Nonoperative Management of Infectious Mononucleosis-Associated Splenic Rupture: A Case Report

Ryan G. McQueen, MD; Edward Harwick, BS; Brian Branchford, MD; John C. Densmore, MD

ABSTRACT

Introduction: Atraumatic splenic rupture is an extremely rare but serious complication of infectious mononucleosis.

Case Presentation: We present the case of an 18-year-old female who presented with atraumatic splenic rupture in the setting of infectious mononucleosis. Her past medical history was significant for postural orthostatic tachycardia syndrome, and she has a sister who was diagnosed with Ehlers-Danlos syndrome. Given her presentation and unique background, she was followed closely by surgery and hematology. The decision was made to pursue conservative management, and she was discharged home 4 days after admission with a 6-week physical activity restriction.

Discussion/Conclusions: This patient's medical and family history warranted unique clinical considerations and multidisciplinary collaboration throughout in-patient management and follow-up. The lessons learned from nonoperative management of pediatric splenic injuries may be applied successfully to medical organ rupture, working in close partnership with hematologists to understand the time course and endpoints for the underlying inflammatory condition.

INTRODUCTION

Infectious mononucleosis (IM) is the self-limiting systemic illness most often resulting from Epstein-Barr virus during adolescence. Common symptoms include pharyngitis, malaise, and lymphadenopathy.[1] An extremely rare, but life-threatening complication of IM is splenic rupture with potential for subsequent hemorrhage that may result in severe anemia, hypovolemic shock, and/or death. The risk of splenic rupture in the setting of IM falls between 0.1% to 0.5%.[2] A systematic review of published case reports found that most IM-associated splenic ruptures to occur in adult males; 86% are absent history of trauma, approximately two-thirds of cases result in surgical intervention (splenectomy vs embolization), and the mortality rate is 9%.[3]

We present the case of an 18-year-old female with IM and a past medical history significant for postural orthostatic tachycardia syndrome (POTS) who developed splenic rupture in the absence of any identifiable trauma. Our aim is to describe the case and successful management of this patient and consider this approach for future pediatric cases, where organ preservation strategies have emanated and now influence adult practice.[4]

CASE PRESENTATION

An 18-year-old female with past medical history significant for POTS and ovarian torsion status post laparoscopic ovarian cystectomy and detorsion 2 years prior presented to urgent care with a 3-day history of fever, generalized body aches, cervical lymphadenopathy, and extreme fatigue. COVID-19 testing was negative. She was diagnosed with a viral upper respiratory infection and symptomatic care was recommended. Four days later, she presented to the emergency department (ED) with similar complaints and was noted to have a fever of 101.8 °F. Viral workup demonstrated a positive monospot test. Supportive care and management were discussed and she was discharged home.

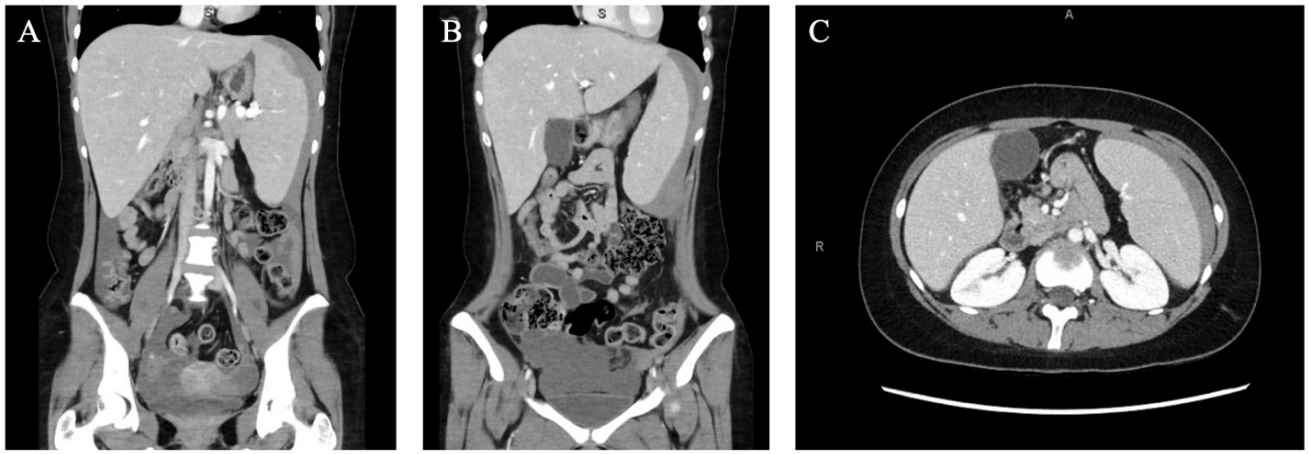
The patient then presented to the ED 8 days later with complaints of sudden left upper quadrant abdominal pain that radiated to her left shoulder, nonbloody and nonbilious emesis, and

• • •

Author Affiliations: Medical College of Wisconsin, Milwaukee, Wisconsin (McQueen, Harwick, Branchford, Densmore); Department of Pediatrics, Division of Hematology and Oncology, Children's Wisconsin, Milwaukee, Wisconsin (Branchford); Department of Surgery, Children's Wisconsin, Milwaukee, Wisconsin (Densmore).

