Cardiol Young 2003; 13: 131–136

ISSN 1047-9511

Original Article

Large pericardial effusions of inflammatory origin in childhood

Geoffrey Chi Fung Mok, Samuel Menahem

Department of Cardiology, Royal Children's Hospital, Melbourne, Australia

Abstract *Objectives:* Our aim was to review the clinical records from children with large pericardial effusions of inflammatory origin presenting to a tertiary referral centre over the last 21 years, with emphasis on their clinical presentation, management and outcome. *Background:* The common identifiable causes of pericardial effusion in children include prior cardiac surgery, bacterial pericarditis, malignancy, and connective tissue disorders. In a significant number of children, however, despite extensive investigation, it is not possible to identify a clear aetiology. A viral cause is often considered, though rarely confirmed. The clinical course of such large idiopathic pericardial effusions in children has not been extensively reported. *Methods and results:* We reviewed retrospectively the records of all patients seen between 1981 and 2001 with large pericardial effusions of inflammatory origin requiring drainage, excluding the effusions related to cardiac surgery or malignancy. We found 31 patients fulfilling our criterions for study. They could be divided into three groups, with 15 patients having no specific identifiable aetiology despite extensive investigation, 12 patients having evidence of bacterial pericarditis, and four with a probable immunologic disorder. Fever was present in only eight patients (53%) in the idiopathic group. All patients in the other groups had fever. Except for fever and the resultant tachycardia, it was not possible to distinguish on clinical grounds, nor on the presence or otherwise of cardiac tamponade, between those with idiopathic aetiology and those with bacterial infection. Of the patients with presumed bacterial pericarditis, five (42%) had both positive blood and pericardial fluid cultures, three (25%) had positive blood cultures, while a further three patients (25%) had only positive pericardial fluid cultures. All patients required drainage of the pericardial effusion, either under echocardiographic guidance or surgically. None of the patients died. The hospital stay was significantly shorter for those with idiopathic as opposed to bacterial pericarditis. Of those with an idiopathic aetiology, six required readmission due to recurrence of the pericardial effusion, with four patients requiring further surgical drainage. No patients required readmission with a bacterial or immunologic aetiology. No patient developed constrictive pericarditis after a median follow-up of 22 months. *Conclusion:* Patients with large idiopathic pericardial effusion had relatively few constitutional symptoms as compared with their gross echocardiographic findings. Those with bacterial pericarditis had more urgent need for treatment. Patients with pericardial effusion of inflammatory origin, when treated appropriately, had an excellent outcome with no mortality or development of constrictive pericarditis.

Keywords: Inflammation; pericardiocentesis; bacterial pericarditis

Pericardial effusions are rare in childhood.[1] The common identifiable causes of such effusions include previous cardiac surgery, bacterial pericarditis, malignancy, and connective tissue disorders.[2] In a significant number of cases, it is not possible to identify the cause, despite extensive investigations.[3] A viral aetiology has been assumed, but often with no confirmatory evidence despite viral serology and cultures. Such idiopathic effusions account for between one-fifth and one-third of cases in series involving adults.[2,4,5]

Information in children, however, is limited. Acute pericarditis causing a large pericardial effusion with cardiac compression necessitating drainage is rare in

Correspondence to: Prof Samuel Menahem, Department of Cardiology, Royal Children's Hospital, Murdoch Children's Research Institute, University of Melbourne, Flemington Road, Parkville, Victoria 3052, Australia. Tel: 61 3 9345 5922; Fax: 61 3 9345 6001; E-mail: sam.menahem@rch.org.au

Accepted for publication 25 November 2002

childhood.[6] Bacterial pericarditis has been more intensively studied because of the importance of prompt diagnosis and early treatment.[7,8] Likewise, pericardial effusions associated with malignancy, or those following cardiothoracic surgery, have been well described.[9,10]

Our purpose, therefore, was to review our experience of large pericardial effusions of inflammatory origin in childhood, paying special reference to their clinical presentation, management and outcome. We hoped to determine if there were features based on the clinical findings and investigations that might help distinguish the aetiology.

