Support Care Cancer (1997) 5:64–66

SHORT COMMUNICATION

Witold Tomkowski
Monika Szturmowicz
Anna Fijałkowska
Janusz Burakowski
Stanisław Filipecki

New approaches to the management and treatment of malignant pericardial effusion

W. Tomkowski, M.D., Ph.D. (✉)
M. Szturmowicz, M.D., Ph.D.
A. Fijałkowska, M.D., Ph.D.
J. Burakowski, M.D. · S. Filipecki, M.D.
Department of Internal Medicine,
National Institute of Tuberculosis
and Pulmonary Diseases,
Płocka 26, PL-01-138 Warsaw, Poland
Tel.: (22) 325149
Fax: (22) 321586

Abstract The purpose of this study was the evaluation of the effectiveness of intrapericardial administration of tetracycline, 5-fluorouracil and cisplatin in patients with recurrent malignant pericardial effusion. In 33 cases with malignant pericardial effusion 46 pericardiocenteses under two-dimensional echo-cardiography were performed. No complications were observed after this procedure. Pericardiocentesis was followed by catheterization of the pericardial space for a mean period of 15 days (range 1–64). In 4 cases bacterial pericarditis was observed during catheterization. The mean volume of the pericardial fluid was 2.4 l (range 0.4–13 l). In cases with bloody pericardial fluid the PO_2, PCO_2 and pH of the fluid were estimated and the results compared with the values for venous blood obtained from the upper limbs. Highly statistically significant differences were documented. Twenty cases of malignant pericardial effusion were treated with direct pericardial administration of cisplatin, 3 with 5-fluorouracil and 2 with tetracycline. Good results (no fluid reaccumulation) were observed only after cisplatin therapy. We conclude that pericardiocentesis performed under two-dimensional echo cardiography, followed by pericardial catheterization and direct pericardial treatment with cisplatin are the methods of choice in cases with malignant pericardial effusion. In cases with bloody pericardial fluid PO_2, PCO_2 and pH analysis can be useful to differentiate the source of the bloody fluid (blood or bloody fluid).

Key words Pericardial effusion · Malignant pericarditis · Pericardiocentesis · Pericardial catheterization · Cisplatin

Introduction

Malignant pericarditis is one of the most frequent causes of recurrent pericardial effusion and cardiac tamponade [5]. Pericardiocentesis, though a life-saving procedure [1], is not sufficient for the management of malignant pericardial diseases as the effusion has a tendency to recur.

Many therapeutic procedures, surgical as well as conservative, have been investigated to avoid fluid reaccumulation after pericardiocentesis [2, 4, 6].

Patients and methods

A group of 33 patients, 10 women and 23 men (mean age 54 years; range 38–69), with malignant pericardial effusion entered our study. The diagnosis of malignancy was based upon histological examination of samples obtained from the primary tumor, and malignant pericardial effusion was diagnosed by the presence of malignant cells in the pericardial fluid and echo-cardiographic examination.

The most frequent histological diagnosis was adenocarcinoma of the lung, gastrointestinal tract, ovary or breast (19 patients). Other reasons for the malignant pericardial effusion were small-cell lung cancer (4 patients), carcinoma planoepitheliale of the

lung (3 patients) and mesothelioma (3 patients). Angiosarcoma, lymphoma and renal cell cancer were represented by 1 patient each.

Pericardiocentesis was performed in the intensive-care unit. The site of the needle puncture was determined by echo-cardiographic examination, the ideal site being when the fluid was closest to the transducer and where the needle avoided the heart, lung and underlying structures. A needle surrounded by plastic sheet was used. After the pericardial fluid had been located the steel part of the needle was removed. The steel needle was never pushed into the right ventricle to avoid puncturing it and no ECG trace was ever obtained from the steel part of the needle.

In cases with bloody pericardial fluid PO_2, PCO_2 and pH were analysed. Data were compared with PO_2, PCO_2 and pH values of venous blood obtained before pericardiocentesis from the upper limbs. In all patients, pericardiocentesis guided by echo cardiography was performed and a polyurethane catheter (Cavafix) was inserted. When the catheter was in place fluid was drained and 10 mg cisplatin in 20 ml normal saline was administered into the pericardial space over 5 min. The procedure was repeated on 5 consecutive days. When fluid reaccumulation stopped, the catheter was removed.

