Cardiac tamponade as the initial presentation of malignancy: is it as rare as previously supposed?

K.W. Muir¹ and J.C. Rodger

Monklands District General Hospital, Monkscourt Avenue, Airdrie ML6 0LJ and ¹University Department of Medicine and Therapeutics, Gardiner Institute, Western Infirmary, Dumbarton Road, Glasgow G11 6NT, UK

Summary: Advanced malignant disease frequently involves the heart and pericardium, and pericardial effusion is a common postmortem finding in such patients. Identification of pericardial effusions in life is uncommon, however, even when symptomatic. Cardiac tamponade occurring as the first presentation of malignancy appears to be uncommon.

We present five cases of cardiac tamponade due to undiagnosed malignancy which presented to a general medical unit over 18 months. The availability of echocardiography was an important factor in correct diagnosis, since clinical features were non-specific. Bronchial adenocarcinoma was the cause in three of the five cases.

Review of the literature confirms adenocarcinomas of the bronchus as the most common cause of this complication. The majority of cases have presented with large volume, haemorrhagic effusions, and cytology (with or without carcinoembryonic antigen measurement) was diagnostic in most patients. Immediate treatment with subxiphoid pericardiectomy is recommended; the role of balloon catheter pericardiectomy remains to be established. Combined chemotherapy and radiotherapy appears to extend survival, which in some cases may be prolonged.

We recommend that early echocardiography should be obtained in all patients presenting with apparent cardiac failure, since early treatment of malignant effusions provides symptomatic relief.

Introduction

Pericardial effusions associated with metastases to the heart or pericardium are a frequent finding at postmortem in malignant disease.¹ The presentation of malignancy with cardiac tamponade appears to be uncommon. A literature search using Medline CD ROM, followed by a review of the references in each paper identified, revealed 73 cases of malignancy presenting as cardiac tamponade that have been reported since 1935. We wish to report five cases of cardiac tamponade presenting to a district general hospital over a period of 18 months in which tamponade was the first manifestation of malignant disease. We suggest that malignant cardiac tamponade may be a more common mode of presentation of malignancy than has been previously supposed, and review the literature.

Case reports

Cardiac tamponade was diagnosed on the basis of right ventricular diastolic collapse on echocardiography,

which was present in all cases at first examination. Details of the cases are given in Table 1. Dyspnoea had acutely worsened in all cases at time of admission but many patients had symptoms for some time prior to the acute event. An example history is outlined for illustration.

Case 2

A 50 year old man presented with acute worsening of dyspnoea after a 6 week history of anorexia, weight loss, exertional dyspnoea, night sweats, non-productive cough and vague left-sided chest discomfort. He had no significant past medical history and smoked 30 cigarettes daily. On examination he had a small left pleural effusion and tender hepatomegaly of five finger breadths below the costal margin.

Blood tests revealed hyponatraemia (serum sodium was 129 mmol/l) and elevated transaminases. Retrospective electrocardiograph (ECG) review found electrical alternans. Chest X-ray showed a globular heart with small left pleural effusion. On echocardiography there was a large pericardial effusion with features of tamponade, and 950 ml of haemorrhagic fluid was aspirated.

Correspondence: K.W. Muir, M.R.C.P.

Accepted: 28 April 1994

Table I Clinical features of cases

Case	Age	Sex	Symptoms	Presentation Signs	Symptom duration	ECG	Pericardiocentesis			Other treatment	Outcome	Histology
							Volume (ml)	Fluid	Cytology			
1	26	M	Dyspnoea, headache, groin pain	Pulmonary oedema, globular cardiomegaly, hepatomegaly, hypotension	2 weeks	Electrical alternans, sinus tachycardia	530	Haemorrhagic	Positive	Chemotherapy	Died 5 months	? Teratoma
2	50	M	Dyspnoea, cough, anorexia, weight loss, night sweats, chest discomfort	Pulmonary oedema, peripheral oedema, globular cardiomegaly, hepatomegaly, left pleural effusion	6 weeks	Electrical alternans	950	Haemorrhagic	Positive	Sclerosis radiotherapy	Died day 69	Bronchial adenocarcinoma
3	63	F	Dyspnoea, orthopnoea, cough, retrosternal pain	Elevated JVP, hypotension, pleural effusions, globular cardiomegaly, pulmonary oedema	1 week	Sinus tachycardia	800	Haemorrhagic	Positive	Nil	Died day 114	Bronchial adenocarcinoma
4	60	M	Dyspnoea, urinary retention, exertional syncope	Epigastric tenderness, pleural effusions, peripheral oedema, ascites, globular cardiomegaly	Unknown	Electrical alternans	550	Haemorrhagic	Probable	Pericardiectomy	Died day 51	Poorly differentiated carcinoma, origin undetermined
5	65	M	Left hemisensory loss, hepatomegaly, dyspnoea	Left extensor plantar, splinter haemorrhages	35 days	Electrical alternans	505	Haemorrhagic	Positive	Pericardial fenestration	Died day 24	Bronchial adenocarcinoma

F = female; M = male; JVP = jugular venous pressure.