Methods and results

We reviewed the records from all patients admitted to a tertiary children's hospital between 1981 and 2001 with a diagnosis of large pericardial effusion. Those who had a pericardial effusion associated with cardiac surgery, neoplasm, or other known cause, were excluded. We divided the identified patients into three subgroups:

- Those with no identifiable aetiology for the effusion despite extensive investigation.
- Those with bacterial pericarditis proven by positive cultures from blood and or pericardial fluid.
- Those with associated autoimmune disease, including connective tissue disorders or inflammatory bowel disease.

The records of each patient were reviewed, and the relevant investigations analyzed. Their management and outcome were summarized. Data were reported as absolute numbers and frequency percentages with mean and standard deviation unless otherwise specified. Categorical data were analyzed by the two-tailed chi-square test or Fisher's exact test where appropriate, while continuous variables with non-Gaussian distribution were compared using the Mann–Whitney U test.[11] The result was considered statistically significant if the p value was less than 0.05.

Characteristics of patients

Over the 21-year period from 1981 to 2001, 31 patients were admitted with large pericardial effusions of inflammatory origin requiring drainage (Table 1). The co-existing disorders discovered in the patients without any identified aetiological feature are not known to be associated with pericardial effusions. One patient with bacterial pericarditis, although not having positive cultures from blood or pericardial fluid, had a cellulitis involving the neck and upper chest wall at the time of the pericardial effusion. Pericardial drainage yielded purulent pericardial fluid and the clinical picture was compatible with bacterial pericarditis. Of the patients with immunologic problems, two presented with a pericardial effusion, and only subsequently developed features suggestive of arthritis. There was a tendency for younger patients to have bacterial involvement, in contrast to older ones who revealed no aetiologic features. There was no sex preponderance in any group.

Clinical presentation

The majority of patients presented with fever, chest pain, and dyspnoea of relatively short duration (Table 2). Only one-half of those in the idiopathic group presented with fever, compared with all the patients having bacterial involvement or immunologic problems ($p = 0.008$). Clinical features of cardiac tamponade were found in one quarter of those with idiopathic effusions, half of those with bacterial

Table 1. Characteristics of patients with large pericardial effusion of inflammatory origin.

	Idiopathic (n = 15)	Bacterial (n = 12)	Immunologic (n = 4)	p value
Age (years, median with range)	9.7* (0.1–14.6)	2.1* (0.4–16)	9.2 (1.3–16.4)	0.13*
Sex				
Male	5 (33%)	7 (58%)	3 (75%)	
Female	10 (67%)	5 (42%)	1 (25%)	
Co-existing disease	Rothmund-Thomson syndrome (1) Soto syndrome (1) Haemoglobin H disease (1)		Juvenile chronic arthritis (2) Mixed connective tissue disease (1) Crohn's disease (1)	
Positive bacterial culture		*Staphylococcus aureus* (4) *Haemophilus influenzae* (4) *Streptococcus pneumoniae* (1) Group A *streptococcus* (1) Coagulase negative *staphylococcus* (1)		

https://doi.org/10.1017/S104795110300026X Published online by Cambridge University Press

infection, and in one of the four patients with immunologic problems. No significant differences were found in the occurrence of other clinical features or cardiac tamponade between those with an idiopathic or bacterial aetiology, with the exception of fever and tachycardia ($p = 0.043$), which may have simply reflected the presence of fever.

Investigations

Table 3 summarizes the relevant investigations. Echocardiography reliably identified the effusions (Fig. 1). There was no significant difference in the presence of echocardiographic evidence of tamponade between those having idiopathic or bacterial effusions. Nor were there significant differences between the idiopathic and the bacterial groups in terms of the total white cell count, neutrophil count, platelet count, erythrocyte sedimentation rate and C-reactive protein. There were no positive cultures from blood or pericardial fluid in those with an idiopathic or immunologic aetiology. In patients with bacterial pericarditis, five patients had positive cultures from both blood and pericardial fluid, while three patients each had positive

Table 2. Clinical presentation of patients with large pericardial effusion of inflammatory origin.

