FATAL PULMONARY EMBOLISM

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Massive pulmonary embolism is a dramatic, often fatal, event. If death is not immediate, embolectomy using cardiopulmonary bypass is feasible, and a number of reports have appeared in recent years attesting to its value (1–5). However, emergency embolectomy is not practical on a wide scale.

In over 300 cases of pulmonary embolism with positive lung-scan findings, we have observed that major or fatal embolization rarely is the first evidence of a thromboembolic process. Most patients have symptoms or signs of small emboli antedating the catastrophic episode by 5–7 days or more. Lung scanning is an effective and widely applicable test for identifying occlusion of lobar, segmental and some subsegmental pulmonary arteries (6,7), while adequate anticoagulation is known to definitely reduce the incidence and mortality from recurrent emboli (8). Detection of these minor or “signal” emboli by lung-perfusion scanning followed by intensive anticoagulation is a potentially effective means of preventing massive embolization.

This paper describes the clinical course and autopsy findings in seven patients with massive pulmonary embolism and suggests that lung scanning may play an important role in reducing the incidence of fatal attacks.

METHODS

In noncritically ill patients 180–350 pCi of 131I-labeled macroaggregated human serum albumin were injected intravenously in an antecubital vein with the patient in the upright position. The posterior scan was begun immediately, followed by anterior and/or lateral views as indicated for better localization of ischemic areas. Critically ill patients were brought to the Radioisotope Department in their hospital beds, and the isotope was administered in the recumbent or semirecumbent position. Usually only an anterior scan could be obtained in these patients. Scans were performed on scanners (Picker Nuclear) with 3 × 2 or 5 × 2-in. NaI(Tl) crystals at speeds of 60–200 cm/min.

CASE REPORTS

Case 1. A 30-year-old male had a history of pneumonia and hemoptysis in 1962. On July 1, 1966, he developed chest pain, cough, and fever and was treated for pneumonia. An x-ray on July 5 showed residual inflammatory disease at the left base. Eight days later he experienced dyspnea, hemoptysis and syncope without fever or pain. A chest film showed no change except possibly slight cardiac enlargement. On July 14 the dyspnea increased. He became cyanotic and had an accentuated pulmonic second sound. The right knee was tender from an injury 5 days earlier. The serum glutamic oxaloacetic transaminase (SGOT) was 67 units (normal <40), and the lactic dehydrogenase (LDH) was 580 units (normal <550). The EKG showed anterior wall ischemia with incomplete right bundle branch block. The chest film demonstrated a prominent pulmonary artery with oligemia of the right lung and hyperemia of the left upper lobe. The lung scan indicated marked ischemia of both bases and the right upper lobe with relatively increased perfusion of the left upper lobe. Ten thousand units of heparin were immediately given subcutaneously followed by 7,500 units intravenously every 6 hr. However, two clotting times in the next 24 hr were only 10 and 18 min (hospital normal <15 min). Because the patient did not improve clinically, a vena cavai plication was performed the following day. The patient’s condition deteriorated during the operation, and emergency embolectomy using cardiopulmonary bypass was attempted. No occlusion could be found in the main pulmonary artery, and even with back flushing from the left atrium very little embolic material could be removed. The pulmonary arterial pressure remained elevated, and the patient expired in surgery. At autopsy the artery to the left lower lobe was com-

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FIG. 1. Anterior (above) and posterior (not shown) scans demonstrate marked ischemia in regions of right upper and middle lobes with lesser ischemia of both lower lobes. Part of perfusion defect in left lower lobe results from cardiac displacement. At autopsy occlusive stricture was found in artery to left lower lobe. All major arteries on right were filled with adherent and nonadherent emboli (shaded area). Partial occlusion of right lower lobe artery became complete during interval between scan and death. Completely occluded by a fibrous ring (Fig. 1). The branches of the right main pulmonary artery were almost completely occluded by emboli of varying age, and many well organized emboli were seen in the smaller arteries of the right lung. The source of the emboli was not determined.

