Clinical Presentation and Long-Term Outcomes of Severe Chronic Idiopathic Pericardial Effusions

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SUMMARY

Objectives
The aim of this study was to determine the frequency, clinical findings, diagnostic methods, treatment, outcome and the long-term prognosis of patients with severe chronic idiopathic pericardial effusion.

Methods
All patients with suspected severe pericardial effusion from 1992 to 2005 were prospectively analyzed following a pericardial disease protocol performed in our institution. Of a total of 152 patients, 54 had severe chronic pericardial effusion, 28 (52%) were finally diagnosed with idiopathic disease and were included in this study.

Results
The mean age was 67 ± 11 years, 82% men, 25 (89.3%) were symptomatic and presented dyspnea, 4 (16%) suffered cardiac tamponade and 10 (35.7%) showed echocardiographic signs of tamponade.
The mean long term follow up was 60 months (3-128). The 3 asymptomatic patients were not undergone pericardial drainage and had a favourable outcome (mean follow up: 42 months).
Twenty-five symptomatic patients were treated with pericardial drainage, 2 patients were lost to follow up, 14 (60.8%) did not have pericardial effusion, 3 (13%) had mild effusion, 2 (8.6%) had moderate effusion and 4 (17.2%) showed a new severe effusion. Three of them had dyspnea III-IV and required pericardiectomy and had a favourable outcome. The fourth patient remained asymptomatic.

Conclusions
Patients with severe chronic idiopathic pericardial effusion may be asymptomatic for a long time.
Despite pericardial drainage is effective in the vast majority of symptomatic patients with pericardial effusion, relapsed can be occur and pericardiectomy is a good option for those patients.

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Key words > pericardium pericarditis, pericardial effusion

Abbreviations >

FC	Functional class	**CP**	Constrictive pericarditis
SCIPE	Severe chronic idiopathic pericardial effusion	**SPB**	Systolic blood pressure
SPE	Severe pericardial effusion		

BACKGROUND

The pericardium is a serous membrane composed by two layers (parietal pericardium and visceral pericardium) which may be affected by infections, physical, traumatic and inflammatory agents, or secondarily by metabolic conditions or general diseases. Pericardial inflammation may be expressed as a simple acute peri-

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carditis or may rapidly evolve with fluid accumulation leading to cardiac tamponade. Eventually, a fibrous and retractile reaction may result in constrictive pericarditis. (1-3)

In spite of a complete diagnostic assessment, etiology cannot be determined in a significant proportion of patients with severe pericardial effusion, and these patients are referred to as having idiopathic pericardial effusions. Unlike coronary heart disease, heart failure or, to a lesser extent, valvular heart disease, there are few data from randomized trials guiding medical management of pericardial diseases. (4)

The aim of this study was to determine the frequency, clinical presentation, diagnostic methods, treatment, clinical outcomes and long-term prognosis of patients with severe chronic idiopathic pericardial effusion (SCIPE).

MATERIAL AND METHODS

Patient inclusion and studies performed

We prospectively included all out-patients and in-patients with suspected severe pericardial effusion (SPE), who were treated at our Institution from June 1992, to April 2005. The assessment was performed according to the following protocol for pericardial disease applied in our Institution:

- Complete clinical chart
- Lab tests: complete cell blood count, blood glucose, erythrocyte sedimentation rate, liver function test, renal function test, thyroid hormones, coagulation tests, Bence-Jones proteinuria, serum protein electrophoresis test, collagen test including antinuclear factor, anti-DNA test, LE cells, latex test for rheumatoid factor, Rose Reagan and c-Anca tests.
- Tuberculin Skin Test.
- Electrocardiogram
- Chest X-Ray.
- Color-Doppler echocardiography

Imaging tests were performed if lab tests failed to identify an etiology and the clinical presentation was suggestive of neoplasms: chest nuclear magnetic images and computerized tomography. Abdominal and pelvic ultrasounds were carried out if necessary.