	Idiopathic (n = 15)	Bacterial (n = 12)	Immunologic (n = 4)	p value*
Symptoms				
Fever	8 (53%)	12 (100%)	4 (100%)	0.008
Chest pain	5 (33%)	0 (0%)	2 (50%)	
Dyspnoea	8 (53%)	6 (50%)	3 (75%)	
Duration of symptoms (days)†	5 (2–30)	2.5 (1–20)	6 (5–14)	
Signs				
Tachypnoea	8 (53%)	10 (83%)	4 (100%)	0.22
Tachycardia	8 (53%)	11 (92%)	4 (100%)	0.043
Hypotension	0	2 (17%)	1 (25%)	
Poor peripheral perfusion	1 (7%)	2 (17%)	2 (50%)	
Pulsus paradoxus	2 (13%)	4 (33%)	1 (25%)	
Peripheral oedema	2 (13%)	1 (8%)	0	
Raised jugular venous pressure	6 (40%)	5 (42%)	3 (75%)	
Muffled heart sounds	6 (40%)	5 (42%)	2 (50%)	
Gallop rhythm	1 (7%)	1 (8%)	1 (25%)	
Pericardial rub	2 (13%)	2 (17%)	2 (50%)	
Hepatomegaly	9 (60%)	8 (67%)	2 (50%)	

*Comparison between idiopathic and bacterial group; †median with range.

Table 3. Investigations of patients with large pericardial effusion of inflammatory origin.

	Idiopathic (n = 15)	Bacterial (n = 12)	Immunologic (n = 4)	p value*
Electrocardiography				
Sinus tachycardia	6 (40%)	10 (83%)	4 (100%)	
ST segment abnormalities	1 (7%)	7 (58%)	1 (25%)	
Low QRS voltage	3 (20%)	2 (17%)	0	
Chest radiography				
Cardiomegaly	14 (93%)	10 (83%)	4 (100%)	
Pleural effusion	6 (40%)	5 (42%)	0	
Consolidation	0 (0%)	3 (25%)	3 (75%)	
Echocardiography				
Subnormal contractility	0	3 (25%)	2 (50%)	
Diastolic compression	7 (47%)	4 (33%)	2 (50%)	0.70
Blood				
Total leucocyte count (10^9/L)	16.2 ± 6.8	20.8 ± 17.1	13.7 ± 7.7	0.46
Neutrophil count (10^9/L)	9.4 ± 6.6	14.3 ± 14.8	9.4 ± 6.6	0.39
Platelet count (10^9/L)	477 ± 174	380 ± 160	562 ± 267	0.14
Erythrocyte sedimentation rate (mm† in 1 hr)	53.3 ± 30.3	95.8 ± 25.7	91.3 ± 25.4	
C-reactive protein (mg‡/L)	121 ± 96.3	187	227 ± 79.9	

*Comparison between idiopathic and bacterial group: †mm: millimeter; ‡mg: milligram.

https://doi.org/10.1017/S104795110300026X Published online by Cambridge University Press

cultures from either blood or pericardial fluid. The remaining patient, with adjacent cellulites, did not have a positive culture, neither from blood nor pericardial fluid. The organisms responsible for the bacterial pericarditis are shown in Table 1. No patient in any group had positive virologic findings from serology or culture.

