

# Pericardial Tamponade as the First Manifestation of Adenocarcinoma

Isabel de la Gándara, Enrique Espinosa, Jorge Gómez Cerezo, Jaime Feliu and Carlos García Girón

From the Services of Oncology (I. de la Gándara, E. Espinosa, J. Feliu), and Internal Medicine (J. Gómez Cerezo), Hospital La Paz, Madrid and the Service of Oncology (C. García Girón), Hospital General Yagüe, Burgos

Correspondence to: Dr. Enrique Espinosa, Service of Medical Oncology, Hospital La Paz, Paseo de la Castellana, 261.28046 Madrid, Spain

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We hereby report on 13 cases of pericardial tamponade as the first manifestation of an adenocarcinoma. The primary tumor was detected in 10 cases: 7 lung, 1 stomach, 1 breast and 1 thyroid. A first cytologic examination of the pericardial fluid yielded the diagnosis of adenocarcinoma in 10 cases, whereas a second cytology was needed in another two cases. The pericardial biopsy was positive in 7 out of 7 patients. The therapeutic procedures included pericardiocentesis in 9 patients (6 of whom had recurrent tamponade), a pericardial window in 4 and pericardiectomy in 4 (without recurrences). The mean survival was 4 months.

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Cardiac tamponade (CT) is a life-threatening but treatable condition. It can be caused by infections, neoplasms, and vasculitis. In some patients the cause is unknown. In the case of a tumor, metastases predominate over primary malignancies. When CT develops, the primary tumor is already known in most cases.

CT as the first manifestation of a neoplasm is a rare event. Its diagnosis and initial management usually correspond to internists or cardiologists, whereas oncologists play a role after the initial workup. The study of this special situation is difficult because occasional reports only include one or two patients. For this reason, it is not known whether these patients have an outcome similar to that of patients with a previously diagnosed neoplasm. A revision of the current literature reflects that adenocarcinomas predominate as the cause of malignant CT. In other words, when a CT is found to be due to a tumor, most cases correspond to an occult adenocarcinoma. We hereby report on 13 cases of adenocarcinoma presenting with CT.

## MATERIAL AND METHODS

In the period 1985–1992, 13 patients (8 male and 5 females) were diagnosed with CT as the first manifestation of adenocarcinoma. This represents 0.22% of all patients seen in our department of medical oncology over that

period. The median age was 47 years (limits 39–63). Clinical history, physical examination, chest x-ray films, electrocardiogram and echocardiography were performed in all cases. The tumor was confirmed by cytology and/or biopsy.

In the same period, 3 patients presented with CT as the first manifestation of lymphoma (2 cases) or esophageal squamous-cell carcinoma (1 case). On the other hand, 56 patients with previously known neoplasms had a CT.

## RESULTS

The most frequent symptoms were dyspnea, chest pain, cough and orthopnea. In general, the symptoms suggested heart failure that developed in a few days in patients without previous heart disease. Two patients presented with angina pectoris: one had paroxysmal atrial flutter and the other suffered a myocardial infarction 15 days later (due to tumoral embolism). One patient had two episodes of cerebral embolism by the time the CT was diagnosed.

With regard to the physical examination, jugular distention appeared in all patients. Hypotension, distant heart sound, peripheral edema and hepatomegaly were also present in most patients. The symptoms and clinical signs are summarized in Table 1.

Chest x-ray films showed cardiomegaly in all cases, pleural effusion in 6 and pneumonic consolidation in 4.

**Table 1**  
*Clinical findings*

Symptoms		Clinical signs	
Dyspnea	10 patients	Jugular distention	10
Chest pain	8	Hypotension	8
Cough	6	Peripheral edema	8
Orthopnea	6	Hepatomegaly	7
		Distant heart sounds	6
		Paradoxical pulse	3
		Kussmaul sign	3
		Pericardial rub	1

These changes were considered as non-diagnostic findings. The electrocardiogram showed reduction in the amplitude of QRS complexes and non-specific alterations of the ST segment in all cases. Electrical alternans was seen in 2 cases, atrial fibrillation in 2 and atrial flutter in 1.

The presence of pericardial effusion was always confirmed by 2D mode echocardiography. This method revealed either posterior movement of cardiac chambers during systole or systolic collapse of the right ventricle or systolic inversion of the right atrium. The possibility of malignant tamponade was not suggested by the echocardiography in any case (although it suggested myocardial infiltration in the patient who later had a tumoral embolism).

Pericardiocentesis was performed in 9 patients and pericardiotomy in 4 as the initial therapeutic procedure. The average amount of effusion was 1050 cm<sup>3</sup> and its characteristics are disclosed in Table 2. A first cytology was positive for adenocarcinoma in 10 patients and negative in 2, but a second cytology yielded the correct diagnosis in these 2 patients. In the remaining patient a biopsy was performed for diagnosis.

Pericardial biopsies were taken in 7 patients. One of them in whom cytology was not performed required a second biopsy because the first one was not diagnostic.

**Table 2**

*Pericardial fluid features. The values represent the mean (standard deviation in parentheses)*

Quantity in ml	1044 (383)
Macroscopic characteristics	
Serohematic	7 cases
Bloody	2 cases
Serous	1 case
Biochemistry	
Protein in g/dL	4.85 (0.66)
LDH in U/L	944 (70)
Glucose in mg/dL	33 (4)
Protein pericardium/serum	0.81 (0.9)
LDH pericardium/serum	2.77 (1.66)
Glucose pericardium/serum	0.37 (0.28)
Positive first cytology	10/12 = 83%
Positive biopsy	7/7 = 100%

The specimen included the parietal layer in all cases and also the visceral layer in 7. Tumoral infiltration was demonstrated in both layers in 4 out of 7 cases. The primary tumors were lung in 7 cases, and breast, stomach (see Appendix) and thyroid in 1 case each.