A 250-mg dose of 5-fluorouracil was administered in 20 ml normal saline directly into the pericardial space over 5 min, and 200 mg tetracycline (Vibramycin) was administered identically.

If fluid reaccumulation had occurred the catheter was kept in place and the courses of cisplatin, 5-fluorouracil and tetracycline were repeated.

To evaluate any toxic side-effects of the intrapericardial treatment, complete and differential blood counts and creatinine levels were monitored during and after therapy. Constant ECG monitoring was performed during each course of intrapericardial instillation of the drugs.

Chest radiographs and echo-cardiographic examination were done after each course of treatment for assessment of response. The duration of response was measured from the beginning of the intrapericardial treatment to the time of fluid reaccumulation or till death if no recurrence of fluid was observed.

Results

Of the 46 pericardiocenteses performed, 76% were from the chest wall (mainly the left sternal borders, apex etc.); only in 24% was a subxiphoid approach chosen. No complications were observed after the procedure described.

In 80% of the pericardiocenteses the pericardial fluid was bloody, the mean PO_2, PCO_2 and pH values of the bloody pericardial fluid being 2.8 kPa (20.8 mm Hg; SD = 11.3), 7.4 kPa (55.77 mm Hg; SD = 14.5) and 7.12 (SD = 0.2).

The mean values of PO_2, PCO_2 and pH of the blood obtained from the upper limbs before pericardiocentesis were 5.2 kPa (39.1 mm Hg; SD = 13.2); 4.9 kPa (36.5 mm Hg; SD = 5.8) and 7.36 (SD = 0.05). Comparison of the mean PO_2, PCO_2 and pH values in bloody pericardial fluid and in venous blood revealed significant differences ($P < 0.001$).

The mean period of catheterization of the pericardial space was 15 days (range: 1–64 days) and the mean volume of total drainage was 2.4 l (range 0.4–13 l). In 4 cases long-term catheterization was complicated by bacterial pericarditis (the mean period of catheterization complicated by bacterial pericarditis was 28 days). Huge pericardial drainage (13 l) was observed in 1 patient with angiosarcoma.

A total of 25 patients received various compounds by intrapericardial administration (20 cisplatin, 3 5-fluorouracil and 2 tetracycline); 8 patients received only conservative treatment (no intrapericardial administration of agents).

Success was observed only after cisplatin in 17 cases (85% of the group treated with cisplatin). In this group 1 patient died during the intrapericardial cisplatin course and in 2 cases fluid reaccumulation was observed after treatment.

Tetracycline and 5-fluorouracil showed no results but the groups of patients were very small (these agents were not administered if good results had been achieved by cisplatin therapy).

Cisplatin was administered in doses of 20–200 mg and this treatment was well tolerated by all patients. In 2 cases mild nausea occurred; in 1 patient supraventricular arrhythmia was observed.

No signs of constrictive pericarditis were observed in the longest-surviving patients.

The duration of response after cisplatin treatment was 1 week to 24 months (mean 5.2 months).

The cause of death in 16 cases receiving cisplatin therapy was neoplastic disease or its complications, but even in cases with fluid reaccumulation, cardiac tamponade was not the reason of death. Four patients from the group treated with cisplatin are still alive. Fluid reaccumulation was observed in all patients who underwent conservative treatment or intrapericardial treatment with 5-fluorouracil and tetracycline. All these patients died.

Autopsies were performed on 10 patients from the group treated with cisplatin and all of these cases still showed neoplastic pericardial involvement. The autopsy examination revealed diffuse fibrofibrinous adhesions between the epicardium and the pericardium in 2 patients and partial adhesion in another 2 cases (1 of them presented with a small amount of residual fluid).

No local complications associated with an indwelling catheter or cisplatin treatment were seen in the pericardial space at autopsy. In 2 cases pericardial fluid was observed at the autopsy.

Discussion

The technique two-dimensional echo-cardiography – guided pericardiocentesis was developed and described by the Mayo Clinic. This study demonstrated the effectiveness of this method.

If the fluid obtained after successful pericardiocentesis is grossly bloody, it has to be tested to determine

whether it clots, or haematocrit values are compared in the pericardial fluid and the blood. However, clotting is a time-consuming procedure and the haematocrit value of the pericardial fluid could be higher than that of the venous blood.

