First Case Report of Spontaneous Pulmonary Hemorrhage Following Heparin Therapy in Acute Myocardial Infarction

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Since its discovery in 1916, heparin has been used extensively for treatment of thromboembolic disorders. Bleeding is its most well-known and frequent complication. We are describing the first case report of overt pulmonary hemorrhage in a patient who received heparin after emergent angioplasty for prevention of coronary artery rethrombosis.

Bleeding is a well-known complication of heparin therapy but spontaneous overt hemorrhage in the lungs following heparin has not been described. The following report describes a case of spontaneous pulmonary hemorrhage that developed after heparin therapy in a patient who underwent angioplasty for his acute myocardial infarction (MI).

Case Report

A 72-year-old man was admitted to the emergency room 30 minutes after the acute onset of severe substernal chest pain. He had a history of end-stage renal disease and hypertension and had been on continous ambulatory peritoneal dialysis for the past 10 months. His blood pressure had been well controlled for the past year without any medication. There was no significant history of respiratory disease except for a right rib fracture sustained as a teenager. There was no history of any bleeding disorder. He had not smoked for more than 30 years and medications prior to admission were epoetin alpha (Epogen) and multivitamin supplement.

Upon arrival, his blood pressure was 122/72 mmHg with pulse rate of 76/min, respiratory rate at 20/min and temperature of 98°F. The physical examination revealed a well-developed man in moderate distress but was otherwise unremarkable. ECG demonstrated hyperacute ST elevation over leads V_2 to V_5. He was given 325 mg of aspirin and underwent emergent cardiac catheterization. Angiography showed a 95% stenosis of his left anterior descending coronary artery, which was treated with immediate angioplasty, resulting in a residual 25% lesion. A bolus dose of 10,000 units intravenous heparin was given prior to angioplasty; followed by continous infusion at 800 units/hr. Within the next 30 minutes, he developed an episode of hemoptysis and heparin infusion was stopped immediately. A Swan-Ganz pulmonary artery catheter was placed and the initial reading of his pulmonary artery pressure was 29/11 mmHg with pulmonary capillary wedge pressure of 17 mmHg and cardiac index of 3.1 L/min/m^2. His hemoptysis resolved the following two hours, at which time heparin infusion was resumed.

Initial laboratory results were hemoglobin 10.2 g/dl; hematocrit 30.2 %; white count 13,500/mm^3; platelet 265,000/mm^3; blood urea nitrogen 64 mg/dl; creatinine 3.8 mg/dl; prothrombin time (PT) 12.0 s (control 10 to 13 s); and activated partial thromboplastin time (PTT) 25.4 s. Arterial blood gas taken on room air showed pH 7.36, Pco_2 44 mmHg, Po_2 74.2 mmHg, oxygen saturation 92.7 %. Chest x-ray showed calcification of the posterior right pleural space, but was otherwise normal.

After heparin infusion was restarted, he developed hemoptysis again, which progressively worsened so that heparin had to be stopped. Repeat PTT three hours after the initial bolus dose was 92 s and it normalized within the next four hours. The bleeding time then was 9 minutes (upper limit of normal 9 min) and platelet count was 104 000/mm^3. Despite normal coagulation studies, he continued having hemoptysis for the next two days, dropping his hemoglobin level to 8.1 g/dl. He was intubated at the time of his respiratory distress. Bronchoscopy was performed which showed presence of large blood clots in the airways. He required transfusion of 5 units of packed red blood cells to maintain his hemoglobin above 10.0 g/dl. His chest x-ray showed pulmonary infiltrates which worsened over the following few days (Fig 1). He responded to supportive measures and his condition gradually improved. He was extubated on his sixth day post MI. Repeat bronchoscopy before extubation revealed presence of blood clots. No endobronchial lesion was seen. The patient was finally discharged from the hospital on the fourteenth day post MI after successfully undergoing cardiac rehabilitation protocol and repeat angiogram, which showed that his coronary artery lesion had remained patent.

Discussion

Heparin has been used in the treatment of unstable angina and acute MI as adjunct treatment to emergent angioplasty or thrombolytic therapy.[1] The most common side effect is bleeding. The lung is not usually known to be a potential site of bleeding. This is the first case report of a spontaneous, overt pulmonary hemorrhage following heparin therapy. A case of occult pulmonary hemorrhage following