Case 2. A 200-lb 23-year-old female developed thrombophlebitis in both legs on Nov. 29, 1964, 6 days postpartum. Her usual cigarette cough was accentuated from a recent “cold” but there was no chest pain and the lungs were clear. On Dec. 1, subcutaneous administration of 5,000 units of heparin four times a day was begun. This was increased to 7,500 units on Dec. 3 and to 10,000 units on Dec. 8 because of inadequate prolongation of clotting times. On Dec. 9 left chest pain, increased cough and tachycardia developed. There was a questionable left parasternal rub, and the pulmonic second sound was accentuated. The electrocardiogram was consistent with acute cor pulmonale. Her condition improved the following day but on Dec. 11 she felt faint and nauseated and had more chest pain. The SGOT and LDH were 12 and 400 units, respectively. A lung scan was consistent with multiple emboli to both lungs. She expired suddenly 3 hr later while being evaluated for possible embolectomy. At autopsy a large antemortem embolus was found at the bifurcation of the main pulmonary artery. Nearly all the large- and medium-sized pulmonary arteries contained both adherent and nonadherent emboli. Only small areas of the right middle and upper lobe and the left apex contained crepitant lung. A 9-cm organized clot was present in the left iliac vein.

Case 3. A 48-year-old male developed sudden onset of severe crushing chest pain, diaphoresis and hemoptysis on Aug. 2, 1965. He had a past history of pulmonary embolism and had been treated 1 month earlier for a pneumonitis although a diagnosis of embolism had also been entertained. A lung scan showed marked ischemia of the right lung and the

FIG. 2. Single anterior scan indicates that perfusion is limited almost totally to left upper lobe. Embolectomy was performed following scan, and large embolus was removed from right main pulmonary artery. No other significant emboli could be removed. At autopsy all major vessels except those to right upper lobe posteriorly and to left upper lobe were occluded with fresh and organizing emboli (shaded area). Resolving infarcts were present in ischemic regions (lined areas).
left base. Embolectomy was immediately performed with total cardiopulmonary bypass, and a large embolus was removed from the right main pulmonary artery. However, the patient could not maintain a normal blood pressure, and he expired. At autopsy only the vessels to the right upper lobe posteriorly and a few segments of the left upper lobe were patent (Fig. 2). The others were occluded by fresh and organizing emboli some of which were adherent. Areas of resolving infarction were also found. The etiology of the emboli was not ascertained.

**Case 4.** A 27-year-old motorcyclist was immobilized on Sept. 8, 1965, for multiple fractures of the right leg. On Sept. 27 he complained of substernal chest pain. His pulse was 140 and his respiration rate 28. The pain persisted during the following week, and his temperature rose to 100.4°F. His white count was 5,200, his SGOT 104 and his LDH 670 units. Incomplete right bundle branch block developed on Oct. 4. The following day he became hypotensive and had a respiratory rate of 44. Decreased breath sounds and a pleural friction rub were present in the left lung. There was evidence of thrombophlebitis in the fractured leg. Atelectasis in the right midlung field and possible pneumonitis in the right upper lobe and at the right base were found on chest x-ray. The lung scan disclosed complete ischemia of the left lung and right lower lung. Intravenous heparin was begun, and an emergency embolectomy with total cardiopulmonary bypass was performed later that day. The main pulmonary artery was clear but some "old clots" were milked from the right and left main branches. The emboli were of varying ages, some containing lines of Zahn and proliferating endothelial cells. A vena cava ligation was then performed. Hypoxia was encountered during the bypass procedure, and the patient never regained consciousness. He expired 4 days later. A massive firm adherent embolus was found distally in the left pulmonary artery at autopsy.

