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Cardiac Tamponade as the Initial Manifestation of an Extracardiac Malignancy

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PRIMARY TUMOURS of the heart are very rarely observed. Cardiac metastases, which are more frequently encountered, have been observed in approximately 10% of the autopsies carried out in cancer patients and, almost exclusively, in those where the disease is disseminated [1–3]. In 80% of the cases, the primary neoplasms are represented by lymphomas, leukaemia and breast and lung carcinomas [2]. Pericardial involvement is prevalent (85%) and often (18–25%) causes haemorrhagic effusion [1–3].

Neoplastic pericarditis generally has a subclinical course so that the *ante mortem* diagnosis is not suspected [2]. Although neoplastic disease is the principal cause of cardiac tamponade [4], it may only rarely represent the first manifestation of a neoplasm. From a review of the data available in the western literature, only 47 cases have been reported since 1935.

The present report concerns a 49-year-old man who, in September 1989, presented with the sudden appearance of cardiac tamponade, requiring hospitalisation. At admittance, chest X-rays and echocardiography confirmed the presence of a pericardial effusion with a "swinging heart" type movement of the cardiac structure. The patient was submitted to an evacuative pericardiocentesis resulting in a total of 1700 cl of clearly haemorrhagic liquid. The cytological examination showed the presence of undifferentiated cells compatible with a neoplastic disease, although the histology could not be better defined. Tests conducted to investigate primary tumour, including computed tomography (CT) of the chest and lung scintigraphy (as a positive indicator) were negative. In the absence of both symptoms and pericardial effusion the patient was discharged after 20 days.

In February 1990, after the appearance of dysphonia from a paralysis of the right vocal cord, thoracic CT showed a nodular lesion of approximately 1 cm diameter in the right apex with superior ipsilateral paratracheal and mediastinal adenopathies which were most likely neoplastic. The bronchoscopic examination confirmed the presence of an expansive process with an extrinsic compression of the main right bronchus, in the absence of endoluminal vegetations. The cytological examination of the material obtained from the bronchial brushing seemed compatible with a diagnosis of an epidermoid lung carcinoma.

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Table 1. Metastatic cancer cases presenting as pericardial effusion (review of literature from 1935 to the present time)

Primary tumour	No. of cases
Lung	26
Unknown	4
Lymphoma	3
Stomach	2
Kidney	2
Leukaemia	2
Rhabdomyosarcoma	1
Pancreas	1
Ovary	1
Thymoma	1
Breast	1
Colon	1
Head and neck	1
Pheochromocytoma	1
Total	47

The patient was treated with a chemoradiotherapy combination which permitted obtaining local disease control. At the present time (14 months from the beginning of the symptoms), the patient is alive with residual lung cancer but without evidence of recurrence of the pericardial effusion.

Of the 47 cases described in literature (Table 1), the primary tumour is represented principally by lung carcinoma showing a total of 26 cases. The clear predominance of lung cancer (55%) is easy to understand, considering the high frequency and the precocity with which this tumour involves the mediastinal lymph-nodes which are a preferential pathway of diffusion for neoplastic cells to the heart [6]. When examining these 26 patients in particular [5–9], the histological examination showed 17 adenocarcinomas, 5 squamous, 3 undifferentiated and 1 adenosquamous carcinoma. The pericardial fluid was between 60 and 2000 cl and the effusion was of a haemorrhagic type in almost all cases. The cytological examination revealed the presence of neoplastic cells in 81% of the cases and was diagnostic for the histological type in 4.

In various studies, the cytological diagnosis of neoplastic pericardial effusion was confirmed in 85–90% of the cases, although not all researchers are in accord. A greater sensitivity of the cytological examination of the pericardial liquid as compared to the bioptic one has also been reported by other investigators [5].

Prognosis of neoplastic pericarditis is poor and the mean survival rate of the 26 patients, at the time of the diagnosis of cardiac tamponade, was 3 months.