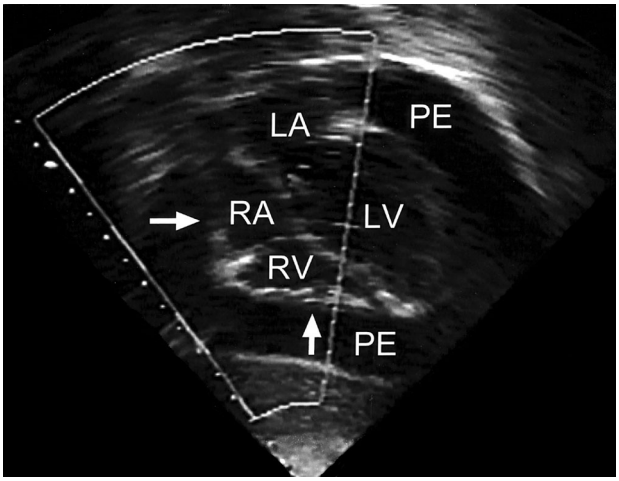

Figure 1.
The echocardiographic findings, in four chamber projection, in a patient with a large circumferential pericardial effusion (PE) of inflammatory origin. Arrows indicate the presence of diastolic collapse of right atrium and right ventricular free wall, which signifies early compression. RA: right atrium; RV: right ventricle; LA: left atrium; LV: left ventricle.

Interventions

All patients required drainage of the pericardial effusion, which was performed either under echocardiographic guidance or surgically. None of the patients developed complications from the drainage (Table 4).

Echocardiographically-guided pericardiocentesis was unsuccessful in two patients who subsequently underwent surgical drainage. A pericardio-pleural window was created in a one-month-old infant at the same time as surgical drainage.

The medications prescribed for the patients are summarized in Table 4. One teenager with an idiopathic aetiology received colchicine after an unsuccessful trial of aspirin, where further reaccumulation necessitated repeated surgical drainage and the creation of a pericardio-pleural window. She remains well more than twelve months later, and no longer requires medication.

Outcome (Table 4)

There were no deaths. Patients with an idiopathic aetiology had a significantly shorter stay in hospital compared with patients having bacterial infection ($p = 0.0001$). No patients with bacterial infection

Table 4. Intervention and outcome in patients with large pericardial effusion of inflammatory origin.

	Idiopathic (n = 15)	Bacterial (n = 12)	Immunologic (n = 4)	p value*
Pericardiocentesis				
Echocardiography-guided	4 (27%)	1 (8%)	3 (75%)	
Surgical	7 (47%)	10 (83%)	1 (25%)	
Both	4 (27%)	1 (8%)	0	
Estimated amounts (range, millilitre)	55–700	50–500	30–600	
Pericardiectomy	2 (13%)	1 (8%)	0	
Medications				
Antibiotics	6 (40%)	12 (100%)	4 (100%)	
Duration (range, days)	1–10	9–28	5–14	
Non-steroidal anti-inflammatory drugs	9 (60%)	2 (17%)	1 (25%)	
Duration (range, days)	21–480	30	14	
Steroid	1 (7%)	0	2 (50%)	
Diuretics	3 (20%)	2 (17%)	2 (50%)	
Inotropes	0	2 (17%)	0	
Outcome				
Death	0	0	0	
Hospital stay (days)	7.2 ± 2.7	18.8 ± 9.3	12.0 ± 2.5	0.0001
Readmission	6 (40%)	0	0	0.02
Reoperation	5 (33%)	1 (8%)	0	0.18
Complete resolution of effusion (days)	109 ± 144	24.0 ± 20.1	14.8 ± 4.7	0.10
Constrictive pericarditis	0	0	0	

*Comparison between idiopathic and bacterial group.

https://doi.org/10.1017/S104795110300026X Published online by Cambridge University Press

or immunologic problems required readmission due to reaccumulation of the pericardial effusion. In contrast, six patients, just under one-half of those with an idiopathic aetiology required readmission following recurrence of the pericardial effusion ($p = 0.02$). They were readmitted from 7 to 90 days after their initial discharge from hospital. Repeated surgical drainage of the pericardial effusion was needed in four, with one needing pericardectomy while the other required creation of a pericardio-pleural window.

The median period of follow-up was 22 months, with a range from 2 to 187 months. None of the patients have developed constrictive pericarditis. The time taken for complete resolution of the pericardial effusion was longer in those with no identified aetiology, but the result was not statistically significant ($p = 0.10$).

