

An Unexpected Complication of Prophylactic Enoxaparin in an Adolescent Female : Case Report

Abdallah Dalabih, MD, MBA¹, Sarah Sylvester, MD², Anna M Onisei, MD³, Claire Foster, MD, MPH¹, Erin Bennett, MD¹

KEYWORDS - Pediatric, enoxaparin, prophylaxis, intracranial hemorrhage

BACKGROUND

Venous thromboembolism (VTE) is a severe medical condition associated with increased morbidity, mortality, hospital length of stay, and healthcare costs [1,2]. While well-documented in adults, managing and understanding pediatric VTE remains challenging for healthcare providers. Currently, there are no validated guidelines for pediatric thromboprophylaxis, leading many hospitals to adopt a stratified approach based on bleeding and VTE risk factors [3]. This case report aims to describe the management and outcome of a 14-year-old female who developed VTE following a motor vehicle collision.

CASE PRESENTATION

A previously healthy 14-year-old female, weighing 76kg with a BMI of 30.5, was ejected from a motor vehicle during a collision. She suffered a closed head injury and was intubated at the scene due to a Glasgow Coma Scale score of 3. Initial CT imaging revealed a few small areas of parenchymal hemorrhage in the right frontal lobe but no other significant findings. The patient was extubated to room air on the first day of hospitalization and an MRI conducted 48 hours later showed multifocal hyperintensities consistent with diffuse axonal injury (DAI). Renal function, hepatic function, and coagulation studies (including PT, PTT, INR, and TEG) were all within normal range.

Due to her prolonged reduced mobility following major trauma, the patient was at high risk for VTE. As there were no planned surgical interventions and thus a low risk of bleeding, she was started on enoxaparin prophylaxis at a dose of 30 mg every 12 hours. On the eighth hospital day, she was transferred to an inpatient rehabilitation service. Two days later, she developed acute agitation, slurred speech, and left hemiparesis without a known inciting event. Repeat head CT revealed interval development of a right frontal lobe intraparenchymal hemorrhage with a 6mm midline shift. Lab work

¹ University of Arkansas for Medical Sciences, Department of Pediatrics, Section of Pediatric Critical Care

² University of Arkansas for Medical Sciences, Department of Pediatrics, Section of Emergency Medicine

³ University of Arkansas for Medical Sciences, Department of Anesthesiology, Section of Pediatric Anesthesia

Corresponding Author:
Abdallah Dalabih, MD, MBA
University of Arkansas for Medical Sciences, Department of Pediatrics, Section of Pediatric Critical Care

Email: Adalabih@uams.edu

at this time showed normal renal and hepatic function, and the anti-Xa peak level was within therapeutic range at 0.58 units/ml despite the prophylactic dosing. The patient received 30mg of protamine via slow IV push (diluted in D5W) over 10 minutes, followed by a craniotomy to evacuate the hematoma. No second dose of protamine was administered.

DISCUSSION

Pediatric VTE is a complex and challenging condition associated with significant morbidity and mortality [1,2]. Due to the lack of validated guidelines for pediatric thromboprophylaxis, hospitals often adopt a stratified approach based on bleeding and VTE risk factors [4]. However, this lack of guidelines may result in inadequate or inappropriate thromboprophylaxis treatment [3]. This case emphasizes the need for a comprehensive VTE prophylaxis protocol that includes routine monitoring of anti-Xa levels in pediatric patients undergoing chemical VTE prophylaxis to ensure sub-therapeutic levels [5].

In this case, the patient's prolonged reduced mobility placed her at high risk for VTE, and she was started on enoxaparin prophylaxis (30 mg every 12 hours). However, despite receiving prophylactic dosing, the patient achieved a therapeutic anti-Xa peak level of 0.58 units/ml (qualified using synthetic chromogenic substrate), which would have been detectable with routine laboratory surveillance. This suggests the benefits of confirming prophylactic dosing of enoxaparin and highlights the importance of routine monitoring of anti-Xa levels in pediatric patients undergoing chemical VTE prophylaxis. In our institution, the targeted anti-Xa level for prophylaxis is 0.1-0.3 units/ml.