**Case 5.** A 60-year-old man had a hemicolectomy for diverticulitis on Sept. 26, 1965. Low-grade fever developed in the postoperative period, but no source of infection could be discovered on re-exploration on Oct. 10. His temperature subsequently rose to 102°F. A single anterior lung scan made on Oct. 19 originally was interpreted as normal but in retrospect demonstrated several oligemic regions. An LDH on Oct. 21 was 710 units, but the patient was not put on anticoagulants. Evidence of thrombophlebitis of the left leg was found on Oct. 25. He suddenly became acutely dyspneic and cyanotic on Oct. 27 and died. The autopsy disclosed a massive saddle embolus. In addition, well-organized emboli which appeared to have been in position for a matter of weeks were found in the branches of the arteries to the left upper and right lower lobes corresponding to the poorly perfused areas seen on the earlier scan (Fig. 3). Thrombi were present in the left femoral and iliac veins.

**Case 6.** A 41-year-old white male with a history of recurrent thrombophlebitis and intermittent chest pain and diaphoresis since 1963 entered the hospital on Aug. 10, 1966, complaining of shortness of breath and pressure in the chest. The lungs and extremities were negative on admission but calf tenderness developed 6 days later. Anticoagulation with heparin and warfarin was begun. A scan on Aug. 14 was consistent with bilateral embolism and this was confirmed by angiography. In addition, both the electrocardiogram and the vectorcardiogram indicated septal infarction. He was discharged as improved on
Sept. 13 on warfarin with a prothrombin time twice normal. On Oct. 3 he became dyspneic and collapsed. The prothrombin time on 2 mg of warfarin daily was 13.5 sec (11 sec control). Five thousand units of IV heparin were given followed by 5,000 units every 4 hr subcutaneously. The white count was 9,900. On Oct. 4, 50,000 units of IV heparin in 1,000 cc 5% dextrose in water was administered at 10 drops/min. Random clotting times were 13, 34 and 23 min. On Oct. 5, a total of 36,000 units of heparin was given, and the clotting times were 28, 42 and 13½ min. A repeat scan the next day indicated new emboli and a vena caval plication was performed. The patient's condition deteriorated during the procedure and an embolectomy on cardiopulmonary bypass followed. With the aid of lung compression "several large emboli" were removed but the patient could not tolerate removal from bypass. An angiogram demonstrated persistent vascular occlusions but further attempts to remove the emboli were only partially successful, and the patient expired. The autopsy disclosed recent and organized emboli distal to the main pulmonary artery occluding the vessels to the left upper lobe and lingula, the right lower and middle lobes, and the branches to the right upper lobe. A thrombus was found in the left iliac vein. In addition, the heart showed severe coronary artery disease and a healed septal infarction.

Case 7. A 48-year-old white female had a cholecystectomy in Aug. 1966. On Sept. 21 she had sudden onset of right flank pain aggravated by respiration. There was no cough or hemoptysis. Her temperature was 100°F. Decreased breath sounds and dullness were found at the right base but evidence of peripheral phlebitis was lacking. The white count was 10,800 with 84% polymorphs. The urinalysis showed 4–6 WBCs/high-power field. The chest x-ray was compatible with pneumonitis or infarction at the right base, and this area was ischemic on the lung scan. Antibiotics were begun the following day, but on Sept. 23 her temperature rose to 101.8°F, the pain worsened and the right lower lobe infiltrate increased in size. The white count was 11,800. A diagnosis of viral pneumonitis was favored over embolism, and no anticoagulation was given. Subsequently, her fever subsided and the white count dropped to 5,700 but the pleuritic pain increased as did the amount of right pleural fluid. On Oct. 14 the patient felt well and was afebrile, but she suddenly developed acute respiratory distress, cyanosis and shock and expired without chest pain. At autopsy an antemortem saddle embolus was found which almost totally occluded both branches of the main pulmonary artery. A small infarct was found in the right lower lobe. The source of the emboli could not be determined.

COMMENTS

The pertinent findings of the seven patients are listed in Table 1. Although one patient had severe coronary artery disease, the primary cause of death determined by autopsy was pulmonary embolism. Had embolization not intervened, all of the patients presumably would have survived.

