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CASE REPORT

Intrapleural hemorrhage due to alteplase use in a 6-year-old boy with pleural effusion

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Background: Intrapleural fibrinolytics have been used successfully worldwide for the management of complicated pleural effusions and empyema. Bleeding complications are usually mentioned as rare side effects, but there is no clear information in the literature addressing the alarming outcome that might result following the use of alteplase as a fibrinolytic in the management of complicated parapneumonic effusions. We present a rare, if not unique, case of intrapleural hemorrhage requiring transfusion after alteplase use as a fibrinolytic in a 6-year-old male with complicated parapneumonic effusion.

Methods: A search of the PubMed database was carried out, using a combination of the following terms: alteplase, fibrinolytic, intrapleural hemorrhage, and side effects.

Results: The majority of studies found in the search concentrated on the efficacy of intrapleural fibrinolytics in the management of pleural effusion, but very few of the reports addressed the bleeding complications which may be caused by the treatment.

Conclusion: Although intrapleural and systemic hemorrhage are rare side effects of intrapleural fibrinolytic use, the health care provider must be watchful for these potentially life-threatening complications. Further studies are needed to understand not only the efficacy of fibrinolytics but also their safety, especially in children.

Keywords: alteplase, tPA, fibrinolytic, intrapleural hemorrhage, pleural effusion

Introduction

Intrapleural fibrinolytics have been used with success worldwide for the management of complicated pleural effusions and empyema. The overall attainment has been reported between 44% and 100%.[1]

The British Thoracic Society guidelines, and studies conducted by the American Pediatric Surgical Association, suggest fibrinolytic therapy as a medical option for the treatment of patients in whom the pleural fluid is thick or loculated.[2,3] The three commonly used fibrinolytics are streptokinase, urokinase, and tissue plasminogen activator (tPA).[4] However, after reviewing the literature, bleeding complications are usually mentioned as rare side effects and no clear literature addresses the alarming complications that might result after the use of fibrinolytics. We present a unique case of intrapleural hemorrhage requiring packed red blood cell (RBC) transfusion due to alteplase use in a previously healthy child.

Case presentation

A 6-year-old male with an unremarkable past medical history and family history, including the mother's prenatal care, was admitted to our hospital due to intermittent

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fever and cough for 2 weeks. There was no vomiting, diarrhea, runny nose, or rash. He was seen in a primary care facility and was diagnosed with pneumonia and was not responding to antibiotic therapy. On admission to the ward, his vital signs were as follows: temperature, 38°C; pulse, 110 per minute; blood pressure, 100 mmHg/60 mmHg; respiratory rate, 42 per minute; oxygen saturation, 96% while on one L per minute of oxygen via nasal cannula; weight, 33.5 kg (>95th percentile); length, 118 cm (75th–90th percentile). His skin had normal texture with no presence of rashes, and there was no hypo- or hyperpigmentation; his capillary refill time was less than 3 seconds. The patient had subcostal retractions with decreased air entry and coarse crackles in right lower and middle zone of the lung. The rest of the physical exam was unremarkable.

Initial laboratory results were as follows: blood group, O(+); negative direct Comb's test; white blood cell, 21,800/μL (neutrophils, 88.2%; lymphocytes, 5.4%; monocytes, 4.9%; and basophils, 0.1%); RBC, 4,100,000/μL; hemoglobin, 12.1 g/dL; hematocrit 36.1%; mean corpuscular volume, 82 fL; mean corpuscular hemoglobin, 25.7 g/dL; RBC distribution width, 13.8%; and platelets, 309,000/μL. Prothrombin time was 10.3 seconds; international normalized ratio, 1.0; activated partial thromboplastin time, 34.3 seconds; C-reactive protein, 440 mg/L; serum glucose, blood urea nitrogen, creatinine, calcium, sodium, chloride, potassium, and liver function tests were normal. Albumin was 28 g/L. Blood culture was negative, and nasopharyngeal swabs for H1N1 and influenza A and B were negative. Chest X-ray with anterioposterior view showed right lower lobe consolidation with minimal pleural effusion along the right lateral chest wall. A chest ultrasound was done immediately after the chest X-ray and showed a small amount of right pleural effusion (approximately 10 mL).

Course of hospitalization

The patient was started on intravenous ceftriaxone 60 mg/kg administered every 12 hours and intravenous vancomycin 60 mg/kg administered every 6 hours. At day 3 of admission, the patient continued to spike with fever up to 39.5°C, and his oxygen requirement increased from 1 L per minute via nasal cannula to 2 L per minute. These developments prompted us to repeat the chest X-ray, which showed right pleural effusion extending to the right upper zone; the right costophrenic angle and right dome of the diaphragm were silhouetted. The repeat chest ultrasound showed that the right pleural effusion volume increased to approximately 100 mL of thick fluid with possible septations. The decision was made to insert a chest tube, and 50 mL of clear fluid were drained. The pleural fluid showed a white blood cell count of 107 (50% neutrophils and 30% lymphocytes); lactate dehydrogenase, 1246 U/L; glucose, 3.7 mmol/L; total protein, 52 g/L; lactic acid, 5.98 mmol/L; and cultures were negative for bacteria and acid fast bacilli.

