The Management of Pericardial Effusion in Cancer Patients*

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The relatively little attention given in the literature to the problem of pericardial effusion in cancer patients reflects the general attitude that if this complication is disclosed, the future of the patient is sealed, and therapy will not change his outcome. We challenge this pessimistic approach, and describe here our experience with seven patients with solid tumors, in whom pericardial effusion was diagnosed; one of them is described in detail. We advocate an active and sometimes even an aggressive therapy, which should always be related to the degree of the hemodynamic impairment. If instant relief is indicated, pericardiocentesis should be done; pericardiectomy is the treatment of choice if the fluid reaccumulates rapidly. After overcoming the urgent problem, the underlying disease and the local pericardial condition should be treated; and in our opinion, a combined approach, such as systemic or local chemotherapy, or both, with or without precordial irradiation, will lead to the optimal result.

There are no statistical data available concerning the prevalence of pericardial effusion in patients with cancer, and the estimates vary from "common" to "uncommon." In 1974, Smith et al were able to collect from the English literature only 35 cases and added their own five cases. In 1975, Flannery et al described another four patients. This small number of reported cases clearly does not correspond to the cases encountered, but the relatively few reports reflect the general attitude of giving too little attention to this aspect of neoplastic diseases, probably due to the concept that if pericardial involvement is disclosed, the future of the patient is sealed, and therapy will not change his outcome. We challenge this pessimistic approach and report herein our experience with patients with solid tumors in whom pericardial effusion was diagnosed. We describe the clinical management of this complication, as well as the average survival time after the diagnosis was made and therapy was started. The importance of evacuation of the fluid and the consideration for additional treatment, such as radiotherapy and chemotherapy (systemic or local), are also discussed.

CASE MATERIAL

This study describes seven patients suffering from solid tumors in whom pericardial effusion was diagnosed during the years, 1970 to 1975. The underlying disease, the clues leading to the diagnosis of effusion, the therapeutic measures taken, the effect of the treatment, and the length of survival of the patient after the appearance of pericardial effusion are summarized in Table 1.

For pericardial puncture, the substernal parasternal approach was used, always performed in the operating theater, with electrocardiographic and blood pressure monitoring. With the patient in a semirecumbent position, a 16-gauge 3½-inch needle was inserted slightly below and to the left of the xyphoid process and was advanced at an angle of 45° towards the right shoulder. During the pericardiocentesis, the maximal amount of fluid was always withdrawn. If local intrapericardial drug administration was planned, a polyethylene tube was thereafter inserted into the pericardial sac and was left there for two to three days.

In cases 1 and 3, the pericardiectomy was performed through a left anterolateral thoracotomy. A large opening ("window") of about 2 × 3 inches was formed by resection of the pericardium between the two phrenic bundles, the aortic and pulmonary arterial reflections in a superior plane, and the diaphragm in an inferior plane. This approach created a direct communication between the pericardial cavity, pleura, and mediastinum, preventing accumulation of fluid in the pericardial sac.

In all of the patients, the diagnosis of malignant involvement of the pericardium was verified by histologic examinations. Although some of the patients received prior irradiation therapy to their chests, the histologic picture clearly defined the malignant nature of the effusion, and postirradiation pericarditis could be ruled out.

For evaluation of the treatment, we used the criteria of O'Bryan et al, as modified by Smith et al, and classified our results as good if (1) the decrease...
or disappearance of pericardial effusion lasted for at least 30 days, (2) symptoms of pericardial tamponade were absent for more than 30 days, and (3) there was no requirement for pericardiocentesis 30 days after the initiation of local or systemic treatment.

ILLUSTRATIVE CASE REPORT

A 53-year-old woman who still menstruated was first examined in May 1973, because of lymphedema of the right arm. A large tumor was palpated in her right breast, and axillary and supraclavicular lymph nodes were apparent. Biopsy of the breast showed adenocarcinoma. A chest x-ray film (Fig 1) and electrocardiogram (Fig 2) were normal.

The patient underwent bilateral oophorectomy and thereafter received radiotherapy to the right breast and lymphatic areas with cobalt, the total dose being 6,000 rad to each field. The response to radiotherapy was partial regression of the tumor. The patient also received testosterone and combined chemotherapy with cyclophosphamide and 5-fluorouracil.