Corresponding Author: Ryan McQueen, MD, email rmcqueen@mcw.edu; ORCID ID 0000-0003-1450-3285

Figure. Anterior-posterior (A and B) and Coronal (C) Computed Tomography Demonstrating Splenomegaly, Perisplenic, and Splenic Subcapsular Hematoma Compatible With Splenic Rupture in the Setting of Mononucleosis



decreased appetite. She was tachycardic to the 140s (beats per minute) with systolic pressures in the 100s mmHg and tachypneic, and saturating well on room air. She reported persistent fevers since she was last seen and an oral temperature of 102.2° F that morning. Her last menstrual period had been 4 days prior. She denied diarrhea, hematochezia, or melena.

On focused exam she was in apparent distress, tachycardic and tachypneic. Her abdomen was not distended, bowel sounds were hypoactive, and the abdomen was soft, with diffuse tenderness and guarding. Cervical adenopathy was also present. Complete blood count was significant for a leukocytosis of 22.7×10^3/μL and a hemoglobin of 10.0 g/dL (baseline of approximately 12), hematocrit of 30.6%, and a platelet count of 124 000/μL. Comprehensive metabolic panel and lipase were unremarkable, and pregnancy testing was negative. Computed tomography (CT) scan of the abdomen demonstrated perisplenic and splenic subcapsular hematoma compatible with splenic rupture, perisplenic fluid tracking down into the paracolic gutters, and hepatosplenomegaly (Figure). Notably, the patient denied any traumatic event leading up to onset of symptoms. She was given intravenous narcotic medication and fluids. Surgery and hematology were consulted immediately, and she was admitted for clinical monitoring.

With adequate pain control, her tachycardia and blood pressure improved. In the setting of hemodynamic stability, immediate surgical intervention was deferred in favor of close observation for signs and symptoms of destabilization. From a hematology standpoint, the patient reported hyper-flexibility similar to her sister, who carries a diagnosis of Ehlers-Danlos syndrome (EDS)—though this patient had never formally been diagnosed herself. She also reported few bleeding symptoms, including easy bruising without hematoma and approximately 2 to 3 episodes of epistaxis yearly lasting 5 to 10 minutes. She denied heavy menstrual periods, history of mucocutaneous bleeding, or gastrointestinal bleeding. She also denied excessive bleeding following her laparoscopic surgery. Therefore, her International Society of Thrombosis and Haemostasis (ISTH) bleeding assessment tool (BAT) score was 2 out of a maximum 56, suggesting a low risk of underlying bleeding disorder prior to the splenic rupture. Given the unique nature of presentation, a first-tier bleeding disorder workup was conducted, including prothrombin time (PT), partial thromboplastin time (PTT), thrombin time (TT), von Willebrand evaluation, and platelet function screen. Overall, results were unremarkable and not consistent with a bleeding disorder.

During her hospital course, her pain was well controlled on patient-controlled analgesia (PCA) narcotics, and her vitals and labs were monitored closely. She initially received nothing by mouth and her diet was advanced slowly. Her hemoglobin reached a nadir of 7.2 g/dL the day after admission, and she received 1 unit of packed red blood cells (pRBC), which increased her ISTH BAT score to 6. Her abdominal pain and hemoglobin improved (9.0 g/dL on discharge). She tolerated a general, age-appropriate diet and was discharged 4 days after admission and placed on a 6-week restriction for participating in vigorous physical activity.

At her outpatient surgery follow-up approximately 2 weeks later, the patient reported persistent pain in the abdomen and continued fatigue. Labs demonstrated a hemoglobin of 12 g/dL and resolved leukocytosis. She was provided with reassurance surrounding the nature of her hospitalization and persistent pain, likely due to ongoing inflammatory process.

She was seen in the hematology clinic approximately 2 months after her hospitalization. She reported doing well overall with improvement in symptoms but noted that she experienced abdominal pain sometimes incited by moderate activity. Her energy was

improved and she had no symptoms of anemia. Platelet aggregation study was ordered to identify any subtle platelet disfunction; results were normal. Surgery and hematology determined no further work-up or management were necessary, and she was instructed to return should any concerns arise.

DISCUSSION

While rare (0.1 to 0.5% of cases), atraumatic splenic rupture in the setting of IM has been well-documented, with numerous case reports in the literature.[5-9] However, features of this case provide unique considerations when diagnosing this rare entity. Understandably, sudden onset of severe left upper quadrant pain in a patient with IM should immediately raise suspicion for splenic rupture. However, this patient's medical and family history introduced important confounders that warranted closer attention.

