation fibers of the pericardium [20]. Paresthesia and thoracic back pain with mixed dermatomal distribution were described and thought to be related to pericardium stretching, leading to interrupted normal vagal innervation [20].

Main differential diagnoses, which should be considered when evaluating PCs, include bronchial cysts, localized pericardial effusion, bronchogenic neoplasm, pericardial fat pad, thymoma, mediastinal teratoma, Morgagni hernia, any simple cystic mediastinal masses, neuroenteric cyst, lymphangioma, congenital cysts of primitive foregut origin [6, 21], esophageal cyst, and congenital diaphragmatic hernia [22].

Diagnostic Modalities

CXRs show an abnormal soft tissue density or an isolated cystic shadow at the cardiophrenic angle in approximately 30% of patients (Fig. 1a) [8••, 21].

TTE is the initial diagnostic modality to evaluate symptomatic patients [23] and is usually the first-line test that incidentally detects a pericardial cyst [23]. TTE usually demonstrates a circumscribed, thin-walled, echo-free space adjacent to the cardiac border filled with fluid that lacks any flow by color Doppler (Fig. 1b) [23]. Common locations for cysts are adjacent to the right atrium and frequently cause extrinsic compression [23]. Diverticulae can be differentiated from PCs by the presence of a defect in the pericardial lining [23]. It is useful to assess the hemodynamic significance of the cyst with respect to right ventricular outflow obstruction or constrictive physiology of the ventricles [24]. The main limitation of TTE

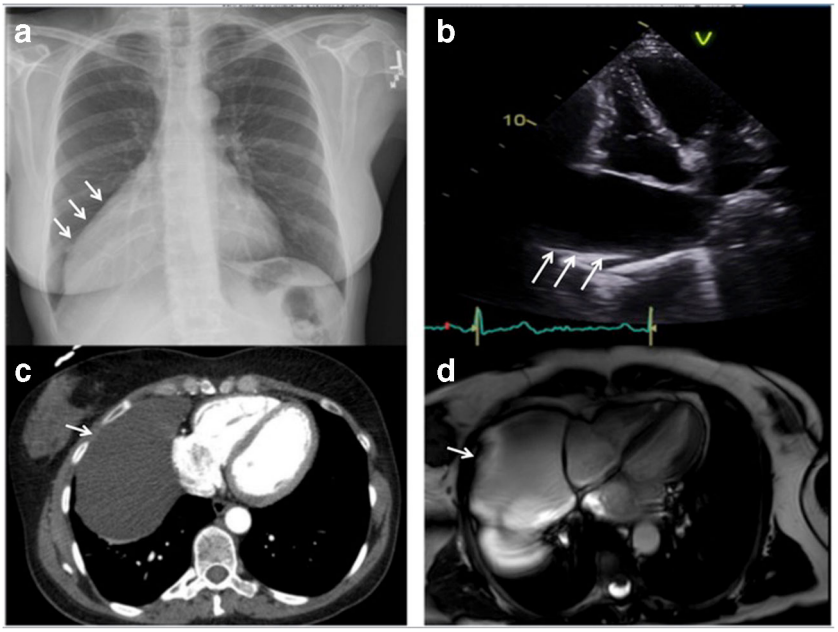

Fig. 1 **a** Chest x-ray shows soft tissue density along the right heart border (*three arrows*). **b** Transthoracic echocardiography shows a thin-walled, echo-free space adjacent to the right atrium (*three arrows*). **c** Chest CT with contrast shows thin-walled, unilocular, ovoid fluid collection, with non-enhancing structure with homogenous values, adjacent to the pericardium in the right cardiophrenic angle (*arrow*). **d** CMR images show low signal intensity in T1-weighted image (*arrow*) of cystic mass within the pericardium to the right of the right heart border

is the low sensitivity in detecting a pericardial cyst [8••]. Out of 103 cases reported by Alkharabsheh et al., TTE was able to detect 34 cases only [8••], although the sensitivity increased to 60% when TTE was used to detect left-sided cysts only [8••]. A possible explanation for this discrepancy could be, in part, the predominant location of the pericardial cyst on the right heart border where imaging quality is limited with traditional echocardiographic windows [8••]. To increase the sensitivity of the detection, off-axis views of the right heart border, e.g., superiorly oriented transthoracic subcostal views, can be used to increase the sensitivity for detection [8••]. Transesophageal echocardiography can better visualize PCs, especially if they are in atypical locations [25].

Cardiac CT provides an excellent delineation of the pericardial anatomy and shows the precise localization and characterization of various pericardial lesions [21]. Pericardial cysts on cardiac CT are typically noted to be thin-walled, well-circumscribed, unilocular, ovoid fluid collections, with non-enhancing structures, and with homogenous attenuation with water-like density. CT will usually confirm the location adjacent to the pericardium in one of the cardiophrenic angles, although they may be also found in other locations in the mediastinum (Fig. 1c) [23, 26]. PCs typically have no communication with the pericardial space and typically reside in the right cardiophrenic angle [23].

