The Use of Cytology to Evaluate Pericardial Effusions

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ABSTRACT

Pericardial effusions from 27 patients were examined cytologically during the five-year period of 1973–1977. Malignant cells were found in eight cases (30 percent). In three of these patients malignancy was unsuspected clinically, and this was the first time the cancer was diagnosed. In addition, cytology often suggested the specific histological types and possible primary sites to be determined. Special stains were also found helpful. There were no false positive reports. Although the pericardial effusions from the remaining 19 patients were negative for tumor cells, metastatic carcinoma to the pericardium was discovered at autopsy in two of these cases. Thus, cytologic examination of pericardial fluid is an important tool in the diagnosis of malignancy, but false negative results may occur.

Pericardial effusions are associated with a wide range of diseases and often present a difficult and perplexing diagnostic problem. Cytological examination of pericardial fluid offers a practical method for establishing a diagnosis. This is especially true for pericardial effusions owing to malignancy. The purpose of this paper is to underscore the usefulness as well as limitations of this important diagnostic modality.

Materials and Methods

The results from pericardial fluid specimens received by the cytopathology laboratory for the five-year period 1973–1977 were reviewed. The cytological reports indicated the presence or absence of malignant cells in the specimens. In the pericardial fluids positive for cancer, the histological type was described. In addition, hospital records including clinical notes, surgical pathology reports and autopsy protocols were reviewed to determine, if possible, the etiology of the pericardial effusions.

The pericardial effusions were brought fresh to the cytology laboratory. The specimens were centrifuged and smears and cell buttons using collodion bags were prepared from the sediment. The smears were stained by the Papanicolaou method. Sections from the cell blocks were stained with hematoxylin and eosin as well as special stains when indicated.

Results

Among the 27 patients included in this
study, malignant cells were found in the pericardial fluid of eight (30 percent). Six of these represented metastases from the lung and two were from the breast. The histological types are summarized in table I. In three of these patients malignancy was not suspected clinically, and the initial diagnosis was made by cytological examination of the pericardial fluid. Since these cases clearly demonstrate the importance of cytology in the investigation of pericardial effusions of undiagnosed etiology, they are briefly reviewed.

Case 1: A 25-year-old Mexican male was admitted with pericardial effusion. He had been in excellent health until three weeks prior to admission.
when he began to experience a non-productive cough and pleuritic chest pain. He had been exposed to an active case of tuberculosis one month prior to admission and had a positive second strength tuberculin skin test. The patient had smoked one pack of cigarettes per day for five years.

Initial physical examination was unremarkable except for a 25 mm Hg pulsus paradoxus. Chest roentgenograms showed a pericardial effusion. The patient’s condition deteriorated rapidly. Pericardiocentesis was performed. Although acid-fast organisms were not identified in the pericardial fluid or numerous sputa, a clinical diagnosis of tuberculous pericarditis was made and treatment with ethambutol and isoniazid was begun. However, cytological examination of the pericardial fluid revealed mucin-producing papillary adenocarcinoma with psammoma bodies (figure 1). Subsequently, examination of sputa and pleural fluid, as well as the pericardium and cervical lymph nodes, showed the same malignancy. Radiological re-examination of the lungs by tomograms demonstrated a nodule in the left upper lobe.

Following palliative radiation therapy, the patient returned to Mexico and expired. An autopsy was not performed.

Case 2: A 46-year-old white female was admitted because of hypotension and progressive dyspnea. Past medical history included smoking two packs of cigarettes per day for 30 years and flu-like symptoms for 10 days prior to admission. Physical examination revealed a 30 mm Hg pulsus paradoxus. A clinical diagnosis of viral pneumonia and pericarditis with cardiac tamponade was made, and a pericardiocentesis was done which showed markedly anaplastic, large malignant cells (figure 2). The pericardial effusion rapidly reaccumulated and the following day a pericardial window procedure was performed. Microscopic sections of the pericardium showed similar malignant cells. No gross pulmonary lesions were noted at the time of surgery. Postoperatively, re-evaluation of the admission chest roentgenogram showed a hilar mass with diffuse lymphangitic spread, and sputum cytology was positive for poorly differentiated carcinoma. After a stormy hospital course, the patient expired. An autopsy was not performed.

Case 3: The patient was a 58-year-old white male who had smoked two packs of cigarettes per day for 30 years. During a recent evaluation for increasing dyspnea, a positive PPD was noted. Despite negative smears and cultures of sputa for acid-fast organisms were not identified in the pericardial fluid or numerous sputa, a clinical diagnosis of tuberculous pericarditis was made and treatment with ethambutol and isoniazid was begun. However, cytological examination of the pericardial fluid revealed mucin-producing papillary adenocarcinoma with psammoma bodies (figure 1). Subsequently, examination of sputa and pleural fluid, as well as the pericardium and cervical lymph nodes, showed the same malignancy. Radiological re-examination of the lungs by tomograms demonstrated a nodule in the left upper lobe.