Figure 1 Two-dimensional trans-thoracic four chamber view echocardiograms in (a) systole and (b) diastole from case 5, demonstrating right ventricular diastolic collapse.

Cytology demonstrated metastatic adenocarcinoma cells.

He required several further pericardiocenteses and was sent for radiotherapy following unsuccessful attempted sclerosis of the pericardial space. The effusion did not subsequently require to be tapped.

Prostatic acid phosphatase, carcinoembryonic antigen, alpha fetoprotein and beta human chorionic gonadotrophin levels were normal. A left hilar mass developed, and the primary tumour was assumed to be lung.

He was well enough to be discharged briefly from hospital but was readmitted with increasingly severe dyspnoea. There was no echocardiographic evidence of tamponade on this occasion. He deteriorated steadily and died 69 days after initial presentation.

Discussion

Metastatic spread of tumours to the heart or pericardium, causing pericardial effusion, is found

in 11.6% of patients with known malignancy at postmortem examination.¹ It is much less common to identify such effusions during life: in one study, only 30% of patients with symptoms referable to their pericardial disease were correctly identified antemortem.² The tumour types most commonly found at postmortem to give rise to pericardial metastases were lung (37%), breast (22%), haematological malignancies (17%) and melanoma (3%).¹ Cardiac tamponade is well recognized but rare in the course of advanced malignant disease. However, 16% of patients with autopsy-identified pericardial metastases had features of tamponade when reviewed retrospectively, despite a lack of clinical suspicion.² Cardiac tamponade has previously been considered to be rare as a presenting feature of malignancy but epidemiological evidence regarding the true incidence of this mode of presentation is lacking. Fraser *et al.* reviewed the literature in 1980 and identified 26 cases, adding three of their own.³ Since that time, further case reports and small series have been added,⁴⁻¹¹ bringing the total number of cases in the literature to 73. Most series are reported from oncology or cardiothoracic surgical units and we believe our report to contain the largest number of cases identified outside a specialist unit. It is undoubtedly the case that ready availability of echocardiography was the main factor in identifying these patients.

Tumour types and frequencies for all reported cases are detailed in Table II. The mean age of presentation was 50 years and there was a male predominance (55 males). Review of the literature shows that in 60% of cases, the primary site was lung. A large proportion of these were adenocarcinomas, with the more common squamous carcinomas being comparatively rare as a cause of tamponade. Overall, adenocarcinomas of any origin accounted for 54% of all cases.

Table II Tumour types presenting as cardiac tamponade reported in literature, 1935-1992 ($n = 78$)

Tumour type	Number	Percentage
Adenocarcinoma lung	29	37
Squamous carcinoma lung	11	14
Bronchoalveolar carcinoma	4	5
Other bronchial	3	4
Mesothelioma	3	4
Adenocarcinoma, unknown primary	8	10
Gastrointestinal tract	4	5
Leukaemia, lymphoma	7	9
Breast	1	1
Ovarian carcinoma	2	3
Other	6	8

The development of tamponade is dependent on both the fluid volume and the rate of accumulation; the majority of malignant effusions presenting as tamponade are large, the average aspirate from one series being 1,200 ml¹² and from all reported cases, 841 ml ($n = 51$). Patients suffered preceding symptoms for a mean of 39 days prior to presentation (range 0–180 days). Right ventricular diastolic collapse on echocardiography or cardiac catheterization is evident prior to the development of hypotension or pulsus paradoxus, and mean arterial pressure is maintained in the early stages of tamponade.