As far as therapy is concerned, radiotherapy of the mediastinum has permitted obtaining control of the neoplastic pericarditis in some cases, as well as systemic chemotherapy or the local instillation of sclerosing chemotherapeutic agents or of radioactive isotopes [2, 3]. Surgical therapy such as pericardiectomy should be reserved for patients with a long life expectancy. The creation of a pleuropericardic window represents an easily tolerated palliative-type therapy which permits obviating recurrences of the effusion after pericardiocentesis. However, the only immediate treatment for cardiac tamponade is the prompt removal of the pericardial liquid. Subsequent treatment for

neoplastic pericarditis is not easily resolved. The data available in literature are still scarce today and survival of these patients continues to be very limited.

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Pneumocystis Pneumonia in a Patient treated with Fludarabine for Chronic Lymphocytic Leukaemia

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FLUDARABINE (9-B-D-arabinofuranosyl-2-fluoradenine) is currently proposed for the treatment of refractory chronic lymphocytic leukaemia (CLL) [1]. In previously treated patients, response rates reached 50–60% for Rai stages III and IV patients [1]. Complete remissions have been maintained in some patients, but the follow-up is still too short [1, 2]. The major toxicity is myelosuppression and severe infections have been reported, especially pneumonia. Pulmonary toxicity has also been noted but interstitial pneumonitis has generally regressed after discontinuation of the drug [2, 3]. A new case has been recently reported, with negative microbiological studies and recurrence after fludarabine had been resumed, in a patient with prolymphocytic leukaemia [4]. However, clinical and radiological features seen in this particular situation can correspond to non-unequivocal mechanisms. We report here a case of pneumocystis pneumonia survening after a single course of fludarabine. This patient recovered and then relapsed after chemotherapy had been resumed.

A 65-year-old woman with Rai stage IV CLL diagnosed in 1981 and refractory to chlorambucil was referred to our centre for treatment with fludarabine (25 mg/m^2 for 5 days each month). 2 weeks after the first course, she developed fever with bilateral pulmonary infiltrates. Fibroscopy with aspiration revealed *Pneumocystis carinii* pneumonia (Gomori silver stain positive). With high-dose cotrimoxazole therapy (100 mg/kg/day sulphamethoxazole for 3 weeks), the patient recovered. As the patient had responded to this first course with a decrease of 50% of peripheral adenopathies and improvement in peripheral blood count (lymphocytosis decreased from 45×10^9/l to 4×10^9/l), we decided to continue therapy with half-dose fludarabine. The patient received two more courses (6 and 10 weeks after the first cycle), and cotrimoxazole was maintained (20 mg/kg/day sulphamethoxazole). Adenopathies and lymphocytosis, however, progressed; thus a fourth course with full dosage of fluadarabine was realised. On day 8 of this fourth cycle, the patient developed fever with interstitial pneumonia. High-dose cotrimoxazole was recommenced without performing another fibroscopy. Chest films improved and the patient was discharged on day 18. Aerosolised pentamidine was prescribed to prevent recurrence of pneumonia.

To our knowledge, this is the second case of opportunistic pulmonar infection reported after fludarabine treatment. Schilling *et al.* [5] recently reported a case of fatal pneumocystis pneumonia associated with cytomegalovirus infection, survening after three courses of fludarabine in a CLL patient. Fludarabine is known to decrease the number of all lymphocyte subgroups, especially the CD4 cells [1], and that could explain such a toxicity. However, immunological deficiency is well-known in CLL, with a decrease of CD4:CD8 ratio and functional abnormalities of T-cell subpopulations [6]. So, patients with advanced CLL are at risk of pulmonary infection or toxicity with fludarabine treatment. Our patient did not receive concomitant corticotherapy, which can increase this infectious risk. The original point in our observation is the fact that pneumocystis infection was recurrent, suggesting a close dose-dependent risk. Particular attention should be paid in such patients treated with fludarabine.

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