Following palliative radiation therapy, the patient returned to Mexico and expired. An autopsy was not performed.

Figure 2. Smear of pericardial effusion (Case 2) showing anaplastic, large, malignant cells (Hematoxylin and eosin, × 600).
fast organisms, pulmonary tuberculosis was diagnosed clinically, and the patient was treated with isoniazid and ethambutol. Soon thereafter, he was readmitted in severe congestive heart failure owing to cardiac tamponade. A pericardiocentesis was done with immediate clinical improvement. Cytological examination of the pericardial fluid revealed squamous cell carcinoma (figures 3A and 3B). The malignant effusion reaccumulated, necessitating a pericardiectomy. At the time of surgery, small nodules were noted in the lungs, pericardium and myocardium. Histologic examination of the pericardium showed squamous cell carcinoma. The patient expired shortly thereafter, and an autopsy was not performed.

Nineteen pericardial effusions did not contain malignant cells. In 17 of these, the effusions were attributed to non-malignant etiologies which included idiopathic (5), tuberculosis (2), rheumatic heart disease (2), myocardial infarction

Figure 3A. Smear of pericardial effusion (Case 3) showing clusters of malignant cells with clear cytoplasmic vacuoles (Hematoxylin and eosin, × 600).

Figure 3B. Cell button of pericardial effusion (Case 3) showing malignant tissue (Hematoxylin and eosin, × 400).
(2), idiopathic cardiomyopathy (1), rheumatoid arthritis (1), uremic pericarditis (1), hypothyroidism (1), trauma (1) and hemorrhagic pericardial effusion secondary to anticoagulant therapy (1). All of these patients have followed a benign course from five to 60 months. However, the two additional patients whose pericardial effusions lacked malignant cells were found at autopsy to have squamous carcinoma of the lung with pericardial metastases. A pulmonary malignancy was recognized premortem in one of these two patients, whereas there was no clinical suspicion of neoplasm in the other patient who was clinically thought to have a pericardial effusion secondary to congestive heart failure (table II).

Discussion

Metastatic tumors to the pericardium and heart are not uncommon in patients with advanced malignant disease. The reported incidence varies among different autopsy series, ranging between 0.1 and 6.4 percent in unselected autopsies and 1.5 and 20.6 percent in autopsies of patients dying with malignant disease.\(^2\) Although theoretically every primary neoplasm can give rise to a cardiac metastasis, the most common are carcinoma of the lung and breast, malignant melanoma, leukemia and lymphoma.\(^1\) Metastases more frequently involve the pericardium than other areas of the heart. Recently, there has been a steady increase in the incidence of cardiac metastases. This is attributed to a general rise in the incidence of lung and breast cancer and to advances in the therapy of malignant diseases enabling patients to live longer and thus develop more extensive tumor dissemination.\(^2\)

Despite the frequency of secondary malignancies of the pericardium and heart, they are often not diagnosed premortem. This is due to a number of factors. Metastatic involvement may sometimes be relatively asymptomatic. When they do result in circulatory impairment, it is often attributed to cardiac disease unrelated to the neoplasm.

A 30 percent rate of positive pericardial fluids in our series is comparable to the 28 percent reported by Zipf and Johnston.\(^3\) In light of a significant frequency of malignant pericardial effusions, it is important to have a high index of suspicion. This is emphasized by the three cases described in which the diagnosis of cancer was clinically unsuspected, and the diagnosis was initially made from the cytological material. This high rate of positivity of pericardial effusions (30 percent) is especially noteworthy in comparison to pleural and abdominal effusions where the positivity rate is 15 percent in the authors' institution.

By means of pericardial fluid cytology, not only can malignancy be documented, but also a specific morphologic classification (adenocarcinoma, squamous cell car-
cinoma, oat cell carcinoma, etc.) as well as a possible primary site can be suggested. Special stains may be helpful. For example, in Case 3, many of the malignant cells in the smears were clustered and contained prominent clear cytoplasmic vacuoles. This appearance suggested a mucin-producing adenocarcinoma (figure 3A). However, in the cell button, where a fragment of malignant tissue suggested a squamous cell carcinoma, the cytoplasmic vacuoles did not stain with mucicarmine and were positive for glycogen using the periodic acid Schiff stain with diastase digestion, consistent with squamous cells (figure 3B). Subsequent tissue biopsy from the lung substantiated the diagnosis of squamous cell carcinoma.

In this series, two patients had a negative pericardial effusion despite involvement of the pericardium as proven by autopsy. Zipf and Johnston also reported two false negatives. This illustrates that pericardial fluid cytology is a very useful diagnostic tool but has limitations. Hence, a negative cytology report may not necessarily eliminate malignancy as a possible cause of pericardial effusion. When there is a strong clinical suspicion of cancer, surgical exploration may be required to establish the correct diagnosis.

References