Phosphorus-32-Colloidal Chromic Phosphate: Treatment of Choice for Malignant Pericardial Effusion

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A 68-yr-old male with agnogenic myeloid metaplasia was given phosphorus-32-colloidal chromic phosphate intrapericardially for the treatment of malignant pericardial effusion. Technetium-99m-sulfur colloid was used to verify catheter placement and to visualize distribution within the pericardium. Estimated dosimetry for this mode of therapy is presented, and it is suggested that pericardial administration of phosphorus-32-colloidal chromic phosphate is the treatment of choice for malignant pericardial effusion.

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Radiocolloids have been used to successfully treat malignant pericardial effusion for nearly 28 yr since Silver's (*1*) original description in 1962. Authoritative cardiology texts from Friedberg (*2*) in 1965 to Braunwald (*3*) in 1984 have advocated this therapeutic approach. Modern chemotherapy, which systemically attacks the patient's malignancy in all body regions, eliminates the need to palliate malignant effusion in many cases, but not in others (*4*). Phosphorus-32 (^{32}P), as chromic phosphate, is felt to be the agent of choice because its high energy, pure beta radiations are clearly cytocidal at the tumor and pericardial surface. Yet beta penetration is so poor that virtually no radiation dose is delivered beyond the pericardium proper. We have recently encountered three patients with malignant pericardial effusion in a 400-bed community hospital. Two responded nicely to systemic chemotherapy for their primary malignancies, requiring only a single pericardial tap. The third case required palliative radiocolloid therapy and is reported here along with estimated radiation doses to pericardial and myocardial tissue provided by the Radiopharmaceutical Internal Dose Information Center at Oak Ridge.

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CASE REPORT

A 68-yr-old white male had been treated for several years for agnogenic myeloid metaplasia. He presented in the summer of 1989 with acute onset of shortness of breath and orthopnea. Chest X-ray showed a large cardiac silhouette and multiple-gated angiocardiogram confirmed a large pericardial effusion. Pericardial taps by the cardiologist revealed bloody fluid containing malignant stem cells. Acute leukemic transformation was later identified by the finding of numerous blasts in blood smears. Anemia and reduced platelet counts of 25,000 were also seen. In spite of vigorous chemotherapy directed at the acute leukemia by the oncologist, three pericardial taps of 1000 cc, 800 cc, and 1200 cc were needed to alleviate pericardial tamponade, with the patient confined to a bed in CCU for 2 wk. Each tap had to be preceded by multiple fresh platelet pack transfusions and was a trying experience for this very ill patient. Phosphorus-32, as colloidal chromic phosphate, was administered by the nuclear medicine physician and cardiologist by means of a standard plastic intracath introduced into the pericardium via the sub-xiphoid route under ultrasound control and by using sterile technique. Before injecting the radiocolloid, 300 cc of pericardial fluid were removed to reduce tension on the pericardial wall, and the catheter position and pericardial volume of distribution (Fig. 1) were verified by introducing 37 MBq (1 mCi) of technetium-99m- (^{99m}Tc) sulfur colloid and imaging the chest with a mobile gamma camera as described in our 1979 textbook (*5*). Sulfur colloid uniformly layers the pericardial surface just as colloidal chromic phosphate does. A 185-MBq (5 mCi) dose of ^{32}P-colloidal chromic phosphate was then injected into the pericardial cavity and the catheter flushed with 10 cc of sterile saline (no preservative). A portable gamma camera was used to obtain additional views of the volume of distribution, and then the catheter was removed. A small pressure bandage was then placed over the injection site. This can usually be removed the following day. The patient was able to sleep flat the next morning and his echocardiogram showed only a small residual effusion. After only 24 hr, he no longer required monitoring and was able to ambulate and care for himself for the first time in a month. The patient left the hospital to an independent existence the day after that. The

FIGURE 1
Anterior view of the chest showing symmetrical distribution of ^{99m}Tc-sulfur colloid in the pericardial space.

patient continued systemic chemotherapy on an outpatient basis without any recurrence of cardiorespiratory distress. The patient succumbed to his acute leukemia ~6 wk later. No postmortem examination was obtained.

DISCUSSION

Malignant pericardial effusion may respond to modern chemotherapy alone. In our institution, a 64-yr-old female with breast cancer, metastatic to bone, developed a 1000-cc malignant pericardial effusion. Her chemotherapy program was modified, and she continues on chemotherapy, 3 yr later, with no recurrent pericardial effusion. A second patient, a 47-yr-old female with bronchogenic carcinoma, developed a 1200-cc malignant pericardial effusion and was started on chemotherapy. This patient has had no recurrence of pericardial effusion for the last 6 mo even though her primary malignancy has progressed. Note that patients who respond to chemotherapy live longer than those who do not. Palliative radiotherapy with ^{32}P is generally essential in patients who respond poorly to chemotherapy and only rarely require a second treatment dose.

