Major Hemorrhage following Administration of Intrapleural Streptokinase

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Severe spontaneous bleeding has not been reported to complicate therapy with intrapleural streptokinase (SK). Recent data have demonstrated intrapleural SK to be devoid of systemic fibrinolytic effect. This report presents a patient who suffered major hemorrhage following the administration of 500,000 units of SK intrapleurally.

Intrapleural SK has been used for 30 years as an adjunct in the removal of hematomas, pus, and fibrinous materials from the thoracic cavity. By a local fibrinolytic effect on fibrinous pleural exudates within the pleural space, SK has improved results of thoracostomy tube drainage. However, due to the lack of controlled randomized studies, significant controversy exists concerning the efficacy of this therapy.

Berglin et al investigated the effect of intrapleurally administered SK on systemic fibrinolysis in ten patients with empyema. No systemic activation of the fibrinolytic system could be detected. We report a patient with apparent systemic activation, which suggests that selected patients may absorb sufficient SK into their systemic circulation to cause severe spontaneous bleeding.

CASE REPORT

A 36-year-old obese white man was hospitalized for treatment of chronic ulcers of the lower extremities secondary to necrotizing vasculitis. The patient had a five-year history of severe rheumatoid arthritis refractory to aspirin, nonsteroidal antiinflammatory agents, penicillamine, and gold. Admission medications included prednisone 30 mg daily (× one year) and indomethacin 50 mg three times daily. An admission chest film showed bilateral pleural effusions with a right upper lobe cavitary lesion believed to be secondary to a necrotizing rheumatoid nodule.

The patient received vigorous wound care of his leg ulcers and was stable until the 21st day of hospitalization when he complained of sharp chest pain and rapidly became dyspneic and hypoxic. The right pleural effusion increased in size and thoracocectomy yielded 1,300 ml of thick yellow fluid from the right pleural space and relieved the patient’s respiratory distress. Analysis of the aspirate was consistent with an exudate: lactate dehydrogenase, 16,000 IU/liter; amylase, 30 units/deciliter; glucose, 16 mg percent; protein, 9.8 g percent; pH, 6.97; WBCs, 29,000/cu mm; Gram-stain did not reveal any organism and results of all cultures were negative. The effusion was felt to be rheumatoid in origin. The effusion persisted and a second right thoracostentesis was performed 12 days after the first and yielded 1,450 ml of thick greenish fluid. However, the lung failed to re-expand with this procedure and six days later a 40-50 percent pneumothorax remained. At this time, a right thoracostomy tube was placed and attached to suction. A continuous air leak persisted and seven days later a second chest tube was placed. Partial re-expansion of the right lung occurred initially, but a 10 percent

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pneumothorax still existed which gradually regressed to a 25 percent right pneumothorax. Due to failure to re-expand the lung and an unresolved bronchopleural fistula, right decortication was performed 60 days after the admission date. Three thoracostomy tubes were placed to provide postoperative drainage, but the system still had a continuous air leak. Postoperative medications included prednisone, 30 mg daily; heparin, 5,000 units subcutaneously every 12 hours; and cimetidine, 300 mg every six hours. Additional therapy included intermittent antimicrobial coverage with various combinations of gentamicin, carbenicillin, penicillin, and amikacin. The patient's postoperative course was complicated by recurrent pneumonias. One month after operation re-expansion of the right lung was incomplete and pleural thickening was noted at the base of the left lung. Large air leaks persisted in all chest tubes. Two months after decortication, a 20 percent right pneumothorax remained with loculations in the right pleural space. A large pleural effusion was now present in the left lung.

Three and one-half months after surgery, intrapleural streptokinase was administered to help break down loculated areas in the right pleural space. A solution containing 500,000 units of SK was administered via the chest tubes. The tubes were then clamped for approximately six hours and returned to suction; at which time 1,450 ml of bloody fluid drained immediately. Hematuria was reported nine hours after SK administration. Within this same time frame, blood was suctioned via nasogastric and endotracheal tubes. In addition, ooze from various puncture sites and epistaxis occurred. Prior to the administration of SK, the prothrombin time and partial thromboplastin time (PT/PTT) had been found to be normal. Approximately 11 hours after SK administration, the PT/PTT was prolonged at 15.9/9.6 seconds (control 12.4/25.9).

Therapy included four units of fresh frozen plasma, 20 mg of vitamin K, and two injections of tetracycline intrapleurally for pleuradeces. The patient previously had a consistently low hematocrit level (30.3 immediately prior to SK therapy), but no major bleeding diathesis was apparent. Over the period of active bleeding the hematocrit dropped to 22.7 and seven units of packed red blood cells were required to maintain the hematocrit above 30. Platelets were adequate ranging throughout this interval between 372,000/cu mm and 182,000/cu mm. No further blood products were required after the third day following the therapy with SK.

Lung re-expansion was never accomplished. The patient expired 140 days after admission, 30 days after therapy with SK. Death was due to sepsis following the development of a mixed Pseudomonas and staphylococcal pneumonia. Autopsy findings included right bronchopneumonia and lung nodules (probably of rheumatoid origin). Exudative pleuritis with bilateral adhesions and pleural effusion were also present. Nonpulmonary findings included pericarditis and adrenal atrophy presumed to be secondary to corticosteroids.

**DISCUSSION**

In the 30 year history of intrapleural SK therapy major hemorrhage has not been reported to complicate treatment. The dosage of 500,000 units administered in this case was no greater than that which has been cited in the literature for intrapleural use. The relative amount of this dose is not particularly large, especially when compared to the amount used systemically for thrombolytic therapy.

Berglin et al. assessed fibrinolytic activity following intrapleural administration of SK, by measuring fibrinogen degradation products, plasminogen, fibrinogen, thrombin time, hematocrit, α2-antiplasmin, and α2-macroglobulin. While fibrinolytic activity in the pleural fluid is maximal within the first hour after administration, no systemic fibrinolytic effect could be detected up to 24 hours after intrapleural administration of SK. Our case appears to be unique in that SK was absorbed from the pleural space into the systemic circulation. Vascular erosion or a bronchopleural fistula may have predisposed this patient to systemic absorption. A bronchopleural fistula was clinically diagnosed due to the continuous air leaks from the chest tubes, but was not readily apparent at the autopsy one month after the hemorrhage. Other potential risk factors predisposing to hemorrhage include concomitant use of carbenicillin and prophylactic heparin. Although no conclusive evidence exists, the patient may have been septic at the time of hemorrhage. Additionally, RBC fragments were found to be present in a blood smear, implicating disseminated intravascular coagulation, concurrent with sepsis, as a possible etiology. Nevertheless, the sudden onset of massive hemorrhage corresponds temporarily with the administration of SK and does not correspond with any clinical change in a septic state.

Given that a similar dose of SK administered intravenously (as dosed in thrombolytic therapy) is only reported to cause major bleeding in 1-3 percent of patients, the likelihood of hemorrhage following intrapleural administration should be rare. However, in view of this report, the following conditions should be considered a relative contraindication to intrapleural SK therapy: (1) coagulation abnormalities; (2) recent bronchial suture; and (3) severe trauma with possible liver, spleen, or intracranial involvement. Bergin et al suggested that these restrictions were unnecessary, as no systemic activity could be measured. Caution should be observed in the above situations, as this case demonstrates a strong association between intrapleural administration and systemic effect. Additional caution should be observed in those patients in whom bronchopleural fistula is suspected.

**REFERENCES**


**Near Fatal Complication Secondary to a Poorly Designed Tracheostomy Connector**

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