Discussion

A prompt diagnosis of bacterial pericarditis allows for early antibiotic therapy.[7,8] Such patients typically present with septicaemia. A septic focus may be identified elsewhere, and may originate from a pneumonia with or without a pleural effusion and/or empyema.[8] In such patients, there is usually a neutrophilia, raised C-reactive protein, and positive cultures are obtained from blood or an infected focus elsewhere, or else from the pericardial fluid itself. Our review has shown, however, that bacterial pericarditis may not be readily distinguished from other causes of pericardial effusion merely on clinical and laboratory grounds without microbiological confirmation. Our patients with bacterial pericarditis were febrile on presentation, and appeared more toxic as a result of the underlying infective process or septicaemia. But there was no significant difference between the groups with respect to the presence of cardiac tamponade. The total white cell count, neutrophil count, erythrocyte sedimentation rate and C-reactive protein were all higher in those with bacterial infection as compared to those with no identified aetiology, while the patients with immunological problems had a high erythrocyte sedimentation rage and C-reactive protein, with only a mild elevation in the white cell count. Their platelet counts were also elevated. We emphasize again the need for positive cultures to diagnose bacterial pericarditis. Thus, pericardiocentesis may not only be therapeutic when the effusion is large, but also diagnostic.

Those with no identifiable aetiological features seem to form a distinct group. Initially, some were considered to have a viral aetiology, but viral serology and culture of the pericardial fluid both proved negative. Fever occurred in only half of these patients, as opposed to all those with bacterial infection or immunologic problems. The classical features of pericarditis, which include fever, chest pain and pericardial rub, were seldom observed in those lacking any aetiologic features. Indeed, two patients were completely asymptomatic at presentation. Only a quarter of the patients had clinical features suggestive of cardiac tamponade, though nearly half had echocardiographic evidence of this feature, with diastolic collapse of the right atrium or right ventricle. In all the patients, echocardiography revealed a large circumferential pericardial effusion exceeding one centimetre in thickness, though signs and symptoms were often relatively mild, being disproportionate to the findings at echocardiography. All of our patients had an excellent outcome after intervention, with none of them having any significant morbidity or late sequels on follow-up.

Idiopathic chronic pericardial effusion, a condition whereby a collection of pericardial effusion persists for more than three months with no apparent cause despite extensive and repeated diagnostic evaluation, has been described mainly in adults.[12] It accounts for between one tenth and one third of pericardial effusions seen in adulthood.[3] By definition, its aetiology is unknown. Many of the patients described in these series were asymptomatic, lacking constitutional symptoms. Nearly all of our patients, in contrast, presented with a relatively short history of non-specific symptoms. It was difficult, therefore, to determine how long the effusion has been present prior to presentation, and to decide whether they should be regarded as having a chronic effusion.

All our patients had their pericardial effusions drained soon after presentation, with no complications occurring when the effusion was drained surgically via the subxiphoid approach or under echocardiographic guidance. Moores et al.[13] showed that subxiphoid pericardial drainage for cardiac tamponade was associated with minimal morbidity in both children and adults. Zahn et al.[14] similarly demonstrated that percutaneous transcatheter drainage was safe and effective in chidlren. Surgical drainage appears to be preferred when there is bacterial infection, since fibrinous deposits may be removed more effectively. None of our patients died. Nor did any develop constrictive pericarditis.[15] That may be explained in part because we did not encounter any instance of tuberculous effusion, an aetiology which is well known to result in constrictive pericarditis[16] (see addendum). Despite previous reports of development of constriction subsequent to bacterial pericarditis,[7,8,17] we have not yet encountered this complication, which may occur even without evidence of earlier pericardial disease.[18]

Based on our experience, we conclude that large pericardial effusions are rare in childhood. When found, a significant proportion of such patients have no identifiable aetiology. These patients usually had relatively few clinical signs and symptoms compared

https://doi.org/10.1017/S104795110300026X Published online by Cambridge University Press

with the echocardiographic findings, and were not constitutionally unwell. It is important to distinguish them from those with bacterial pericarditis, which warrants urgent drainage and aggressive antibiotic treatment to decrease the associated mortality and morbidity. Further studies are now required to clarify the aetiology of those having neither bacterial infection nor immunological problems.