Pericardiocentesis was performed in the following cases:

- Suspected purulent pericarditis.
- Cardiac tamponade.
- SPE with serious symptoms related to effusion (CF III-IV dyspnea or dysphagia) or electrocardiographic signs of cardiac tamponade.

Pericardial fluid was analyzed as follows:

- Bacteriological tests: Gram stain, acid-fast bacillus smear (Ziehl-Nielsen method), Indian ink preparation (fungi detection); bacterial and TB culture; radiometric culture; detection of adenosine deaminase activity or polymerase chain reaction.

Pericardial biopsy was done when pericardiocentesis failed to resolve cardiac tamponade or when this condition relapsed after pericardial drainage.

During the first year following pericardiocentesis, patient follow-up was performed every 3 months; if pericardial efussion relapsed, a new pericadiocentesis was carried out and patients were then followed-up every three months. If a new symptomatic recurrence occurred, patients underwent pericardiectomy.

Follow-up

Patients' follow-up was carried out at the out-patient's clinic, by telephone or by their primary physicians, every 3 months during the first year, and once a year thereafter.

Definitions

Severe pericardial effusion: anterior and posterior echo-free space during diastole >20 mm.

Chronic idiopathic SPE: SPE lasting for more than three months, without a positive etiologic diagnosis after having performed the aforementioned study protocol.

Cardiac tamponade: systolic blood pressure (SBP) less than 90 mmHg, paradoxical pulse (reduction greater than 10 mmHg in SBP during inspiration) and jugular engorgement.

Incipient echocardiographic signs of cardiac tamponade: SPE with right ventricle or right atrium collapse at the echocardiogram.

Acute idiopathic pericarditis: Acute idiopathic pericarditis: self-limited acute pericarditis of unproven etiology despite complete screening.

Pericardial tuberculosis: Positive Koch bacillus or caseous granuloma in pericardial fluid, pericardial tissue or in any other site in presence of pericardial involvement.

Purulent pericarditis: purulent pericardial exudates with positive bacteriologic tests.

Neoplasm-related pericardial effusions: presence of neoplastic cells in pericardial fluid or tissue.

Pericardial effusion associated with systemic disorders: in patients with uncontrolled systemic diseases, such as lupus, hypothyroidism, etc.

Statistical analysis

Quantitative data analysis was carried out using media with the corresponding standard deviation or range and categorical data were expressed in percentages. Event-free survival (SPE, need of a new pericardiocentesis or pericardiectomy) was estimated by the Kaplan-Meier method.

RESULTS

Between June 1992 and April 2005, 152 patients with pericardial diseases were assessed; 39 patients (25.6%) had acute noneffusive pericarditis, 23 (15.1%) presented with constrictive pericarditis (CP) and severe pericardial effusion was present in 90 patients (59.2%). In the group of 90 patients with SPE, 40% (n = 36) had acute or sub-acute efussions (lasting less than 3 months) and 60% (n = 54) presented chronic pericardial effusions (lasting more than 3 months).

Among those 54 patients with chronic SPE, 28 (51.8%) were finally diagnosed as idiopathic disease and an etiology could be identified in 26 patients (48.2%).

Figure 1 shows the etiology of the 54 patients with chronic severe pericardial effusion (SPE).

Among the 28 patients with SCIPE, mean age was 67 years (43 to 81 years) and 23 (82%) were male.

Table 1 shows the basal characteristics of the population.

During initial assessment, 25 patients (89.3%) were symptomatic. Dyspnea was the most frequent symptom: 8 patients (32%) were in New York Heart Association (NYHA) functional class (FC) I-II and 17 (68%) in FC III-IV. Cardiac tamponade was present in 4 patients (16%), and 10 patients (40%) had incipient echocardiographic signs of cardiac tamponade.

The most common electrocardiographic findings are shown in Table 2.

Chest X-Ray was abnormal in all patients, with an increase in cardiothoracic index, and 3 patients exhibited associated pleural effusion.

