Pericardial Effusion following Radiation to the Chest*

Report of a Case

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Among the various causes of chronic massive pericardial effusion, radiation injury has been cited on only one previous occasion.1 We have had the opportunity to observe a patient who developed such an effusion two years after massive radiation to the left anterior chest for carcinoma of the breast. Although the histologic appearance of the pericardium of our patient did not have the "elephant skin" quality as described in the case reported by Blumenfeld and Thomas,1 the clinical courses of the two cases are similar and we consider them both to be a result of radiation injury.

Case Report

The patient, a Negro woman, was 43 years old when first admitted to Cook County Hospital in June, 1961. For two years, she had had a persistent ulcerative lesion in the precordial area of the thorax and in the month preceding admission had had increasing orthopnea and exertional dyspnea. Past history revealed that she had had mild hypertension since 1957, but had received no treatment. In July, 1958, she had had a radical mastectomy at another hospital. Following surgery and in the period between July 27 and September 3, 1958, she received radiation therapy in 49 treatments to the left anterior chest, left axilla and left supraclavicular areas to a total of 10,000 r. It is estimated that this delivered between 1,800 and 3,200 r to the heart and pericardium and was given as follows: 1) two 10 x 15 cu ports directed to the left anterior chest wall from the medial and lateral side. Total 2,000 r (air) to each port; 2) two opposing 10 x 15 cu ports — one anterior and one posterior directed to the left axilla. Total 2,000 r (air) to each port; 3) one 10 x 15 cu port in the left supraclavicular region with a total of 2,000 r (air) to this port; 4) factors: 200 KV; F.S.D.—50 cu; H.V.L. 1 mm cu. Chest x-ray film taken in the eighth week of therapy showed minimal left ventricular enlargement (Fig. 1). A follow-up x-ray film taken six months later showed distinct enlargement of the cardiac silhouette. In June, 1959, the mastectomy scar began to ulcerate.

Physical examination revealed a healthy woman with an ulcerating lesion in the area of the mastectomy scar. The blood pressure was 180/120. A P-A x-ray film of the chest revealed a large cardiac silhouette, a streaky density in the left infracostal area, and pathologic fractures of the 4th, 5th and 6th ribs on the left. The rib fractures were believed to be the result of radiation necrosis. Routine laboratory procedures which included a complete blood count, blood urea nitrogen, blood sugar and liver profile were within normal limits. Histologic examination of a biopsy from the border of the ulcer revealed

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Figure 1: Chest x-ray film taken September 22, 1958 during radiation therapy showing minimal cardiomegaly.
necrosis and inflammation. The ulcer decreased in size with topical therapy but did not heal.

She was hospitalized on two subsequent occasions in 1961 for pain at the site of the ulceration. Additional biopsies revealed a histologic picture compatible with radiation necrosis. An x-ray film of the chest taken in July of that year showed a massive cardiac silhouette.

In December, 1961, she was hospitalized because of a "heavy" sensation beneath the left scapula; and precordial pain and pressure which had been present for the previous month. Exertional dyspnea had become more severe. Blood pressure was 190/125, neck veins were distended and pulse rate was 130 per minute and regular. The ulcerating lesion had extended from the left sternal border to the left anterior axillary line. The liver was palpable three finger-breadths below the costal margin. Chest x-ray film revealed an extremely enlarged flask-shaped cardiac silhouette. ECG showed left ventricular hypertrophy and strain. The patient was treated with digitalis, diuretics and reserpine with partial relief of symptoms.

In August, 1962, during a prolonged admission for treatment of the ulcerative skin lesion, she continued to complain of dyspnea and orthopnea. Physical examination revealed blood pressure of 160/100 on expiration and 154/100 during inspiration. The pulse was 120/minute and regular. The neck veins were distended. The first heart sound was best heard at the left lower sternal border. The second sound was normally split and best heard in the second left intercostal space. There was no abnormal heart sound or murmur. Chest x-ray film again revealed an enlarged cardiac silhouette (Fig. 2).

Pericardiocentesis yielded 300 ml of clear straw-colored fluid. The protein content was 7 grams per cent. A post-pericardiocentesis x-ray examination following injection of air into the pericardial cavity revealed a normal sized heart and a thin parietal pericardium (Fig. 3). Routine cultures and cultures for tubercle bacilli were negative. Histologic examination of a cell block failed to reveal malignant cells. A pericardial biopsy (October, 1962) revealed pericardial fibrosis.

In February, 1963, a chest x-ray film revealed reaccumulation of the pericardial fluid. After pericardiocentesis, and despite her cardiac symptoms, an attempt was made to skin graft the ulcerated area. Postoperative wound infection and pneumonia led to death a few days after surgery.