The clinical picture of the patient was not improving, so another decision was made to use intrapleural fibrinolytics 2 days after chest tube insertion. In practice, we generally use streptokinase as intrapleural fibrinolytic, but as it was unavailable, one dose of 3 mg (0.1 mg/kg) of tPA diluted in 30 mL of normal saline was administered. The chest tube drained 550 mL of serosanguinous fluid, which eventually changed to frank blood. The patient started to show signs of weakness and was tachypneic and pale; however, the patient's neurological examination was unremarkable, and there were no other sites of bleeding. A repeat test for hemoglobin showed 7.6 g/dL, the international normalized ratio was 2.0, and partial thromboplastin time was 21.4 seconds. Alteplase was not resumed, and the patient was transfused with packed RBC at 15 mL/kg. The patient did not require fresh frozen plasma or cryoprecipitate transfusion therapy. Hemoglobin and coagulation profile were normalized. The chest X-ray on discharge showed a small nonhomogeneous opacity in the right lung base with the possibility of minimal residual right-sided pleural effusion. The chest tube was removed 8 days after insertion. The patient was discharged 10 days after admission and remained on oral augmentin for 11 days. He was afebrile and in a good condition. The parents are health care providers and did not consider a follow-up in the outpatient clinic was necessary, as the patient's physical exam at home was normal.

Discussion

Respiratory diseases remain the leading cause of morbidity and mortality among children.[5] Simple parapneumonic effusion is thought to occur in up to 57% of patients with pneumonia and could be associated with a 15% increase in mortality.[6]

Fibrinolytics is thought to dissolve fibrin deposits and loculations in the pleural space. Streptokinase, urokinase, and alteplase have been in use as fibrinolytics agents; however, alteplase is the least described in the literature.[4] Studies in children have shown that intrapleural fibrinolytic (mean duration of fibrinolytic treatment 4.3 days) treatment is an effective and safe adjunctive therapy in children with thoracic empyema and can obviate a thoracotomy in most cases.[7] Other researchers consider fibrinolytic treatment to be the

better economic option, yielding the same clinical outcome as compared to video-assisted thoracoscopic surgery.[8]

The Pediatric Infectious Disease Society outlines two approaches for alteplase use: the first method is treatment with 4 mg in 40 mL of 0.9% saline, intrapleural administration. The first dose is given at the time of chest tube placement, with a 1-hour dwell time. This is repeated every 24 hours for 3 days (total of three doses). The alternative approach is to administer 0.1 mg/kg (maximum 3 mg) in 10–30 mL of 0.9% saline, intrapleurally. The first dose is given after pigtail catheter (or chest tube) placement, with a 45-minute to 1-hour dwell time, and repeated every 8 hours for 3 days (total of nine doses).[9]

Only a few studies have reported complications of intrapleural tPA, and the patient populations are either adults or individuals on anticoagulant agents. In one study of 41 adult patients, one developed hematuria after tPA administration.[10] In a different study of 120 adult patients, there was a 2% rate of bleeding at the chest tube site.[11] Gervais et al[12] reported a 7% overall bleeding risk using a dose of 4–6 mg/day in 10–50 mL of normal saline for 3 days; however, the patients were on anticoagulant medications. Walker et al[13] presented a case report of a 62-year-old woman with an increase of partial thromboplastin after intrapleural tPA use, although coagulation profiles are not thought to be altered by tPA use as an intrapleural fibrinolytic agent. Moreover, Ben-Or et al[14] assessed the effectiveness and risks associated with intrapleural tPA use. The study was conducted on 118 adult patients, with some receiving anticoagulant medications. The tPA dose was 25 mg. Two patients developed self-limited bleeding after two doses of tPA, and one patient had minor bleeding after three doses; however, the authors did not specify if the three patients were on anticoagulants.

There have been very few studies published on tPA treatment in children. A study conducted by Weinstein et al[15] showed that intrapleural tPA is effective in the treatment of pleural effusion in children. Effectiveness was measured by total fluid drainage. The study stated that no child treated with tPA developed local or systemic bleeding. Also, Ray et al[16] reviewed the clinical course of six pediatric patients with complex empyema who were treated with tPA. The study showed that tPA is efficacious as a fibrinolytic in treating complex empyemas in children. The efficacy was assessed by measuring pleural fluid drainage after tPA infusion. No major complications were reported in that study. Finally, Goralski et al[17] published a case report of a child with complicated parapneumonic effusion, who developed intrapleural hemorrhage after tPA administration. However, the child had chronic renal failure and was on hemodialysis.

Conclusion

Intrapleural and systemic hemorrhage is a rare side effect of intrapleural fibrinolytic use; however, the health care provider must be watchful for the mentioned serious side effect. The majority of studies conducted on intrapleural fibrinolytics concentrate on their efficacy in the management of pleural effusion, but very few address the bleeding complications. Further studies are needed to investigate not only the efficacy of fibrinolytics, but also their safety, especially in children.

Disclosure

The authors report no conflicts of interest in this work. There is no financial relationship with any company.

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