Therapeutic pericardial drainage was performed in 25 patients (89.2%) through a subxiphoid approach; a tube was placed in 21 patients and 4 patients underwent percutaneous catheter drainage. Mean tube drainage time was 2 days (1 to 13 days). No complications were reported during the procedures. The mean duration of the disease at the moment of pericardial drainage was 16.9 moths (3 to 60). Pericardial fluid was examined in all patients; the gross appearance was serohemorrhagic in 14 patients (57%), serous in 8 patients (32%) and hemorrhagic in 3 patients (12%). Pericardial biopsies showed unspecific chronic pericarditis in all patients.

Mean long-term follow-up was 60 months (range, 3 to 128) in 26/28 patients (92%, 2 patients were lost). Of all the 23 patients who had undergone pericardial drainage and completed follow-up, 14 (60.8%) did not show recurrence, 3 (13%) evolved with mild pericardial effusion and 2 (8.6%) presented moderate pericardial effusion. These patients were asymptomatic during follow-up and still remain under periodical controls. Among four patients (17.2%) with severe recurrent pericardial effusion, 3 presented dyspnea in NYHA FC III-IV and required new pericardial drainage. Subsequently, as these patients remained symptomatic with recurrent effusions, they underwent pericardiectomy with favorable outcomes; no complications were reported during surgery and they are currently free of symptoms. The remaining patient refused to undergo a new drainage and remains free of symptoms with SPE.

Figure 2 shows the event-free survival curve (SPE, new drainage and pericardiectomy).

Three patients with SCIPE did not undergo percutaneous catheter drainage; they remain asymptomatic after a mean time of 42.3 months since the beginning of the disease.

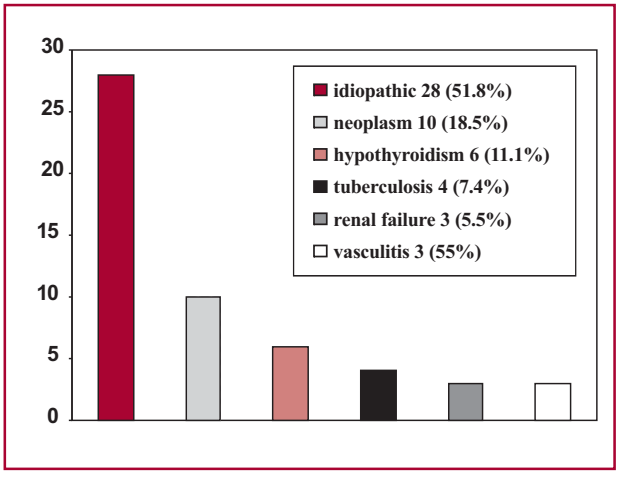

Fig. 1. Chronic severe pericardial effusion in 54 patients. Etiology

DISCUSSION

Pericardial inflammation is a response to different insults, which is generally accompanied by fluid accumulation. If fluid collection installs suddenly, hemodynamic impairment due to life-threatening cardiac tamponade occurs and pericardial drainage should be performed immediately. On the contrary, if fluid

Table 1. Population characteristics (n = 28)

Variables	n (%)
Age (mean ± SD)	67 (11.4)
Male sex	23 (82)
Hypertension	9 (32.1)
Dyslipemia	9 (32.1)
Smoking habbits	6 (21.4)
Diabetes Mellitus	3 (10.7)
Bronchial asthma	2 (7.1)
COLD	2 (7.1)

SD: Standard deviation. COLD: Chronic obstructive lung disease.

Table 2. Frequent electrocardiographic findings

Variables	n (%)
Sinus tachicardia	22 (80)
ST elevation	4 (14.2)
Atrial fibrillation	4 (14.2)
Negative T waves	3 (10.7)
Low voltaje QRS complexes	3 (10.7)
Electrical alternans	1 (35)