Pericardial seeding by malignant cells is probably insufficient to cause tamponade: lymphatic obstruction seems to be an additional requirement. As described by Fraser *et al.*, lung tumours spread to mediastinal lymph nodes, from where retrograde spread occurs to the epicardial lymphatic plexus. Slow accumulation of large volumes of fluid may then occur. Tumours which metastasize primarily by the haematogenous route, or those that rarely spread to mediastinal nodes rarely cause tamponade. Many tumours that metastasize to heart or pericardium very rarely present with tamponade through a combination of lack of lymphatic obstruction and earlier presentation with local symptoms, for example, breast, colon, pancreas, stomach, ovary, melanoma. Similarly, squamous carcinoma of the lung may be a rare cause of tamponade as it is typically endobronchial and symptoms of haemoptysis, cough or bronchial obstruction may cause earlier presentation than adenocarcinomas, which are more usually situated distally in the pulmonary parenchyma.

The most common clinical features of malignant cardiac tamponade are non-specific. Since malignant tamponade usually develops as an acute event superimposed on a background of a large, slowly developing pericardial effusion, the clinical appearance is often more suggestive of congestive cardiac failure. In a review of malignant tamponade pooling several series,¹ the most common symptoms were dyspnoea (79%), cough (47%), thoracic pain (27%), orthopnoea (26%) and dysphagia (18%). Physical signs encountered were pleural effusion (51%), tachycardia (50%) and signs of systemic venous congestion such as elevated jugular venous pressure, hepatomegaly and peripheral oedema. Signs considered typical of pericardial effusion – pulsus paradoxus, a pericardial rub and Kussmaul's sign – occurred in only 30%, 12% and 5%, respectively. Although abnormal ECGs were reported in over 90%, the changes were all non-specific save electrical alternans which occurred in only 5%. The need to maintain a high index of suspicion in patients presenting with apparent cardiac failure and hypotension of unknown aetiology is vital if the diagnosis is not to be

delayed. Delay in diagnosis of cardiac tamponade, even in the face of typical clinical features was a feature of our series. This has been noted in other reports.¹² Earlier and more widespread use of echocardiography in the investigation of patients with apparent cardiac failure may facilitate diagnosis. The assumption of an ischaemic aetiology is not necessarily safe even in patients with known coronary artery disease, as illustrated by case 4, and the administration of angiotensin converting enzyme inhibitors to patients with extrinsic myocardial compression may precipitate sudden circulatory collapse.

The immediate drainage of pericardial fluid is life saving and brings about symptomatic relief. It also provides a diagnosis of malignancy in the majority of cases. In reported cases, aspirated fluid was haemorrhagic in 59 of 67 cases where information was available (88%) and cytology positive in 56 of 67 (84%). Measurement of carcinoembryonic antigen (CEA) in pericardial fluid may provide additional diagnostic help, as elevated levels are found in many malignant effusions. In one series, a combination of cytology and CEA measurement was 100% sensitive and specific for malignancy.¹³

Subacute management of malignant pericardial effusion requires either sclerosis of the pericardial space or pericardial fenestration. Operative pericardial fenestration requires thoracotomy under general anaesthesia and unsurprisingly carries an immediate mortality of approximately 8%.¹⁴ A safer procedure with low recurrence rates (approximately 3%) is subxiphoid pericardiotomy, which may be performed under local anaesthetic. A more recently developed alternative is balloon catheter pericardiotomy, first reported in 1991 by Palacios *et al.*¹⁵ and critically reviewed by Keane and Jackson.¹⁶ This technique effected prolonged relief of tamponade in 94% of a series of 35 patients.¹⁷ Its place in the management of patients with malignant effusions is not clear at the present time as considerable operator skill is required, the equipment is costly, and results are not presently superior to subxiphoid pericardiotomy. Tetracycline instillation after pericardial drainage has been successful in two reported series,^{18,19} but a mean of three instillations over the course of several days is required and an *in situ* drain was needed for a mean of 9 days. The use of corynebacterium parvum as a sclerosant has not previously been reported for pericardial effusion but it is commonly used for pleurodesis.

Whilst the prognosis for patients presenting with cardiac tamponade is poor, survival for several months is the norm and prolonged survival may be possible. Including our patients, mean survival for all patients in whom survival times are quoted in the literature was 144 days ($n = 66$, range 4–1,400 days). Prolonged survival in those patients with

tumours amenable to systemic chemotherapy, for example, haematological and gynaecological malignancies, is possible. Ten patients (13%) in reported series survived for over a year. Chemotherapy alone did not prolong survival in one series,¹² but combined radiotherapy and chemotherapy did.

