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First use of andexanet alfa in the management of massive delayed hemothorax

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Abstract:

In emergency medicine practice, massive hemothorax represents a life-threatening condition in patients with comorbidities. We present the case of a 75-year-old female patient with a massive delayed hemothorax, which developed following a chest injury sustained during a low-height fall. The patient had been on long-term rivaroxaban, a direct oral anticoagulant, due to underlying comorbid conditions. To reverse the anticoagulant effect, andexanet alfa was administered, followed by the placement of chest drainage. After evacuating the bloody pleural effusion from the pleural cavity, full lung reexpansion was achieved, with only minimal residual drainage within an hour. Following drainage removal, the patient was subsequently discharged without any complications. After follow-up, the patient remained in good condition. This case demonstrates that andexanet alfa can be an effective reversal agent in life-threatening cases of massive delayed hemothorax.

Keywords:

Andexanet alfa, delayed hemothorax, massive hemothorax

Introduction

Hemothorax is defined as the accumulation of bloody fluid with hematocrit of at least 50% in the pleural cavity.[1] Blunt chest injuries often result in rib fractures,[2] particularly in older individuals.[2] These fractures are frequently associated with hemothorax, with an incidence of 27.5%.[3] A rare variant is delayed hemothorax in the pleural cavity.[4] This condition is particularly life-threatening as it is associated with a high mortality rate of 6.8%.[5] Therefore, it necessitates prompt action, especially in patients on long-term direct oral anticoagulants (DOACs). The use of DOACs has significantly increased,[6] as it is associated with an elevated risk of hemorrhages.[7] Reversal of DOAC effects can be achieved with andexanet alfa, which is approved for use in severe life-threatening hemorrhages.[8] Its use has been reported in situations such as preoperative management before aortic surgery requiring cardiopulmonary bypass,[9] during the exchange of an occluded cardiopulmonary bypass[10] as well as in cases of intracerebral hemorrhage[7] and gastrointestinal bleeding.[8] To the best of our knowledge, its use in cases of hemothorax has not been documented in the literature. Before the introduction of andexanet alfa, no effective and specific therapies were available for reversing DOACs.[6]

We report the case of a patient who developed a massive delayed hemothorax following a low-height fall, which resulted in rib fractures. The patient was on long-term

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rivaroxaban therapy. Andexanet alfa was administered to reverse its effects. Subsequently, chest drainage was used.

Case Report

A 75-year-old female with a history of chronic illnesses – including heart failure, persistent atrial fibrillation, Hashimoto's disease, and atherosclerosis – had previously undergone hip joint endoprosthesis surgery. She was receiving long-term rivaroxaban therapy at a dose of 20 mg once daily. Following a fall from standing height at home, she presented to the emergency department. A chest X-ray (CXR) scan revealed rib fractures from VII to VIII on the left side without extravasation and lung contusions with free pleural spaces [Figure 1a]. Eight days after the fall, her condition deteriorated. Emergency medical services were called, finding her difficult to communicate with, experiencing shortness of breath, with an oxygen saturation of 60%. Passive oxygen therapy was applied, resulting in a brief improvement in saturation to 95%. A suspected pneumothorax was decompressed on-site, yielding approximately 40 ml of blood.

Upon arrival at the emergency department, the patient was conscious and drowsy but able to maintain logical verbal contact. Pupils were equal, medium-sized, and reactive to light. Shallow, diaphragmatic breathing was observed. Breath sounds were absent over the left lung field, with normal vesicular sounds on the right. The patient had last taken rivaroxaban at 8 PM, before she arrived at the emergency department at 1 AM. Her vital signs were as follows: heart rate 83/min, blood pressure 140/57 mmHg, temperature 36.6°C, saturation 98% while receiving oxygen at 7 L/min via face mask. Laboratory tests revealed anemia due to hemorrhage, with reduced red blood cells (RBC; 2.72×10^6/µl), hemoglobin (8.8 g/dl), and hematocrit (28.4%). Thrombocytosis (443,000/µl), elevated INR (1.81), elevated fibrinogen (623 mg/dl), respiratory acidosis (pH = 7.24), and elevated inflammatory parameters were also noted.

