The Role of Cytology in the Evaluation of Pericardial Effusions*

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Pericardial effusions from 47 patients were examined for cancer cells. Fluids from 13 of the 15 patients with neoplasm involving the pericardium were decisively “positive.” There were no false positive reports. Three patients had malignancy localized to the chest, but not metastatic to the pericardium. Effusions from these three patients contained no tumor cells. The accumulation of fluid in a patient with a known or suspected malignancy does not necessarily mean metastatic disease. Cytologic evaluation of these fluids is helpful in establishing a prognosis and mode of therapy.

The presence of effusions in body cavities can be a confusing clinical problem in differential diagnosis. The examination of pleural and peritoneal fluids by cytologic methods has already proved to be of decisive value in the diagnosis of malignant, as well as non-malignant disease.1–8

Surveys of the possibilities and limitations of pericardial fluid cytology have been limited, probably because pericardial fluids constitute less than 1 percent of the serous fluids examined in a cytology laboratory. The purpose of this paper is to show that the cytologic examination of pericardial fluids may play a significant role in the differential diagnosis of pericardial effusions.

MATERIALS AND METHODS

Each year at Duke Hospital, 25-30 pericardiocenteses are performed. In two-thirds of these, the pericardial effusions are of known etiology, usually uremic pericarditis. In eight to ten patients per year, however, the etiologies of the effusions are not certain, and samples of the fluid are submitted to the cytopathology laboratory for evaluation.

In recent years, 70 pericardial fluid specimens have been examined in the cytopathology laboratory at the Duke University Medical Center. In 47 of these patients sufficient histologic or clinical information was available to leave no doubt about the absence or presence of a neoplasm involving the pericardium. Fifteen of the 47 cases had histopathologic confirmation (by open pericardial biopsy or autopsy examination) of a neoplasm involving the pericardium. The absence of pericardial neoplasm in the other 32 cases included in the study was confirmed by histopathologic examination or by adequate clinical followup.

Until 1966, the pericardial fluids were mixed with equal parts of 10 percent formalin prior to being brought to the cytology laboratory. These specimens were centrifuged, and smears and cell blocks were prepared from the sediment. Since 1966, the fluids have been heparinized, (1-3 units of heparin per ml of effusion) at the time of pericardiocenteses and submitted immediately and unfixed to the laboratory. From these fluids membrane filter preparations fixed in 95 percent ethanol and stained by the Papanicolaou method have been used exclusively.

Sixty-one pericardial fluid specimens from the 47 patients were received for cytologic evaluation. Nearly all cytologic examinations were reported to be either "positive, diagnostic for cancer," or as "negative, no evidence of cancer in the specimen." On several occasions it was not possible to be definitely conclusive of the malignancy of atypical cells in a specimen, and for statistical analysis these "suspicious" cases have been regarded as negative. Slides from each case were reviewed in a blind and random fashion by the authors.

RESULTS

Table 1 compares the final confirmed diagnoses with the initial cytologic reports.

Twenty-two pericardial taps were performed on the 15 patients with tumor involving the pericardium. Malignant cells were reported in 15 of the 22 specimens. These 15 positive specimens had been obtained from 12 (80 percent) of the patients with pericardial metastases. There were three false negatives. These three patients had had five pericardial taps, four of which were originally reported as containing cells which were suspicious for, but not diagnostic of, malignancy. No tumor cells were seen...
in the fifth specimen. On review, malignant cells were found in two specimens from one of these patients originally reported as "suspicious." Even on review, cells diagnostic for malignancy could not be found in specimens from the other two patients. Both patients had undifferentiated carcinomas with origins thought to be in the lung. Autopsy examination of one patient demonstrated the pericardial metastases to be covered by a fibrinous exudate which apparently prevented exfoliation of the malignant cells.

With each "positive" diagnosis an opinion was expressed as to the type of cell composing the neoplasm. Table 2 compares the cytologic appearance of cell type with the site of origin of the tumor. The majority of the tumors metastasizing to the pericardium were adenocarcinomas (Fig 1 and 2).

The carcinomas of the breast and stomach were poorly differentiated histologically as well as cytologically. The squamous cell carcinoma was fairly well differentiated histologically, but the malignant cells disseminated in the pericardial fluid did not have differential features. The lymphosarcoma cells were readily differentiated from the inflammatory cells of benign pericarditis (Fig 3, 4, and 5).

Forty pericardiocenteses were performed on the 32 patients who had no tumor involving the peri-
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FIGURE 3. Malignant lymphoma, pericardial effusion. The malignant characteristics of these cells include a thin rim of cytoplasm, jagged irregularities of the nuclear membrane, clearing and clumping of the nuclear chromatin, large irregular acidophilic nucleoli, and an extrusion of the nucleoplasm which has the appearance of a proboscis (arrow). Millipore filter, Papanicolaou stain, × 1000.