Addendum

Since compiling our data, we have encountered one child with a large tuberculosis pericarditis who required surgical drainage and a brief course of steroids. No evidence of constrictive pericarditis was noted a year later. A further adolescent presented with ascites, having had an early right serous pleural effusion drained, and was found to have a large pericardial effusion. It recurred after percutaneous drainage, and it proved necessary to create a pericardial-peritoneal window. She continued to develop ascites, only settling over six months after high dose pulsed steroids, and failed to respond to treatment with aspirin, colchine, azathioprine, and diuretics. She was considered to have a seriotitis of uncertain cause.

References

1. Rheuban KS. Pericardial diseases. In: Allen HD, Gutgesell HP, (eds). Moss and Adams' heart disease in infants, children, and adolescents: including the fetus and young adult. 6th ed. Lippincott Williams & Wilkins, 2001, pp 1287–1296.
2. Sagristà-Sauleda J, Mercé J, Permanyer-Miralda G, Soler-Soler J. Clinical clues to the causes of large pericardial effusions. Am J Med 2000; 109: 95–101.
3. Soler-Soler J, Sagristà-Sauleda J, Permanyer-Miralda G. Management of pericardial effusion. Heart 2001; 86: 235–240.
4. Callahan JA, Seward JB, Nishimura RA, et al. Two-dimensional echocardiographically guided pericardiocentesis: experience in 117 consecutive patients. Am J Cardiol 1985; 55: 476–479.
5. Gibbs CR, Watson RD, Singh SP, Lip GY. Management of pericardial effusion by drainage: a survey of 10 years' experience in a city centre general hospital serving a multiracial population. Postgrad Med J 2000; 76: 809–813.
6. Roodpeyma S, Sadeghian N. Acute pericarditis in childhood: a 10-year experience. Pediatr Cardiol 2000; 21: 363–367.
7. Sagristà-Sauleda J, Barrabés JA, Permanyer-Miralda G, Soler-Soler J. Purulent pericarditis: review of a 20-year experience in a general hospital. J Am Coll Cardiol 1993; 22: 1661–1665.
8. Dupuis C, Gronnier P, Kachaner J, et al. Bacterial pericarditis in infancy and childhood. Am J Cardiol 1994; 74: 807–809.
9. Medary I, Steinherz LJ, Aronson DC, La Quaglia MP. Cardiac tamponade in the pediatric oncology population: treatment by percutaneous catheter drainage. J Pediatr Surg 1996; 31: 197–200.
10. Tsang TS, Barnes ME, Hayes SN, et al. Clinical and echocardiographic characteristics of significant pericardial effusion following cardiothoracic surgery and outcomes of echo-guided pericardiocentesis for management. Chest 1999; 116: 322–331.
11. Bland M. An introduction to medical statistics. 2nd ed. Oxford Medical Publications, 1995.
12. Sagristà-Sauleda J, Angel J, Permanyer-Miralda G, Soler-Soler J. Long-term follow-up of idiopathic chronic pericardial effusion. N Engl J Med 1999; 341: 2054–2059.
13. Moores DW, Allen KB, Faber LP, et al. Subxiphoid pericardial drainage for pericardial tamponade. J Thorac Cradiovasc Surg 1995; 109: 546-552.
14. Zahn EM, Houde C, Benson L, Freedom RM. Percutaneous pericardial catheter drainage in childhood. Am J Cardiol 1992; 70: 678–680.
15. Blake S, Bonar S, O'Neill H, et al. Aetiology of chronic constrictive pericarditis. Br Heart J 1983; 50: 273–276.
16. Hugo-Hamman CT, Scher H, DeMoor MM. Tuberculous pericarditis in children: a review of 44 cases. Pediatr Infect Dis J 1994; 13: 13–18.
17. Cheatham JE, Grantham RN, Peyton MD, et al. *Hemophilus influenzae* purulent pericarditis in children. J Thorac Cardiovasc Surg 1980; 79: 933–936.
18. Ferreira SMAG, Ferreira Jr. AB, Morais AdoN, Paz WS, Silveira FAA. Constrictive chronic pericarditis in children. Cardiol Young 2001; 11: 210–213.