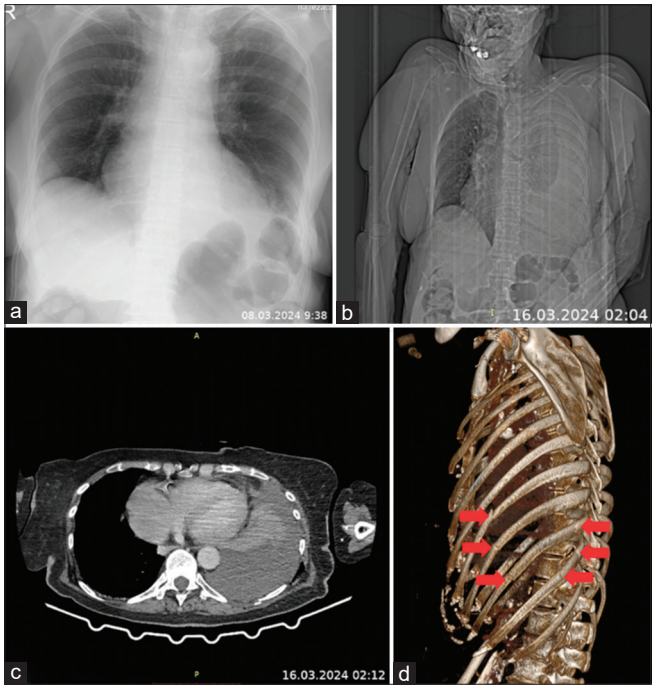

Figure 1: (a) Anteroposterior chest X-ray on the day of the patient's fall, showing fractures of the 7th and 8th ribs on the left side. (b) Axial chest computed tomography (CT) demonstrating a large left-sided hemothorax with near-complete lung collapse and mild rightward mediastinal shift. (c) Axial CT showing fluid in the left pleural cavity, causing near-complete left lung collapse. (d) Three-dimensional CT projection depicting ribs fractures from 7th to 10th on the left side. Fracture sites are marked by red arrows

A computer tomography (CT) scan revealed multiple rib fractures from VII to X on the left side, along with a large amount of hyperdense fluid in the left pleural cavity, consistent with hemothorax, causing near-complete collapse of the left lung [Figure 1b-d].

A thoracic surgeon was consulted and recommended transfusion of RBCs and fresh frozen plasma (FFP). Due to worsening respiratory failure, the patient was induced into a clinical coma and subsequently intubated using rapid sequence intubation and connected to a ventilator. In addition, hypotension and tachycardia were observed. 400 mg of andexanet alfa was administered in an intravenous bolus during the transfusion of 3rd unit of RBC. 40 min after administration, a chest tube was inserted in the 6th intercostal space and connected to active suction, evacuating 1700 ml of bloody fluid. A follow-up CXR, performed 30 min later, showed complete re-expansion of the left lung [Figure 2a]. Over the next hour, 50 ml of bloody fluid was drained. A total of five RBC units and four FFP units were transfused. Due to hypovolemic shock, the patient was transferred to the intensive care unit. 4 h postdrainage, follow-up CXR and biochemical tests were performed, which showed gradual improvement: RBC (3.77×10^6/µl), hemoglobin (11.3 g/dl), hematocrit (34.8%), platelets (312,000/µl), normal INR (1.06), fibrinogen (529 mg/dl), pH = 7.41, and elevated inflammatory parameters. Increased blood pressure and decreased heart rate were noted. Prophylactic antihemorrhagic treatment and anticoagulant therapy with enoxaparin were initiated, and third-generation cephalosporins were administered. Analgosedation was gradually reduced, leading to extubation on the 2nd day; passive oxygen therapy was administered with oxygen flow of 3 l/min. The patient was transferred on the 4th postoperative day to the department of thoracic surgery for further treatment. The chest tube was removed [Figure 2b]. Subsequently, she was discharged in good general condition after 7 days, with a prescription for anticoagulant – enoxaparin and external chest stabilizer (Pani Teresa© Medica). At the 3-week

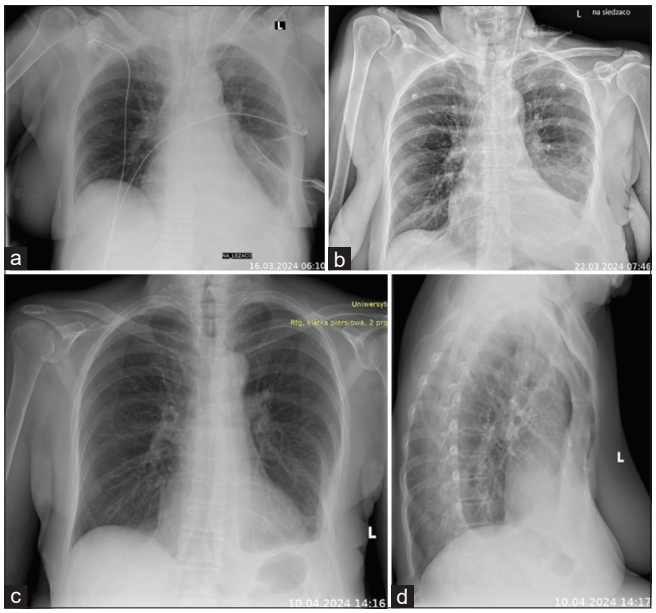

Figure 2: (a) Anteroposterior chest X-ray (CXR) performed 30 min after drainage, demonstrating complete reexpansion of the left lung. (b) Anteroposterior CXR after drain removal. (c and d) Follow-up anteroposterior (c) and lateral (d) CXRs taken 3-week postprocedure