FIGURE 4. Chronic inflammation, pericardial effusion. This pericardial exudate is composed of acute and chronic inflammatory cells and reactive mesothelial cells. The large mesothelial cells have abundant cytoplasm, a smooth nuclear boundary and indistinct nucleoli. The clumping along the inner aspect of the nuclear membrane represents degenerative changes (arrow). Millipore filter, Papanicolaou stain, × 1000.

FIGURE 5. Chronic inflammation, pericardial biopsy. This histologic section from the same patient as Figure 4 demonstrates thickened pericardium with an inflammatory infiltrate consisting of neutrophils, plasma cells, lymphocytes and monocytes. The mesothelial cells are hyperplastic (arrow). No tumor was seen. Hematoxylin and eosin, × 250.

Table 3—Pericardial Effusions without Associated Pericardial Metastases

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulomatous pericarditis</td>
<td>14</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4</td>
</tr>
<tr>
<td>Tumor elsewhere</td>
<td>3</td>
</tr>
<tr>
<td>Idiopathic pericarditis</td>
<td>11</td>
</tr>
</tbody>
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A variety of processes accounted for these non-malignant effusions and are summarized in Table 3. Fourteen effusions were due to a granulomatous pericarditis and in most of these a clinical or bacteriologic diagnosis of tuberculosis pericarditis was made. Four cases were associated with uremic pericarditis. Three patients had a malignancy elsewhere (one with carcinoma of the breast and two with Hodgkin's disease), but histologic examination demonstrated no pericardial involvement. These effusions were thought to have accumulated as a result of x-ray therapy to the chest or due to a "sympathetic effusion" induced by an inflammatory reaction to tumor adjacent to the mediastinum. No definite etiology could be determined in the remaining 11 cases, but all cases of idiopathic pericarditis were associated with rheumatic heart disease, viral pneumonitis, myocardial infarction, rheumatoid arthritis or polyarteritis.

There were no false positive reports; however, seven of the earlier patients with reactive mesothelial cells and hyperplastic but benign acinar elements were originally reported as suspicious (Fig 6 and 7). On review and with more experience it was apparent that these should have been reported as severe inflammation or reactive mesothelial cells. During the past five years, no "sus-
Kiel HI: Reactive mesothelium, pericardial biopsy. This histologic section from the same patient as Figure 6 demonstrates the hyperplastic but benign nature of the clumps of mesothelial cells present in the fluid. Reactive mesothelial cells line the thickened pericardium. These cells have a moderate amount of cytoplasm. The nuclei are large and pleomorphic, but the chromatin is evenly distributed and nucleoli are not present. Some of the cells are multinucleated (arrow). Hematoxylin and eosin, X 400.

DISCUSSION

Pericardial fluid cytology is not of value in making an early diagnosis of cancer, although on several occasions positive cytology did expose an undiagnosed malignancy. More commonly, it provides the information that a known or suspected cancer has metastasized, in which case corrective surgery is contraindicated.

In most cases it is possible from examination of exfoliated cancer cells to classify the neoplasm into its histologic type; however, it is not possible to suggest with confidence the primary site of the neoplasm.

A negative report does not eliminate cancer from the differential diagnosis, but it does make pericardial metastases unlikely. Even in patients with previously treated cancer, the accumulation of fluid does not always mean disease and should not be considered as such especially if no cancer cells are detectable in the fluid. If the presence of malignancy is clinically suspected, other diagnostic procedures should be relied upon. The study of pericardial fluid is most valuable when the cytologic examination is accompanied by a bacteriologic analysis. In particular, smears and cultures for acid-fast bacilli are most rewarding.

REFERENCES

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Giant Birds of New Zealand

Dinornis maximus, a moa, stood ten feet high and must have had an appetite for grass equivalent to that of a large cow. Dinornis lost all trace of even a rudimentary wing. Recent research has shown that the giant Dinornis was alive as late as about AD 1500; and the Polynesians encountered, slew and ate it. An other large moa was Europteryx, of no mean size, for it stood on its short massive legs as high as a man. With no vestige of wings the great moas strode about, cropping the tussock pastures. Their huge egg must have been a bonne bouche for the Polynesian who, after sucking the contents through a small hole, used it for storing water—as the Bushman does today with ostrich egg. The only moa-like bird to survive for certain today is the national bird of New Zealand, the kiwi. Kiwi bones date back at least before the last Ice Age.