MALIGNANT PERICARDIAL EFFUSION (MPEs)

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The finding of pericardial effusion in a patient with cancer requires from the attending physician a quick evaluation to choose the diagnostic method and the appropriate therapeutic procedure.

The chance of an MPE being due to metastatic tumor is 40 times greater than being due to a primary cardiac tumor (mesothelioma, sarcoma) (1).

It is known by autopsy studies that a patient with **metastases** in the pericardium, has metastatic disease in other sites in 100% of the cases and is surely incurable.

But in turn, it should be known also, that a patient with pericardial effusion and cancer does not necessary have MPE, since between 33% and 66% of patients have nonmalignant etiology for the effusion (1)(2)(3), and for this reason other causes should be ruled out, such as radiation-induced, infectious, or drug-induced pericarditis.

However, when there is no evidence of inflammatory disease (fever, pericardial rub, or pain) and the patient **presents (with)** clinical tamponade, **very probably** this is **probably** a malignant invasion of the pericardial space. (4)

The **most common** tumours that metastasize in the pericardium **more often** are **due to** lung cancer, lymphomas, leukemia, breast and gastrointestinal cancer**. tract tumours**. (5)

The most frequent cause (43.8%) of requirement for pericardiocentesis in a series of 219 patients from a General Hospital in Boston was cancer.(6) The cytologic confirmation of metastatic disease is achieved through periocardiocentesis in up to 92% of these patients. (7)

Cardiac tamponade could be the form of presentation of the malignant disease. In a study of 58 patients with malignant pericardial effusion, 45 had known cancer, but in 13 the diagnosis was known through pericardiocentesis performed due to tamponade.(1)

Patients with cancer and pericardial effusion may present with

1) Clinical tamponade (shock with jugular ingurgitation, paradoxical pulse, etc.)
2) Tamponade by echocardiogram: RV diastolic collapse, atrial collapse by more than 30% of the cardiac cycle.
3) Echographic effusion without tamponade (with inspiratory collapse of the inferior vena cava)
4) Effuso-constrictive pericarditis (ECP). (8)

DIAGNOSTIC METHODS

Chest X-ray: it may allow to suspect **the** diagnosis if there is **growth an enlargement** of cardiac **sillouhette** and even more, if a prior X-ray confirms that this cardiomegaly did not exist previously. In turn, it allows evaluating whether there is pleural effusion associated and possibly visualizing the cause (nodule or pulmonary infiltrate).

Electrocardiogram: **is** not of great value, since the presence of electrical alternans and microvolt (defined as R+S in DI+DII+DIII<15 mm) are only seen in 20% of massive effusions, according to a publication by the Spanish group.(9) The Nebraska study only found a correlation coefficient of 0.29 between QRS voltage and effusion magnitude. (10)

CT: useful to visualize thickening, masses, and calcification in the cases where ECP is suspected. It may assess mediastinal adenopathies, pleural effusion, and the presence of pulmonary lesions.

Echocardiography: it is of great value, not just for the diagnosis of the effusion, but for the evaluation of the signs of the imminence of tamponade (RV collapse) or by the possibility of a form of ECP, where the presence of calcium, bridles, and the Doppler pattern may lead to think that jugular pressure will not drop after pericardiocentesis, due to the concomitant presence of constriction, and effusion.

Examination of pericardial fluid: Pericardiocentesis is indicated in clinical tamponade (Class I evidence for the Guidelines by the Spanish Society of Cardiology)(8) and the European Guidelines 2004, with a B level of evidence.(11)

Diagnostic performance of pericardiocentesis for malignant cells in absence of tamponade is 5% (in the total pool of effusions) and is between 50 and 100% of MPEs according to the series.

In patients with symptomatic pericardial effusion but without tamponade, the indication of pericardiocentesis has a lower level of evidence (IIa); however, pericardiocentesis is not advised according to the Duke University study, when indicated only by search of malignant cytology. (12)

Current studies discourage the indication of pericardiocentesis blindly for diagnosis. In the case that performing it blindly is necessary, the subxiphoid pathway is preferred, and not the apical pathway; on the other hand, several papers find advantages with the apical pathway when pericardiocentesis is made under echographic imaging.(13)(14)

If fluid is obtained, it should be taken into consideration that 75% of it is serobloody, regardless of etiology.(10)

Pericardial biopsy:

In patients with tamponade, the performance of biopsy to find neoplastic tissue will not go beyond 35% and is lower (5%) without tamponade.

The low performance of taking the sample of the parietal pericardium is explained, since it is in the visceral pericardium where the neoplastic disease usually lays.

Usually, the same diagnostic procedure is used to place a drainage or to make a window to the peritoneum through the subxiphoid pathway, or to the pleura by thoracoscopy or subxiphoid access.

Indications of pericardial biopsy with drainage are (8):

1. Unresolved cardiac tamponade with pericardiocentesis or post-pericardiocentesis recurrence (Class I evidence).
2. Histologic and bacteriological study of pericardial tissue in patients with clinical activity in spite of three-week treatment being allegedly appropriate (Class IIa).

MANAGEMENT

When we face an MPE, we should ask ourselves before acting:

1) What is the life expectation of this patient?

2) Does he/she have chances to respond to some systemic management **treatment** in a short while **time**?
3) What **How** is the general state **status** of the patient?
4) What is the best diagnostic and therapeutic method I have in the institution?

Pericardiocentesis as a single procedure, leads to insufficient management for malignant effusion, due to the high percentage of recurrence.(15) Effusion has a chance of recurrence in up to 62% of these patients.(16)(17)

Some years ago, the choice of management of malignant pericardial effusion could not avoid surgery, whether by the conventional method or by thoracoscopy.

Surgery is based on making **open a** windows to the pleural or peritoneal space. Both cavities are lined by a great area of mesothelial cells with absorption capacity. The window should be wide so that it does not tend to close the defect and lets it work.

Pericardiectomy in MPE is left just for effuso-constrictive pericarditis cases, where derivative/drainage methods fail.(12)

Currently, placing a permanent catheter is becoming popular, and a review by the Mayo Clinic that included patients with all kinds of etiologies of pericardial effusion, showed that the rate recurrence is only 14%.(18)

The percutaneous pathway has enabled the introduction of balloon catheters and making windows for the management of tamponade.(19) Many publications with a small number of cases allow showing the usefulness of the method when there is trained staff. (20)

Since the FDA disapproved tetracycline instillation (1996), multiple attempts with intrapericardial antineoplastic drugs have attempted to prove useful to prevent effusion recurrence. Bleomycin in a single 20-mg dose and cisplatin (total dose of 50 mg, at 10 mg/day during 5 days) have only been published in small and nonrandomized studies, although the rate of success is around 80%.(21)

Recently, an Italian study was published with good **acceptable** results with the use of intrapericardial thiotepa.(22) The protocol is complex due to the requirement of lidocaine and steroids to prevent local adverse effects, unlike the cisplatin protocol, about which there are references of excellent tolerance.

The European guidelines suggest thiotepa is more useful in MPEs by breast cancer and cisplatin in those secondary to lung cancer.(11)

Personal experience with cisplatin has been similar to the Spanish group, with minimal recurrence and scant **low** adverse effects.(23)

There is a chance that external radiotherapy could be useful in radiosensitive tumors. Although a 93% effectiveness has been described in lymphomas and leukemias, the risk of radiation-induced myocarditis in patients with prolonged survival expectations makes it necessary to look for other therapeutic alternatives.

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