follow-up, the patient returned for suture removal; a CXR confirmed full re-expansion of the lung [Figure 2c and d]. Enoxaparin treatment was continued. At the 5-week follow-up visit, her condition was good, and she resumed rivaroxaban treatment.

Written consent for publication of this case was obtained from the patient.

Discussion

We are describing an unusual case of a patient with rib fractures and massive delayed hemothorax caused by persistent bleeding, likely due to ongoing rivaroxaban use. Based on the cases presented by Ritter and Chang,[11] the definition of delayed hemothorax can be formulated as any hemothorax that occurs after an initial negative imaging result, regardless of the time elapsed. In this case, the hemothorax was diagnosed 8 days after initial admission. Treatment required administration of andexanet alfa, which is used in life-threatening situations,[8] to reverse the effects of rivaroxaban, which is a factor Xa inhibitor.[7] Studies confirm the effectiveness of andexanet alfa, showing a significant decrease in factor Xa inhibitor activity,[8] leading to rapid pro-coagulation.

Delayed hemothorax is a rare complication, with incidence ranging from 2.1% to 7.4%,[4] following blunt chest trauma due to a fall.[12] In elderly patients who usually have additional comorbidities such as stroke and atrial fibrillation,[13] where additional treatment using rivaroxaban is recommended,[13] such injuries pose a particular threat to health and warrant special attention.[12] In addition, delayed hemothorax presents diagnostic challenges due to its absence on initial examination.[11] Based on our experience, we suggest considering the replacement of rivaroxaban with enoxaparin in similar cases, as this may help reduce the risk of delayed hemothorax.

The management of hemothorax depends on the amount of bloody fluid accumulated. If <300 ml is present, conservative management is usually recommended. For larger hemothoraces, chest drainage is advised. Surgical intervention is recommended if the evacuated bloody fluid exceeds 1000–1500 ml within 24 h or 200–500 ml/h for two to three consecutive hours.[14] Despite evacuating 1700 ml of bloody fluid, surgical intervention, which is indicated in cases of massive hemothoraces,[14] defined as the loss of over 1500 ml of blood,[12] was not pursued. This decision was based on minimal subsequent bleeding with a loss of 50 ml of bloody fluid within 1 h, complete left lung reexpansion on CXR, and normalization of biochemical parameters, which were attributed to andexanet alfa.

While andexanet alfa effectively reverses factor Xa inhibition, concerns about thrombotic events and high cost limit its routine use. In this case, its benefits outweighed the potential risks due to the life-threatening nature of the hemorrhage. From our clinical experience, in some cases, due to persistent postoperative high drainage, thoracotomy followed by rethoracotomy combined with packing is required. However, in certain patients, this approach is ineffective, and the expected outcome is not achieved.

The introduction of andexanet alfa has expanded treatment options for patients taking DOACs in emergency situations. Before the emergence of reversal agents, management was challenging and relied on nonspecific therapies such as activated factor VII, high doses of prothrombin complex concentrates, activated prothrombin complex concentrates, FFP,[15] hemodialysis, activated charcoal administered orally, and hemoperfusion with activated charcoal.[15] This case highlights the potential utility of andexanet alfa in managing life-threatening delayed hemothorax.

Conclusion

This case demonstrates that the administration of andexanet alfa effectively reversed the effects of rivaroxaban in massive delayed hemothorax in an unstable patient, which is a result that was previously not feasible in an efficient manner. These findings underscore the need for further studies on the role of andexanet alfa in traumatic hemothorax and its potential integration into emergency protocols.

Author contributions' statement

MK: Conceptualization (lead), Supervision (lead), Project administration (lead), Writing - review and editing (equal), Investigation (lead), Resources (lead). JA: Writing - original draft (equal), Writing - review and editing (equal), Project administration (equal), Visualization (equal). AC: Writing - original draft (equal), Writing - review and editing (equal), Project administration (equal), Visualization (equal). KC: Writing - original draft (equal), Writing - review and editing (equal), Project administration (equal), Visualization (equal). PN: Project administration (supporting), Resources (supporting), Investigation (supporting).

Conflicts of interest

None Declared.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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