Agnogenic myeloid metaplasia (or myelofibrosis) is characterized by the growth of neoplastic stem cells outside of the bone marrow. Spleen and liver are involved, leading to organ enlargement. Fibrotic replacement of marrow leads to symptomatic anemia, thrombocytopenia and leukopenia, and death in four to five years. Leukemic transformation, as in our patient, occurs in 5%–10% of cases. Leukemic infiltrates may involve any organ, including the heart and pericardium, thereby producing malignant pericardial effusion.

The care and treatment of these patients is a cooperative effort involving the cardiologist or thoracic surgeon, oncologist, and nuclear medicine physician. The availability of well qualified experienced cardiologists and oncologists who regularly perform pericardial, pleural, and peritoneal taps and/or therapy with nonradioactive agents makes it unnecessary and inadvisable for nuclear physicians or radiotherapists with less experience to carry out treatment alone. The nuclear physician should prescribe the proper dosage, verify the identity, and quantify the activity of the chromic phosphate before administration, verify the accurate placement of the pericardial catheter, and assist with the dose administration. This cooperative effort greatly improves the likelihood of a satisfactory outcome for the patient.

Although the use of radiocolloids in therapy is well documented, dosimetry for the intracavitary use of radiocolloids has been difficult to determine, and dosimetry for intrapericardial administrations has never, to our knowledge, been done. An estimation of the dose to pericardial and myocardial tissue was made by the Radiopharmaceutical Internal Dose Information Center using extrapolations of values from a dosimetry model for radioactivity contained in the peritoneal cavity published by Watson et al. (*6*). It is assumed that the heart is covered with a uniformly thin layer of radiocolloid with a volume of ~30 ml and a thickness of 0.08 cm. Estimated doses to the myocardial wall as a function of depth are shown in Table 1 for both ^{32}P and ^{99m}Tc. The observed cytotoxic effect of ^{32}P on malignant pericardial tissue can be explained by the extremely high surface dose resulting from a 185-MBq (5 mCi) administration. Radiation dose estimates to the remainder of the body due to the intrapericardial administration of ^{99m}Tc-sulfur colloid are shown in Table 2.

Radioactive phosphorus, when used as colloidal chromic phosphate, is a useful, palliative treatment for

TABLE 1
Radiation Dose Estimates for the Myocardial Wall from Intrapericardial Administration of ^{32}P or ^{99m}Tc*

		^{32}P	
		Estimated radiation dose	
	Distance† (cm)	(mGy) 185 MBq	(rad) 5 mCi
^{32}P			
	0.006	6.6×10^5	6.6×10^4
	0.018	4.7×10^5	4.7×10^4
	0.030	3.7×10^5	3.7×10^4
	0.12	1.3×10^5	1.3×10^4
	0.21	5.6×10^4	5.6×10^3
	0.30	2.0×10^4	2.0×10^3
	0.40	4.1×10^3	4.1×10^2
^{99m}Tc			
	0.001	35	3.5
	0.002	29	2.9
	0.004	21	2.1
	0.008	9.6	0.96
	0.012	2.6	0.26
	0.016	0.28	0.028
	0.020	0.016	0.0016

* Activity assumed to be in the thin sac around myocardium, volume = 30 ml, thickness = 0.08 cm. Because of the range of the betas or electrons, ^{32}P was treated as a thin plane source and ^{99m}Tc was treated as semi-infinite volume source. No biologic removal assumed.

† Distance from source into myocardial wall.

TABLE 2
Radiation Dose Estimates to Remainder of the Body from Intrapericardial Administration of ^{99m}Tc*

Organ	Estimated radiation dose (mGy) 37 MBq	(rad) mCi
Heart wall†	4.8	0.48
Lungs	0.51	0.051
Thymus	0.85	0.085
Ovaries	0.0071	0.00071
Red marrow	0.13	0.013
Bone surfaces	0.18	0.018
Testes	0.00071	0.000071
Total body	0.19	0.019
Effective dose equivalent	0.53	0.053

* Activity was assumed to be in thin sac around the myocardium with no biologic removal.
† Photon dose only.

patients suffering from recurrent pericardial tamponade caused by malignant pericardial effusion which is resistant to chemotherapy. The extremely high dose to affected pericardial tissue combined with the substantially lower dose to underlying tissue makes this therapeutic approach a valuable adjunct in the care of these patients.

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