One year later, she developed metastatic involvement of the left breast and the liver. The patient's chemotherapeutic regimen was then changed to methotrexate, triethylenethiophosphoramide (thio-TEPA), vinblastine, and prednisone.

One and a half years later, the patient was urgently admitted to the hospital, because of severe dyspnea. Physical examination revealed respiratory distress, with a respiratory rate of 40 respirations per minute. The pulse was irregular, at a rate of 112 beats per minute. Pulsus paradoxus was noted (25 mm Hg). The blood pressure was 150/100 mm Hg. Marked jugular venous congestion was seen. The heart sounds were distant. Venous pressure was 24 cm H₂O. A chest x-ray film demonstrated a markedly enlarged cardiac shadow (Fig 3). The ECG showed low voltage of complexes, and diffuse ST-T changes (Fig 4).

Later during the day, the patient's blood pressure dropped to 50 mm Hg, and she went into circulatory collapse. Tamponade was diagnosed, and emergency pericardiocentesis was performed, withdrawing 300 ml of blood-stained fluid. Immediately after pericardiocentesis, the blood pressure returned to normal values, and the dyspnea improved. Histologic examination of the pericardium revealed metastatic adenocarcinoma of the breast. The patient was discharged home in good condition. She remained free of disease for 30 months, but died of peritoneal metastasis after a recurrence of fluid.
logic examination of the fluid showed adenocarcinoma cells. During the following day, gradual deterioration was observed in the patient’s circulatory and respiratory condition, and the cardiac shadow on the chest x-ray film enlarged. Therefore, thoracotomy and pericardial fenestration were performed, with evacuation of 1,200 ml of blood-stained fluid. During the following three days, 30 mg of triethylene-thiophosphoramide were infused twice a day, for a period of 30 minutes each time, through a pericardial drainage tube. Thereafter, the patient received intramuscular injections of triethylene-thiophosphoramide (10 mg/day). One week later, the patient was discharged in a satisfactory general condition.

During the next six months, the patient was free of symptoms and very active and received weekly injections of triethylene-thiophosphoramide. Two weeks before her last admission to hospital, the patient again started to complain of dyspnea. Marked bilateral pleural effusion was seen on the chest x-ray film, but no enlargement of the heart was present. Shortly thereafter, the patient died of respiratory insufficiency.

**DISCUSSION**

The pericardium may be invaded by a malignant process either by direct intrathoracic invasion, or by retrograde lymphatic spread from mediastinal nodes. In both cases the accumulation of fluid in the pericardial sac will inevitably lead to the development of symptoms and signs of cardiac compression and will aggravate the patient’s condition. With further accumulation of fluid, inflow obstruction and the clinical picture of cardiac tamponade will develop, and the life of the patient becomes acutely endangered, in many occasions much before the time his basic disease would have reached a terminal stage. Therefore, the alertness of the physician is important to diagnose this condition early and to provide therapy.

This first diagnostic clue may be an enlarging of the cardiac silhouette, as pointed out by Harvey, followed by elevation of jugular venous pressure, pulsus paradoxus, and electrocardiographic changes. The importance of this last diagnostic procedure was recently pointed out as one of the most, if not the most, reliable feature of pericardial involvement. If these simple measures do not provide...
enough information, the more sophisticated procedures (such as angiocardiograms, precordial scan, or echocardiograms) should be used.

The malignant nature of the fluid is verified by the finding of malignant cells. There is a high rate of malignant findings in the pericardial effusion on cytologic examination, as demonstrated in our material, as well as in previously reported cases.2-4

The ammunition we have at our disposal in the battle against malignant pericardial effusion includes systemic chemotherapy, local radiotherapy, local introduction of chemotherapeutic or radioisotopic agents into the pericardial sac, pericardiocentesis (with or without prolonged evacuation), pericardial "window" operation, pericardiectomy, or a combination of these procedures.

In our opinion, in patients with apparent hemodynamic impairment, pericardiocentesis is the immediate therapy of choice. This procedure was applied soon after the diagnosis of pericardial effusion was made in six of our patients. Only one of them (case 3) could be managed for 24 months on systemic chemotherapy alone, requiring pericardial tap only thereafter. In several instances, our patients required a pericardial tap as an emergency procedure because of tamponade; and in our opinion, in this situation, such a procedure is preferable over immediate pericardiectomy, especially since the general condition of these patients is usually poor.