In our study, cases with bloody pericardial fluid PO_2, PCO_2 and pH were analysed and the data obtained suggest that this is a very easy procedure that rapidly differentiates bloody pericardial fluid and blood from the right ventricle.

Venous blood obtained from the upper limbs showed PO_2, PCO_2 and pH values very similar to the values for mixed blood from the right ventricle. The PO_2 value for the upper-limb venous blood was are a little less, PCO_2 was a little higher and the pH was a little less than the values for mixed blood from the right ventricle.

In residual bloody pericardial fluid, oxygen is utilized by morphological elements of fluid and cells surrounding the pericardial space. Carbon dioxide is transferred into the pericardial fluid. In bloody pericardial fluid PO_2 is expected to be less than in mixed right-ventricle blood, PCO_2 is expected to be higher and the pH lower. Simple comparison of the values mentioned shows the origin of the bloody fluid: blood from the right ventricle or the bloody pericardial fluid.

Pericardial drainage could be huge, as in the case with angiosarcoma. Prolonged drainages should be avoided because of the possibility of bacterial pericarditis, which happened in 12% of our patients.

In this study intrapericardial agents were administered in 25 cases. The treatment was successful only in 17 cases treated with cisplatin. In the majority of patients the production of pericardial fluid stopped after the administration of 50 mg cisplatin. This method of treatment was first used by Markmann and Howell [6]. Recently published data (as well as ours) [3, 8–10] has suggested that intrapericardial cisplatin therapy is very effective.

Drug delivery by polyurethane catheter was safe, and we did not observe any serious toxic side-effects of this treatment. Mild nausea was very rare.

The interesting autopsy finding was the presence of neoplastic pericardial involvement in all patients, although there was no effusion in 8 patients.

These data indicate that the good results following local cisplatin treatment probably depend on an unknown, non-specific anti-inflamatory action of this drug.

The neoplastic involvement found on autopsy was asymptomatic in 8 cases. The pericardial effusion observed on autopsy in 2 cases was not the cause of death.

The length of survival of our patients after pericardiocentesis and intrapericardial instillation of cisplatin compared favourably with those described in other reports [7].

We therefore recommend pericardiocentesis performed under two-dimensional echo-cardiography, followed by pericardial catheterization and direct pericardial treatment with cisplatin as an effective symptomatic treatment of recurrent effusion in malignant pericarditis.

The cost-effectiveness ratio of the method described seems to be better than the cost-effectiveness ratio of other surgical methods of treating malignant pericardial effusion, published in the literature [7].

References

1. Celermajer DS, Boyer MJ, Bailey BP, et al (1991) Pericardiocentesis for symptomatic malignant pericardial effusion: a study of 36 patients. Med J Aust 154:19–22
2. Davis S, Sharma SM, Blumberg ED, et al (1978) Intrapericardial tetracycline for the management of cardiac tamponade secondary to malignant pericardial effusion. N Engl J Med 299:1113–1114
3. Fiorentino MV, Daniele O, Morandi P, et al (1988) Intrapericardial instillation of platin in malignant pericardial effusion. Cancer 62:1904–1906
4. Gaast A van der, Kok TC, Linden N van der, et al (1989) Intrapericardial instillation of bleomycin in the management of malignant pericardial effusion. Eur J Cancer Clin Oncol 25:1505–1506
5. Kralstein J, Frishman W (1987) Malignant pericardial diseases: diagnosis and treatment. Am Heart J 113:785–790
6. Markman M, Howell SB (1985) Intrapericardial instillation of cisplatin in a patient with a large malignant effusion. Cancer Drud Deliv 2:49–52
7. Okamoto H, Shinkai T, Yamakido M, et al (1993) Cardiac tamponade caused by primary lung cancer and the management of pericardial effusion. Cancer 71:93–98
8. Tomkowski W, Szturmowics M, Fijałkowska A, et al (1991) Intrapericardial cisplatin in malignant pericardial effusion. Eur J Cancer 27 [Suppl 3]:57
9. Tomkowski W, Szturmowicz M, Fijałkowska A, et al (1993) Intrapericardial cisplatin in patients with malignant pericardial effusion. Eur J Cancer 29 [Suppl 6]:110
10. Tomkowski W, Szturmowicz M, Fijałkowska A, et al (1994) Intrapericardial cisplatin for the management of patients with large malignant pericardial effusion. J Cancer Res Clin Oncol 120:434–436