We would suggest that the occurrence of cardiac tamponade as the first manifestation of malignancy is more common than hitherto appreciated. A high degree of suspicion is necessary, but all of our cases could have been identified by clinical features and careful review of radiographic and electrocardiographic data. Echocardiography should be mandatory in patients with apparent cardiac failure where aetiology is unclear. Pericardiocentesis will provide

a diagnosis in over 80% of cases, and may allow diagnosis in an even greater proportion if cytology is combined with carcinoembryonic antigen measurement. Definitive treatment of the malignant effusion by means of subxiphoid pericardiectomy or percutaneous balloon pericardiectomy, or sclerosant therapy with tetracycline may allow prolonged symptom-free survival. Combined chemotherapy and radiotherapy may prolong survival regardless of tumour type.

Acknowledgement

We wish to thank Dr A.J.S. Gardiner for his permission to report case 5.

References

1. Press, O.W. & Livingston, R. Management of malignant pericardial effusion and tamponade. *JAMA* 1987, **257**: 1088–1092.
2. Thurber, D.L., Edwards, J.E. & Achor, R.W.P. Secondary malignant tumours of the pericardium. *Circulation* 1962, **26**: 228–241.
3. Fraser, R.S., Vilorio, J.B. & Wang, N.S. Cardiac tamponade as a presentation of extracardiac malignancy. *Cancer* 1980, **45**: 1697–1704.
4. Aggarwal, P. & Sharma, S.K. Cardiac tamponade as the initial presentation of malignancy. *Int J Cardiol* 1989, **22**: 157–159.
5. Hwang, M.H., Brown, A., Piao, Z.E. & Scanlon, P.J. Cardiac lymphoma associated with superior vena caval syndrome and cardiac tamponade: case history. *Angiology* 1990, **41**: 328–332.
6. Cercato, M.C., La Ferla, G., Pericoli, N., Fedele Scinto, A., Saccij, I. & Cognetti, F. Cardiac tamponade as the initial manifestation of an extracardiac malignancy. *Eur J Cancer* 1991, **27**: 670–671.
7. Krisanda, T.J. Atrial fibrillation with cardiac tamponade as the initial manifestation of malignant pericarditis. *Am J Emerg Med* 1990, **8**: 531–533.
8. Blanco, C., Cobo, J., Gomez-Cerezo, J., Ramos, F. & Molina, F. Infarto agudo de miocardio y taponamiento cardiaco como manifestacion inicial de un adenocarcinoma. *Rev Clin Esp* 1990, **187**: 210–211.
9. Rinkevich, D., Borovik, R., Bendett, M. & Markiewicz, W. Malignant pericardial tamponade. *Med Ped Oncol* 1990, **18**: 287–291.
10. Forslund, T., Forsen, K.O. & Maenpaa, J. Cardiac tamponade due to ovarian carcinoma. *Arch Gynecol Obstet* 1991, **248**: 161–165.
11. Sharma, S., Balaney, B. & Mandke, J.V. Cardiac tamponade as a presentation of mucoepidermoid bronchogenic carcinoma. *J Assoc Phys India* 1989, **37**: 183–185.
12. El Allaf, D., Burette, R., Pierard, L. & Limet, R. Cardiac tamponade as the first manifestation of cardiopulmonary malignancy: a study of ten cases. *Eur Heart J* 1986, **7**: 247–253.
13. Tatsuta, M., Yamamoto, R., Ichii, M., Lishi, H. & Noguchi, S. Carcinoembryonic antigens in the pericardial fluid of patients with malignant pericarditis. *Oncology* 1984, **41**: 328–340.
14. Gregory, J.R., McMurtrey, M.J. & Mountain, C.F. A surgical approach to the treatment of pericardial effusion in cancer patients. *Am J Clin Oncol* 1985, **8**: 319–323.
15. Palacios, I.F. Percutaneous balloon pericardial window for patients with malignant pericardial effusion and tamponade. *Cathet Cardiovasc Diagn* 1991, **22**: 244–249.
16. Keane, D. & Jackson, G. Managing recurrent malignant pericardial effusions. *Br Med J* 1992, **305**: 729–730.
17. Ziskind, A.A., Pearce, C., Burstein, S. *et al.* Percutaneous balloon pericardiectomy for the treatment of pericardial effusion and tamponade: report of the registry. *J Am Coll Cardiol* 1992, **19**: 265A.
18. Davis, S., Rambotti, P. & Grignani, F. Intrapericardial tetracycline sclerosis in the treatment of malignant pericardial effusion: an analysis of 33 cases. *J Clin Oncol* 1984, **2**: 631–636.
19. Shepherd, F.A., Morgan, C.D., Ginsberg J.S. *et al.* Control of malignant pericardial effusion by tetracycline sclerosis. *Proc Am Soc Clin Oncol* 1986, **5**: 246.