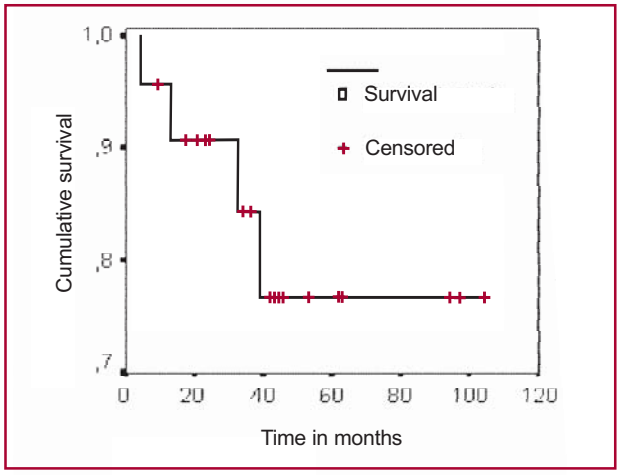

Fig. 2. Survival curve free of severe pericardial effusion (following first pericardial drainage)

accumulation is progressive, pericardial sac may tolerate huge amounts of fluid for months or even years before the patient develops symptoms. (5) Pericardial drainage is clearly indicated in two clinical situations: cardiac tamponade and suspected purulent pericarditis (with or without cardiac tamponade). (6). Indications for pericardial drainage in presence of severe pericardial effusion without clinical signs of cardiac tamponade should be individualized in the other situations. (7-9). Thus, pericardiocentesis may result unnecessary in young patients with severe pericardial effusion related to acute pericarditis who show good response to anti-inflammatory drugs. (6) Mercé et al. performed a 6-year follow-up of 71 patients with severe pericardial effusion of different etiologies (acute pericarditis, systemic diseases), without cardiac tamponade or suspected purulent pericarditis. Twenty six patients underwent a pericardial drainage procedure; diagnostic yield was 7% and none of 45 patients who did not have pericardial drainage initially (including 25 patients with right atrium or right ventricle collapse in the echocardiogram) developed cardiac tamponade during follow-up, and severe pericardial effusion was present only in two patients at the end of the follow-up period. In consequence, the authors concluded that pericadiocentesis is not necessary in such cases. (10)

According to the same authors, management of patients with idiopathic (when no underlying cause was found despite a complete screening) pericardial effusions would be different. (10)

Sagristá-Sauleda et al. published in 1999 the most important study regarding this issue, during a median 7-year follow-up of 28 patients (mean age, 61 years), of whom 13 were initially asymptomatic and 8 presented cardiac tamponade. Therapeutic pericardiocentesis was performed in 24 patients (5 with early pericardiectomy); 11 patients experienced severe recurrent effusion requiring pericardiectomy, with favorable outcomes. They concluded that despite severe idiopathic pericardial effusions are generally well tolerated, some patients may develop unexpected cardiac tamponade, suggesting that therapeutic pericardiocentesis should be performed in all patients, leaving pericardiectomy in case of recurrences. (4) Based on this study, the Spanish Society of Cardiology and the European Society of Cardiology recommend performing pericadiocentesis in all patients with SCIPE, even in the absence of cardiac tamponade or symptoms. (11, 12) Previously, these approaches had been recommended by expert consensus. (13) Nevertheless, there are some arguments against this opinon. (7)

In our Institute of Cardiology and Cardiovascular Surgery, Fundación Favaloro, SCIPE represented 18.4% of 152 patients treated for pericardial diseases during 13 years. This incidence might be overestimated, since our institution is a tertiary centre of reference mainly of cardiovascular diseases, where patients with PE associated with neoplasms, endocrinology disorders or renal failure are rarely admitted, as opposed to general hospitals. Anyway, and in spite of this, it is not an uncommon disorder, and little is known about its natural history and optimal management. (4, 6). Our experience is similar to the one reported by Sagristá-Salueda et al., with a mean follow-up of 5 years. Time between the moment of the diagnosis and the performance of the first drainage was long (mean, 16.9 months), during which patients remained asymptomatic. Subsequently, successful pericardial drainage was performed through a subxiphoid approach in all patients who developed symptoms (4 of them with cardiac tamponade); no complications were reported. The procedure solved the condition in 60% of patients. In the remaining patients, mild to moderate recurrent, well tolerated effusions occurred in most cases, and 4 patients (17%) presented severe effusion, with serious symptoms (FC III-IV dyspnea) in 3 cases requiring a new drainage and consequent pericardiectomy, with favorable outcomes.