Post-mortem examination revealed 100 ml of blood-tinged fluid in the pericardial cavity. The pericardial cavity was lined by a fibrinous exudate. The heart weighed 370 grams. The left ventricle was slightly enlarged. All the valves were normal. The coronary arteries showed a moderate degree of atherosclerosis. Histologic examination of sections from ventricles and atria revealed a fibrinous pericarditis. Beneath this relatively thin exudate, there was a thick layer of dense connective tissue with a moderate degree of focal cellular infiltration comprised chiefly of lymphocytes and occasional macrophages (Fig. 4). The sub-epicardial fat tissue was replaced by dense fibrous connective tissue. Sections from the left ventricle disclosed extensive replacement fibrosis of the myocardium. Sections from the right ventricle disclosed a moderate degree of septal fibrosis.

**Discussion**

The heart is believed to be markedly resistant to radiation injury. Hartman et al. exposed hearts of dogs and sheep to radia-
tion and, in those animals surviving 30 days to five months, found pericardial effusion. They were unable to demonstrate significant gross or microscopic changes in the pericardium. Leach and Sugiuira\(^4\) directed up to 20,000 roentgens to the hearts of adult rats and confirmed the radioresistance of the pericardium. They observed pericardial effusions in a few animals, but no significant histologic changes in the pericardium.

Recently, reports of radiation-induced myocardial infarction and fibrosis seen clinically and produced experimentally have appeared.\(^5\)\(^6\)\(^7\) Moss et al,\(^8\) by selective cardiac irradiation of dogs, produced changes which simulated acute-myocardial infarction. They noted pericardial effusion (150 ml serosanguineous fluid) in two dogs 21 days after irradiation. Pericarditis was noted by Phillips, Reid and Rugh\(^9\) in four of seven dogs after irradiation. Two dogs had pericardial effusions.

Symptoms of acute pericardial involvement have been described in patients receiving chest or mediastinal radiation. The so-called "mediastinal-cardiac reaction" was initially described in three patients whose thyroid glands were irradiated in treatment of thyrotoxicosis.\(^10\) The symptoms appeared during or immediately following treatment and consisted of pyrexia, retrosternal pain and electrocardiographic changes suggestive of pericarditis. These manifestations disappeared without apparent residual effects. Similar symptoms were described in patients receiving radiation of thymomas in treatment of myasthenia gravis.\(^11\)\(^12\)\(^13\) Jones and Wedgewood\(^14\) reported two patients who developed rather severe pericardial effusions, and attributed this reaction to conditioning of the pericardium when invaded by radiosensitive neoplastic tissue.

Catterall and Evans\(^1\) recorded electrocardiographic changes suggestive of pericardial injury in patients receiving roentgen-ray therapy to fields which included the heart and found no such changes in a control group of patients receiving similar therapy to the mediastinum, but directed to avoid the heart. Pearson reported myocardial infarction following therapeutic radiation of the chest.\(^1\) Vaeth, Feigenbaum and Merrill\(^2\) studied 20 patients who received heavy doses of x-ray to fields which involved at least 35 per cent of the myocardium. Electrocardiographic changes were noted in seven and these changes were associated with significant elevations of serum glutamic oxalo-acetic transaminase values in six.\(^3\)

Freid and Goldberg,\(^4\) in studying changes in lungs of 18 patients who received radiation to the chest, observed four instances of pericarditis and parietal pericardial adhesions and four additional patients had small pericardial effusions. Leach\(^5\) described three patients who had pericarditis following roentgen-ray treatment for neoplasms of the chest and mediastinum. All had chronic infection of the thoracic wall, ribs and left lung. Secondary infection by contiguity was implicated as the cause of the pericardial lesions.

Chronic pathologic alterations, secondary to irradiation of the heart, have been described. Tricot, Baillet and Hekmcke\(^6\) observed constrictive pericarditis following radiation for carcinoma of the left breast. Windsor\(^7\) found thickening of the pericardium characterized histologically by hyaline collagen and chronic inflammatory cells in a patient who had received x-ray therapy for carcinoma of the lung. He attributed the patient's death during surgery to myocardial damage from the radiation. Blumen-
feld and Thomas' case (mentioned above) is the only case associated with chronic pericardial effusion which was attributed by the authors to radiation of the pericardium.

Since there is no distinctive pathologic picture which defines roentgen-ray injury to the pericardium, the relationship to previous therapy can only be presumptive. In our patient, the absence of other causes for effusion and the evidence for severe radiation injury in the adjacent tissues make radiation injury the most plausible explanation for the chronic effusion. It seems evident that roentgen therapy can cause changes in the heart and pericardium, but the mechanism by which it produced massive pericardial effusion has not been explained. Two explanations seem plausible. Particles and macromolecular substances are poorly absorbed from the pericardial cavity through lymphatic channels which are not numerous and are located mostly at the base of the heart and along lines of fat deposition. 14-16 Radiation injury to lymphatic channels might be the factor which converts the acute pericardial injury into a chronic effusion. An alternate hypothesis is that this is a variant of the post-traumatic pericarditis syndrome. 17 The trauma is the x-ray injury and a secondary "auto-immune mechanism" perpetuates the effusion.

References

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