CMR of pericardial cysts typically shows a non-enhancing thin-wall mass. The fluid content of the cyst will demonstrate low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (Fig. 1d) [27, 28•]; and due to their avascularity and the absence of fibrous structure, they typically do not enhance with gadolinium-based contrast media administration [23]. Similar to TTE, PCs are distinguished from diverticulae by the presence of a complete wall and the absence of an open communication with the pericardium [8••]. Consistent with other diagnostic imaging modalities, PCs are more likely to be located in the right heart border (81%), followed by the left heart border (17%), and the least common location is the anterior mediastinum (3%) [8••].

The American Society of Echocardiography (ASE) recommends cardiac CT or CMR if a pericardial cyst is suspected by CXR or TTE [23]. CMR is superior to CT in defining the fluid nature of the cyst as some cysts may contain non-serous fluid, which has high attenuation on CT and can be mistaken for a solid mass [23]. On contrast CMR, these cysts maintain characteristically high signal intensity when imaged with T2-weighted sequences, regardless of the nature of the cyst's contents [29]. If pericardial cysts are in unusual locations, it may be difficult to distinguish them with certainty from bronchogenic or thymic cysts [23].

Finally, prenatal PCs were previously reported [11]. If present, they are more likely to be detected by 25-week sonographic examination [11]. For this population, serial sonographic examinations are suggested to reassess fetal size, sonographic characteristics, and size of cysts, potential for compression of vessels, amniotic fluid volume, and fetal hydrops [22]. After birth, neonates should be evaluated by imaging and followed for symptoms [22]; however, the frequency of follow-up in the neonatal period has not been established [23, 30].

Complications

PCs might cause compression of nearby structures leading to right ventricular outflow tract obstruction, superior vena cava syndrome, or obstruction of the right main stem

bronchus [1•]. They may also get infected or mask an underlying malignancy [1•]. Rarely, pericardial cysts can be associated with serious complications such as heart failure, cardiac tamponade, hemorrhage, rupture, constrictive pericarditis, obstruction of the right main stem bronchus, and sometimes, sudden cardiac death [4, 10, 18]. Inflamed, asymptomatic cysts may lead to increased fluid accumulation within the cyst and subsequently cyst rupture into the pericardial space, which may lead to cardiac tamponade [21]. Mitral valve prolapse and atrial fibrillation have been associated with PCs in some instances [7].

Follow-up and Management

A recent report of 103 patients with pericardial cysts who were followed for up to 2 years showed that one-third of pericardial cysts decreased in size on repeat imaging, and interval enlargement of pericardial cysts, if present, was infrequent and unlikely to be clinically significant [8••]. The current ASE recommendations for pericardial disease support serial follow-up monitoring with CT or CMR every 1 to 2 years [29]. Alkharabsheh and colleagues suggested decreasing the frequency of serial imaging to at least 3 to 5 years unless indicated by a clinical change in the patient, as the majority of patients in their study did not show significant change in the recommended follow-up imaging [8••]. Most PC cases resolve spontaneously [31]. The mechanism by which this occurs is believed to be secondary to cyst rupture, without significant pericardial effusion or tamponade [31].

Treatment options include percutaneous aspiration [32], ethanol sclerosis [33, 34], resection through video-assisted thoracoscopic surgery [18, 35], thoracotomy [18, 36], median sternotomy [8••], or laparoscopic resection [1•]. Cases that might be concerning for malignant potential should undergo operative management [1•]. Minimally invasive approaches, such as thoracoscopic surgery or laparoscopic approach, are recommended when possible, as that cyst aspiration is associated with a recurrence rate of up to 30% [1•, 4]. In a recent case series, among 11 symptomatic patients with pericardial cysts, one patient underwent aspiration and sclerosis of the pericardial cyst but developed recurrence of the pericardial cyst [8••].

The European Society of Cardiology guidelines recommend percutaneous aspiration and ethanol sclerosis as first-line treatment options if available [13••]. Although this approach is less invasive and can be done emergently [8••], it lacks the ability to make a histopathological diagnosis and is associated with higher recurrence rate due to fluid accumulation [18] with recurrence rate up to 33% within 3 years and the possibility of injury to the surrounding structures [37]. Sclerosis has been shown to decrease the recurrence rate after aspiration [7]. Indications for the surgical resection are symptomatic cases, large size, and uncertain malignant potential to prevent complications [7].

Conclusions

PCs are rare entities and are frequently underestimated. They are more likely to be single and simple. Congenital or idiopathic types are the most common etiologies. Patients are usually asymptomatic, and chest pain is the most likely complaint if present. PCs are usually detected incidentally by CXR or TTE and confirmed by cardiac CT or CMR. Large cysts might lead to serious complications such as cardiac tamponade, which can result in sudden death. Most cases resolve spontaneously, and if they become symptomatic, they can be treated by aspiration or surgical resection, with the minimum invasive surgery being the preferred technique. Clinicians should be aware of this entity and identify its course and potential complications.

Compliance with Ethical Standards

Conflict of Interest Allan L. Klein has received research grant support from Kiniksa, advisory board SOBI.

Mohamed Khayata, Saqer Alkharabsheh, and Nishant P. Shah declare that they have no conflict of interest.

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- •• Of major importance

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