Nine patients needed a pericardiocentesis initially and 6 of them had recurrent CT 2 to 21 days later. The second surgical procedure was a pericardial window in 4 cases and a new pericardiocentesis in 2, without recurrences. On the other hand, pericardiotomy was performed in 4 cases, with good results. Eight patients received chemotherapy: 7 with cisplatin + ifosfamide + mitomycin for lung tumors and 1 cisplatin + adriamycin + mitomycin for a tumor of unknown origin.

The average survival from the diagnosis was 113 days (15–206), although it was longer in those patients with lung cancer who received chemotherapy (144 days).

## DISCUSSION

Heart tumors are usually metastatic: 2–22.7% of patients dying of cancer have heart metastases, usually silent from the clinical point of view (1). The clinical alterations may be due to infiltration of the pericardium, myocardium or endocardium (2), pericardial effusion being the most common manifestation (3, 4). Twenty-nine percent of patients with pericardial metastases develop symptoms and only 16% have a CT. The correct diagnosis of CT is reached in only 30% of cases before death (3). More than half of all cardiac metastases are due to lung and breast tumors. Mesothelioma, lymphoma, leukemia, sarcoma, melanoma, head and neck, digestive, genital and renal tumors account for the rest (5, 6).

CT as the first manifestation of a neoplasm is a rare event. In the past five years over 50 cases have been described, most of them secondary to lung adenocarcinoma or sarcomas. Several cases of mesothelioma, acute monoclonal leukemia, lymphoma and thymoma have also been reported. There are single reports of squamous cell carcinoma of the thymus, squamous cell carcinoma of the lung, esophageal carcinoma, papillary thyroid carcinoma, Hodgkin's disease, Kaposi's sarcoma and teratoma. In our experience, 16 out of 72 patients with malignant CT did not have a known tumor, and adenocarcinomas accounted for 81% of such cases. The present series is one of the largest ever reported of CT as the first manifestation of adenocarcinoma.

The diagnosis of CT requires the clinical suspicion, although the typical signs (paradoxical pulse, Kussmaul sign) are usually absent. Chest x-ray films and electrocardiograms show non-specific alterations in most cases. Echocardiography is the method of choice to diagnose a CT (5).

Why do lung adenocarcinomas predominate in this particular group of patients? Cardiac metastases may occur by

lymphatic or hematogenous dissemination, as well as by direct extension from the mediastinum. Fraser's hypothesis of tumoral retrograde lymphatic dissemination from involved mediastinal lymph nodes is the most accepted theory. Neoplasms with early metastases to mediastinal lymph nodes may present as CT, which explains the predominance of lung cancer in this setting. On the other hand, breast cancer invades the pleural space or the lung (hematogenously) before it extends to mediastinal lymphatic vessels, which may explain why CT is extremely unusual as the first manifestation in spite of cardiac metastases being so frequent in its evolution.

Cytology of the pericardial fluid yields the diagnosis in 70–90% of cases (77% in our series) (1), although it is sometimes necessary to take more than one sample. The pericardial biopsy was positive in 85% of our patients.

CT requires urgent drainage of fluid. Pericardiocentesis is effective in 90% of patients, with 1% of major complications, but is associated with a high rate of recurrence (3), 66% in our series. In expert hands, subxiphoid pericardial drainage may obtain the best results: in a series of 155 patients (82 with cancer), the relapse rate was less than 3% (7). Some authors have suggested that the instillation of cytostatics (bleomycin, cisplatin) (8, 9) or tetracycline may decrease the recurrence rate. Grau reported a series of 11 patients in whom oxytetracycline (500–1000 mg/day per 6 consecutive days) was administered via an indwelling pericardial cannula, after the extraction of as much pericardial fluid as possible (10). All the patients died of progression at sites other than the pericardium, with no evidence of pericardial relapse. In a recent series from the NCI the value of the instillation was unclear (11). Sclerotherapy with radionuclides offers no advantage (8).

Surgery is advisable for patients with uncertain diagnosis in order to obtain a biopsy. Subxiphoid pericardiectomy is the procedure of choice: compared with the pericardial window, it is easier to perform, more efficacious (recurrence rate 3%) and has a lower morbidity (3, 8). However, some authors favor the use of a pericardial window (11–13).

Other therapeutic options are pericardiectomy (if other measures fail), radiotherapy (useful for lymphomas) and chemotherapy. Chemotherapy may be useful for leukemias, lymphomas, small-cell carcinomas and breast tumors (8).

The presence of CT usually indicates advanced disease and is associated with a short survival. In the series by Moores, the 30-day mortality was 32.9% for patients with cancer and 5.4% for patients with benign diseases (7). In our series, the average survival was 113 days, rather long, which may be due to the fact that some patients with lung cancer respond to chemotherapy. However, the average survival of patients with non-small cell lung cancer is 7–9 months in the absence of CT, which supports the idea that CT as the first manifestation of a tumor correlates with a poor survival.

APPENDIX: the case of the patient with gastric carcinoma has been published in *Am J Gastroenterol* 1990; 85: 1431 (letter).

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