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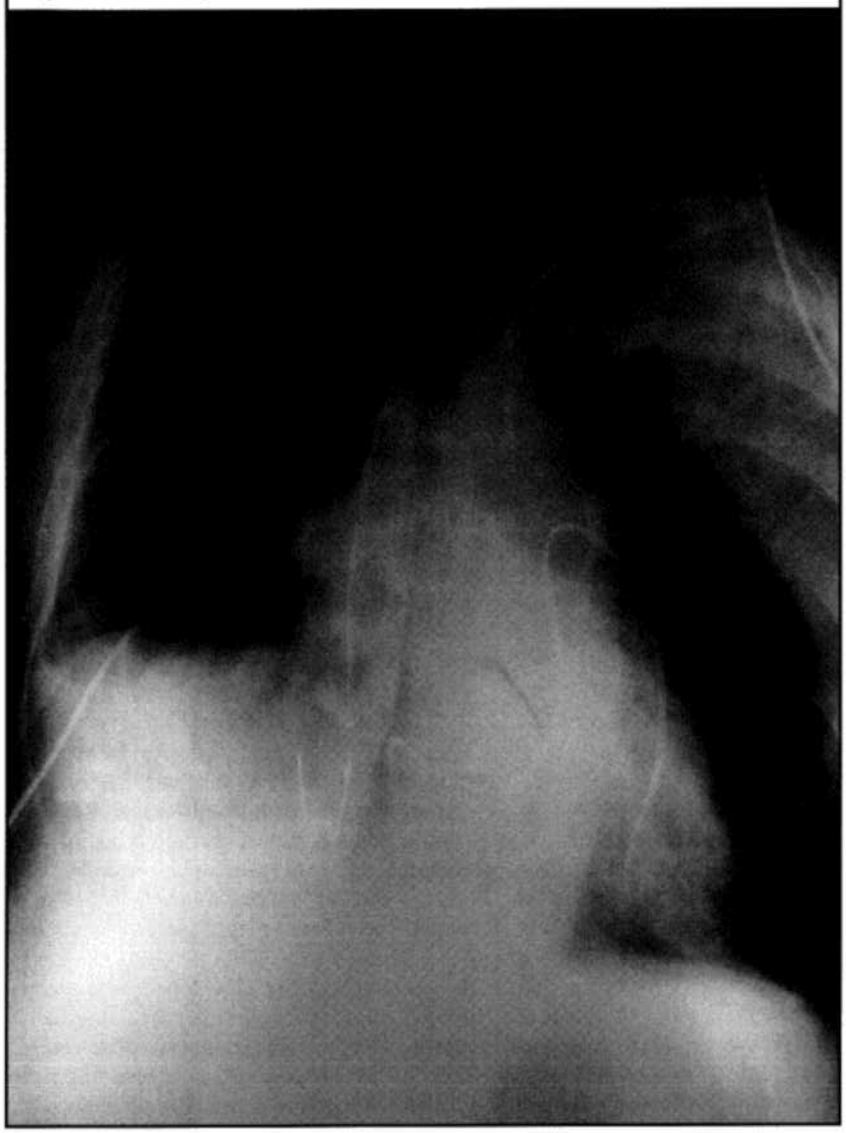
Fig 1.—Chest x-ray



heparin therapy has been described earlier by Finley and colleagues.[2]

There have been three case reports in the English literature documenting pulmonary hemorrhage as a complication following thrombolytic therapy. In all three cases, the diagnosis was made based on the triad of hemoptysis, falling hemoglobin, and new pulmonary infiltrate on x-rays. Awadh and colleagues described a patient with pulmonary hemorrhage following streptokinase and heparin therapy.[3] Both streptokinase and heparin therapies may have contributed to the bleeding. Disler and Rosendorff[4] reported a case of pulmonary hemorrhage following intravenous streptokinase in a patient who had recently recovered from a lower respiratory tract infection. An unresolved pneumonia was implicated to have contributed to this complication. Nathan et al[5] described a similar case of pulmonary hemorrhage following thrombolytic therapy and in their case the patient had a Swan-Ganz pulmonary artery catheter placed prior to the onset of the hemoptysis. Thrombolytic therapy and the catheter may have contributed to this complication. Our patient received only heparin therapy, had no prior history of pneumonia or any lung disease, and developed an episode of hemoptysis prior to insertion of the pulmonary catheter, the proper position of which was confirmed radiologically. Continous monitoring of the wedge pressure did not show dampening to suggest *overwedging*.

There are two mechanisms whereby heparin is eliminated from the body. There is the rapid clearance by binding of heparin to receptors on endothelial cells and macrophages, whereby it is internalized and depolymerized. And the other is a slower mechanism of clearance which is mainly renal.[1] Renal failure is a known risk factor for heparin-associated bleeding.[6] However, in the presence of decreased renal clearance, hemostatic abnormalities such as prolonged bleeding time, impaired platelet adhesion or aggregration are usually reversible following dialysis. Age also has been shown to increase the incidence of bleeding with heparin use as demonstrated in a study by Jick et al[7] but the underlying mechanism of which is not well defined. Renal impairment and advanced age may have played a significant role in the development of spontaneous pulmonary hemorrhage in our patient.

Even though pulmonary hemorrhage is a clinical diagnosis based on the presence of hemoptysis, new radiographic pulmonary infiltrate, and falling hemoglobin; occult pulmonary hemorrhage without hemoptysis has been described.[2] Therefore this diagnosis should be kept in mind when dealing with patients who had thrombolytic and/or heparin therapy with progressive anemia. Magnetic resonance imaging (MRI) and diffusion capacity of carbon monoxide gas (DLco) have been described to aid in diagnosing the presence of blood in lung parenchyma. Both methods require specialized equipment and patients' cooperation which are not easily suitable for unstable patients. Bronchoscopy with bronchoalveolar lavage would be a more helpful tool in confirming the diagnosis. Hemosiderin score (an arbitrary score of hemosiderin content present in the mean of 100 macrophages) has been described to aid in the diagnosis, especially in occult hemorrhage.[2]

Conclusion

In summary, we report the first case of spontaneous overt pulmonary hemorrhage following heparin therapy. The patient's advanced age and renal condition have contributed to this complication. Heparin should therefore be used with caution in elderly renal patients. Awareness of this potential complication may help minimize the morbidity and mortality inherently present with its use.

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