The three initially asymptomatic patients and a fourth patient who suffered an asymptomatic recurrence after drainage remain in good conditions for 42.3 months.

Based on our experience and on published articles, we propose to perform pericardiocentesis in symptomatic patients with SCIPE, and to carry out a close follow-up every three months in asymptomatic patients. If symptoms develop, pericardial drainage should be performed, as 4 patients (16%) evolved with sudden cardiac tamponade and other 10 patients (40%) presented incipient echocardiographic signs of cardiac tamponade and FC IV dyspnea.

In our series of patients no further additional etiologic diagnosis was made during follow-up, confirming that pericardial effusions initially considered idiopathic were correctly classified according to our effective study protocol. Diagnostic yield of pericardial biopsy performed in patients without cardiac tamponade is too low (5% to 7%), increasing to 35% when it is carried out in patients with cardiac tamponade. (11)We performed pericardial biopsy when pericardiocentesis failed to resolve cardiac tamponade or when it recurred after pericardial drainage; pathology findings in all cases were consistent with unspecific chronic pericarditis, ruling out the presence of other infectious or neoplastic diseases.

No deaths occurred during follow-up, suggesting that the treatment was safe. Medical treatment was conducted according to primary physicians' criteria, and, in consequence, no valid conclusions could be drawn. In addition, we did not perform intrapericardial sclerosis or a pleuropericardial window, which may be more efficient procedures than pericardial drainage through subxiphoid approach and may be considered a therapeutic alternative in patients in whom etiological-based strategies cannot be achieved.

CONCLUSIONS

Patients with severe chronic idiopathic pericardial effusion may remain asymptomatic for a long time. Nevertheless, thy can develop symptoms and, in some circumstances, cardiac tamponade. Despite pericardial drainage is effective in the vast majority of symptomatic patients with pericardial effusion, recurrences can occur and pericardiectomy is a good option for these patients.

RESUMEN

Presentación clínica y evolución alejada de los derrames pericárdicos crónicos severos idiopáticos

Objetivo

Determinar la frecuencia, la presentación clínica, los métodos diagnósticos, el tratamiento, la evolución y el pronóstico alejado en pacientes con derrame pericárdico crónico severo idiopático.

Material y métodos

Se analizaron prospectivamente todos los pacientes con sospecha de derrame pericárdico severo, desde junio de 1992 a abril de 2005. Fueron evaluados de acuerdo con un protocolo de enfermedad pericárdica que se aplica en nuestra Institución. De un total de 152 pacientes, 54 presentaron derrame crónico severo, de los cuales 28 (52%) fueron catalogados como idiopáticos e incluidos en el presente estudio.

Resultados

La edad media fue de 67 ± 11 años, el 82% eran hombres, 25 (89,3%) se encontraban sintomáticos por disnea, 4 (16%) con taponamiento cardíaco y 10 (35,7%) con signos ecocardiográficos incipientes de taponamiento. El seguimiento promedio fue de 60 meses (3-128 meses). Los 3 pacientes asintomáticos no fueron drenados y tuvieron una evolución favorable (seguidos en promedio durante 42 meses). Los 25 pacientes sintomáticos se trataron con drenaje pericárdico y se realizó seguimiento en 23 (2 perdidos). En 14 (60,8%) de ellos no hubo recidiva de derrame, 3 (13%) presentaron derrame leve, 2 (8,6%) derrame moderado y 4 (17,2%) derrame severo. De estos últimos, 3 estaban con disnea III-IV, por lo que requirieron pericardiectomía, con buena evolución ulterior. El paciente restante permaneció asintomático.

Conclusiones

Los pacientes con derrame pericárdico crónico severo idiopático pueden permanecer asintomáticos durante largo tiempo. El drenaje pericárdico es eficaz en la mayoría de los casos en los que se desarrollan síntomas graves. En los pacientes sintomáticos con recidivas de derrame severo posterior al drenaje, la pericardiectomía resulta una solución eficaz.

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