Pulmonary symptoms developed a minimum of 8 days before death in all patients. Based on the recorded history and physical findings, pulmonary embolism should have been a major consideration in the differential diagnosis in these patients. However, in two the diagnosis was not strongly consider-

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical diagnosis</th>
<th>Interval between initial symptoms and death</th>
<th>Interval between positive scans and surgery or death</th>
<th>Autopsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>30</td>
<td>Pneumonitis</td>
<td>15 days</td>
<td>24 hr</td>
<td>Fresh and organizing emboli in large and small pulmonary arteries.</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>23</td>
<td>Postpartum thrombophlebitis</td>
<td>13 days</td>
<td>3 hr</td>
<td>Saddle embolus. Adherent and non-adherent emboli in large and medium sized vessels.</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>48</td>
<td>Pneumonitis</td>
<td>1 month</td>
<td>1 hr</td>
<td>Fresh and organizing emboli in segmental vessels. Resolving infarcts.</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>27</td>
<td>Leg fracture</td>
<td>8 days</td>
<td>6 hr</td>
<td>Fresh and resolving emboli in large arteries.</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>60</td>
<td>Postoperative infection</td>
<td>17 days</td>
<td>8 hr</td>
<td>Massive saddle embolus with well organized segmental embolus.</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>41</td>
<td>Thrombophlebitis, pulmonary emboli</td>
<td>2 months</td>
<td>2 months</td>
<td>Recent and organized emboli in lobar and segmental vessels.</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>48</td>
<td>Pneumonitis</td>
<td>23 days</td>
<td>23 days</td>
<td>Massive saddle embolus with old pulmonary infarction.</td>
</tr>
</tbody>
</table>
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erered until the patients developed thrombophlebitis or failed to respond to therapy for thrombophlebitis. Three were treated for some form of pneumonitis. Of the remaining two, the signs and symptoms in one were attributed to a postoperative infection while the other had no diagnosis made until he developed major embolization. Four of the patients received no anticoagulation or only terminal heparinization. The others were receiving anticoagulants, but full therapeutic levels were not maintained.

The lung scans in all the patients were abnormal although one, based on a single anterior scan, was interpreted as normal initially. At autopsy, all the patients had gross evidence of emboli, some of which were adherent. Since fixation to the intima requires a minimum of 4–5 days (9), lung scans would have been positive well in advance of massive embolization. In the three who did have scans performed 8 days or more antemortem, one patient was correctly diagnosed and treated for pulmonary embolism; in the second, the ischemic area at the lung base was attributed to pneumonitis rather than infarction; and in the third the scan was incorrectly interpreted as normal.

In all seven autopsies, the sites of vascular occlusion correlated well with the ischemic areas seen on the scans (Figs. 1–3). However, in three cases massive saddle embolization intervened between the time of the scan and the patient’s death (Cases 2, 5 and 7) and in another a partial lobular arterial occlusion became complete (Case 1).

In the past decade there has been a sharp rise in the recognition of pulmonary-embolic disease both clinically and pathologically. However, because of the great frequency with which the diagnosis still is not made, no reliable morbidity or mortality statistics are available. In the last 4 years, we have scanned over 700 patients with suspected pulmonary embolism. Most were referred from medical services with just a few from the surgical, orthopedic and obstetrical services. Of this number the seven fatal cases reported here represent the total known deaths in which pulmonary embolism was the primary and not a contributory or incidental finding. None of the patients had congestive heart failure or known malignant disease. Six were young, and all were potentially salvageable.

The three patients with a working diagnosis of pneumonitis deserve special attention. While it is well recognized that many findings in bacterial pneumonitis mimic those of pulmonary infarction, several features are found in these patients which should increase the suspicion of embolism or infarction. These include the development of “pneumonitis” in relatively young people without obvious predisposing conditions; a history of recurrent unexplained pneumonias; little or no elevation of the white blood cell count; poor response to antibiotic therapy; or history of pulmonary embolism, thrombophlebitis or hemoptysis. Although lung scans may not help in differentiating the etiology of the ischemia in areas of infiltrate seen on a chest film, the presence of other ischemic areas in roentgenographically normal lung is characteristic of embolism because it has been found that emboli to the lungs are usually multiple.