The patient in this case experienced intraparenchymal hemorrhage with midline shift, a significant complication which can lead to considerable morbidity and mortality. After reviewing other risk factors and excluding them, the suprathreshold level of enoxaparin was determined as the most likely cause. The child made a full recovery following hematoma evacuation and was transferred back to the rehabilitation unit the following week. VTE prophylaxis was not contraindicated in this child, even with punctate hemorrhages observed on the initial CT scan, and a 48-hour observation period showed no additional signs or symptoms of bleeding [6]. Routine monitoring of anti-Xa levels after prophylactic dosing of enoxaparin is not typically performed in adults and adult-sized pediatric patients [5]. However, the development of this complication suggests the need for closer monitoring of pedi-

atric patients initiating VTE prophylaxis and the importance of prompt intervention if any concerning signs or symptoms arise.

CONCLUSION

This case underscores the significance of careful monitoring and individualized decision-making in VTE prophylaxis for pediatric patients. Although this complication is rare, the potential harm warrants thorough consideration of chemical anticoagulation prophylaxis in children. Currently, there are no validated guidelines for pediatric thromboprophylaxis, and hospitals often categorize patients based on bleeding and VTE risk factors. However, it is crucial to assess the risk-benefit ratio of VTE prophylaxis and ensure appropriate dosing. Monitoring anti-Xa levels in pediatric patients undergoing chemical VTE prophylaxis is of utmost importance as it helps guarantee the administration of an effective and appropriate dose. Further research is needed to establish evidence-based guidelines for pediatric VTE prophylaxis, incorporating indications for initiation and appropriate ongoing monitoring while considering the unique needs and characteristics of this patient population.

AUTHORS' CONTRIBUTIONS

Abdallah Dalabih, Erin Bennett: made substantial contributions to the conception of the work and the acquisition of data. Drafted the work or revised it critically for important intellectual content, and approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Sarah Sylvester, Anna M Onisei, and Clair Foster: revised it critically for important intellectual content, and approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURES AND DECLARATIONS

All authors indicate that they received no funding for this work, and has no financial or non-financial interests, study received an IRB exemption for the UAMS IRB.

REFERENCES

- 1 Goudie A, Dynan L, Brady PW, Fieldston E, Brilli RJ, Walsh KE. Costs of Venous Thromboembolism, Catheter-Associated Urinary Tract Infection, and Pressure Ulcer. United States: American Academy of Pediatrics; 2015;136:432–9. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26260712>
 - 2 Monagle P, Cuello CA, Augustine C, Bonduel M, Brandão LR, Capman T, et al. American Society of Hematology 2018 Guidelines for management of venous thromboembolism: treatment of pediatric venous thromboembolism. United States: Elsevier Inc; 2018;2:3292–316. Available from: <https://dx.doi.org/10.1182/bloodadvances.2018024786>
 - 3 Bennett E, Delgado-Corcoran C, Pannucci CJ, Wilcox R, Heyrend C, Faustino EV. Outcomes of Prophylactic Enoxaparin Against Venous Thromboembolism in Hospitalized Children. United States; 2022;12:617–25. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/35531629>
 - 4 Heit JA. Epidemiology of venous thromboembolism. England; 2015;12:464–74. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26076949>
 - 5 Mahajerin A, Croteau SE. Epidemiology and Risk Assessment of Pediatric Venous Thromboembolism. Switzerland: Frontiers Research Foundation; 2017;5:68. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28443269>
 - 6 Kahn SR, Lim W, Dunn AS, Cushman M, Dentali F, Akl EA, et al. Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. United States: American College of Chest Physicians; 2012;141:e195S-e226S. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/22315261>
-