Occasionally in such cases, 700 to 1,000 ml of fluid can be evacuated, with immediate relief.

In rare cases, a pericardial tap alone may be sufficient to relieve the patient and avoid reaccumulation of the fluid, as described by Hirsch et al.9 who witnessed a five-year remission following a single tap in a patient suffering from breast carcinoma; however, in our experience, because of the tendency of the malignant effusions to reform, additional measures are required. Precordial irradiation seems to be an appropriate procedure to follow the evacuation, especially in those patients who had no previous precordial or mediastinal irradiation with a maximal dose.4 Although Lokich10 advocated precordial irradiation alone as the "treatment of choice" for malignant pericardial effusion and described successful treatment of approximately one-half of the reported cases treated by this method, in our opinion the prior evacuation of the fluid is an essential prerequisite to the success of the subsequent irradiation.

Surgical procedures, such as the creation of a pericardial "window" or partial pericardiectomy, are regarded as major interventions, and we believe that they should be reserved for the very advanced cases, in which fluid reaccumulates too rapidly to be manageable by repeated pericardial taps. Such was the situation in our patient 1, who had a fairly long (six-month) survival after such an operation. On the
other hand, patient 3 did not survive this surgical intervention. We generally share the view expressed by Smith et al.,8 that patients treated in the "conservative" way, including pericardiocentesis and local or systemic chemotherapy or radiotherapy, or both, maintain a longer symptom-free interval than those treated with pericardial operations. Lokich10 expressed the opinion that surgical interventions are reserved for patients in whom previous exposure of the cardiac structure to irradiation precludes the use of radiotherapy.

Intrapericardial administration of chemotherapeutic agents or radioactive material is an important adjunct to other therapeutic measures, and we applied this to two of our patients. Suhrland and Weisberger11 achieved resolution of the effusion in three patients with intrapericardial administration of 5-fluorouracil, while Rose12 found only "rare" favorable responses to this therapy in patients with pericardial effusions.

Poudrage with talc has occasionally been suggested as treatment for this condition, and a case successfully treated by this method was described by Goldman and Pearson.2

The chances for survival once pericardial effusion has been diagnosed are not clearly described in the literature, but undoubtedly it is classified as a "late" manifestation, as compared to neoplastic pleural or peritoneal effusions.18 Only two of the 15 patients diagnosed during a 19-year period with this condition (Goldman and Pearson2) were discharged from the hospital alive. In ten of the fatal 13 cases, the pericardial effusion was considered either the primary cause of death or a major contributing factor. According to Smith et al.,8 a mean survival of 11.7 months is experienced when conservative measures alone were employed, while the mean survival in patients treated with a pericardial "window" and any other treatment was 6.4 months in nonhematologic malignant disease. A significant interference with cardiac action was observed by Thurber et al18 in 85 percent of the patients with pericardial involvement. In our series, only one patient (case 3) seemed to have unimpaired hemodynamic and cardiac function for about two years, while all others suffered from some degrees of cardiac incapacitation.

The pericardial effusion due to invasion of the malignant process should be differentiated from that occurring as a late sequela of irradiation of the left side of the chest. In this last category, therapy with corticosteroids has been tried successfully, while others claim that pericardiectomy is the treatment of choice, especially in view of the frequent transformation of this entity into the constrictive type of pericarditis.

It is our conclusion that the appearance of pericardial effusion in patients with cancer does not necessarily herald a turn into the terminal stage. This complication should be actively and sometimes even aggressively treated; and clinical improvement, subjective and objective, frequently ensues for periods long enough to justify the therapeutic efforts. The management should be related to the status of the patient. If urgent hemodynamic complications required relief, pericardiocentesis should immediately be done. If rapid reaccumulation of the fluid threatens the life of the patient, pericardiectomy is indicated. After the hemodynamic impairment has been overcome, or during the stage when such impairment does not present an urgent problem, the underlying disease and the local pericardial condition should be treated by systemic or local chemotherapy or precordial irradiation, or some combination of the three. This "combined" approach seems to provide the desired melioration of the impaired hemodynamic status and is efficient in alleviating the malignant pericardial process.

REFERENCES