While the increased use of lung scanning combined with early anticoagulation will not eliminate the mortality from pulmonary embolism, it offers a reasonable alternative to the two less practical procedures of routine prophylactic anticoagulation and emergency embolectomy. Anticoagulation of high-risk groups, such as elderly patients with hip fractures, has reduced or eliminated fatal pulmonary embolism (8). However, in the absence of specific indications there has been a general reluctance on the part of physicians to use anticoagulant prophylaxis to prevent pulmonary embolism. This stems not only from concern over possible hemorrhagic complications but also from a lack of awareness of the efficacy of this approach as well as from difficulties in patient selection. The availability and use of cardiopulmonary bypass on an emergency basis has stimulated interest in embolectomy, but surgical treatment, once massive embolism has occurred, presents even more problems with potentially little chance of success. A survey of cardiovascular surgeons who have attempted this procedure elicited a mortality rate of 57% in 137 patients (10). In defense of these apparently poor results, it is assumed that the mortality would have been 100% without surgery. Many questions remain to be resolved in evaluating emergency embolectomy, but the basic problem is that patients, who because of mechanical obstruction could survive only with removal of the embolus, rarely survive long enough to institute even partial cardiopulmonary bypass. In a study of 283 fatal cases of emboli proved at autopsy on the surgical service of the Massachusetts General Hospital, Donaldson estimated that only one out of five patients survived long enough to institute a surgical procedure (11). In those who survive massive embolism for more than several hours but remain in critical condition, the data are still too few to indicate that embolectomy is to be preferred over intensive medical support.

The rationale behind prevention of fatal pulmonary embolization rests as much on adequate therapy as it does on the diagnosis of warning or “signal” emboli. A review of the anticoagulant program in the three patients in this series who received therapy...
24 hr or more before death as well as others who did not suffer fatal complications demonstrates a generally ineffectual use of these agents. Heparin was usually given by the deep subcutaneous route in doses rarely exceeding 30,000–40,000 units/day. Although the clotting times would sometimes be well in the therapeutic range, adequate anticoagulation was not maintained continuously. Therefore, the effectiveness of treatment was reduced or lost. Intermittent intravenous heparin given in doses of 10,000 or more units every 4 hr for at least the first 24–48 hr following the first signs of embolism with clotting times maintained at least two times the standard normal at all times is now the recommended therapeutic program. A detailed review of the rationale of heparin therapy in thromboembolism has recently been published and need not be reviewed further here (12).

Expansion of nuclear-medicine programs in most major hospitals and many smaller hospitals means that the scanning equipment necessary for detection of pulmonary emboli is now available to a large segment of the medical community. As pulmonary emboli are diagnosed with greater frequency, it becomes apparent that the disease does not carry the relatively high mortality that has been attributed to it in the past. Nevertheless, pulmonary embolism has been found to be the most common fatal pulmonary disease seen at autopsy and ranks among the top three nonfatal pulmonary diseases (13). The disease is an important one which can now be recognized and in many cases treated successfully.

**SUMMARY**

In 700 patients with suspected pulmonary embolism, massive embolism was the primary cause of death in seven. Of these seven, all had signs or symptoms of emboli preceding the fatal episode by 1 week or longer. At autopsy adherent emboli in major vessels or branches were present in six and correlated well with the areas of ischemia in the scan. Because lung scanning can detect ischemia produced by occlusion of vessels greater than a few millimeters in diameter and because adherence of the emboli to the intima indicates presence within the vessel for at least 4–5 days, the nonlethal embolic episodes could have been detected in time to institute prophylactic anticoagulation.

Lung scanning, by early confirmation of developing pulmonary embolic disease, combined with adequate anticoagulation should materially reduce the mortality from this disorder.

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Fatal Pulmonary Embolism

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