POTS is a syndrome marked by orthostatic intolerance with associated cardiovascular changes (tachycardia) and accompanying symptoms that may include fatigue, palpitations, cognitive disturbances, presyncope, and nausea.[10] As such, attention should be called to the overlapping symptoms of POTS and splenic rupture, namely tachycardia and orthostasis. While recognition of splenic rupture was not delayed in this case, it is imperative that clinicians maintain an open mind when considering the etiology of nonfocal or generalized symptoms in patients with unique medical histories. POTS previously has been described as a sequela of IM,[11] but in this case, POTS preceded the development of her Epstein-Barr viral infection.

Given the rare and grave nature of atraumatic splenic rupture, subsequent bleeding disorder evaluation was completed, including factor XIII deficiency.[12] This patient's history of hypermobility and a sibling with EDS was also a potential contributor. Connective tissue disorders, including EDS, are known to be associated with bleeding tendencies.[13] In fact, a recent study found the mean ISTH-BAT score of 0.1 for healthy subjects and 9.1 for subjects with EDS.[14] While this patient's elevated ISTH-BAT score alone is not diagnostic of EDS, it did reiterate the need for a focused bleeding assessment. Two EDS subtypes are more commonly associated with bleeding—hypermobile and vascular—and are inherited in an autosomal dominant fashion. This raised the possibility that this patient could have undiagnosed EDS given her known affected sister.

Case reports exist of traumatic splenic rupture in the setting of EDS, so it was prudent for this patient to undergo further workup.[11,15] Thorough hematologic workup revealed initial prolongation of prothrombin time (PT) and partial thromboplastin time (aPTT), the latter of which did not correct on 1:1 mixing with normal plasma. Follow-up testing revealed normal PT and aPTT values. Reflex testing of factors VIII, IX, XI, and XIII demonstrated normal to minimally elevated values. Von Willebrand factor antigen (vWF), GPIbM activity, and collagen III binding were above the reference range, consistent with acute phase reaction but not concerning for an underlying von Willebrand disease. Platelet function was normal by both platelet function assay (PFA-100) screening test and light transmission aggregometry. In the absence of any abnormalities on this workup, we did not perform further analysis by genetic testing.

Finally, the patient's 6-week physical activity restriction aligns with previous recommendations for patients with splenic injury; however, there is no consensus for resuming physical activity following IM with or without splenic rupture. Proposed recommendations vary from 3 weeks to 6 months and stem from studies demonstrating an average healing time of 3 and 8 weeks for grade I and II splenic injuries, respectively, peak spleen size at 2 weeks on ultrasound following IM diagnosis, and the majority of documented splenic injuries from IM occurring within the first 3 weeks.[5-6] Other factors, such as the presence of systemic symptoms and type of contact sport, must be considered during clinical decision-making. It is important to also recognize that this is a single report, and the findings herein cannot be applied directly in a broader context. However, these findings and considerations are valuable in the field of pediatric surgery with regards to conservative management of organ rupture.

CONCLUSIONS

Atraumatic splenic rupture is a rare entity. Consideration of the diagnosis in the setting of epigastric and left upper quadrant pain is imperative to prompt recognition. Laboratory studies and axial imaging are essential in the prevention of life-threatening complications.

This case outlines a typical presentation of atraumatic splenic rupture in the setting of IM and details the resolution in the setting of careful observation and supportive care. However, the patient's medical and family history provide unique confounders that required further consideration as contribution to her presentation. The lessons learned from nonoperative management of pediatric splenic injuries may be applied successfully to medical organ rupture, working in close partnership with hematologists to understand the time course and endpoints for the underlying inflammatory condition.

Financial disclosures: None declared.

Funding/support: None declared.

Statement of informed consent: Verbal and written consent was obtained from the patient for publication of this case report.

Acknowledgement: This manuscript was prepared using the CARE guidelines (http://www.care-statement.org).

REFERENCES

1. Sylvester JE, Buchanan BK, Silva TW. Infectious mononucleosis: rapid evidence review. *Am Fam Physician*. 2023;107(1):71-78.

2. Putukian M, O'Connor FG, Stricker P, et al. Mononucleosis and athletic participation:

an evidence-based subject review. *Clin J Sport Med*. 2008;18(4):309-315. doi:10.1097/JSM.0b013e31817e34f8

3. Bartlett A, Williams R, Hilton M. Splenic rupture in infectious mononucleosis: a systematic review of published case reports. *Injury*. 2016;47(3):531-538. doi:10.1016/j.injury.2015.10.071

4. Bairdain S, Litman HJ, Troy M, et al. Twenty-years of splenic preservation at a level 1 pediatric trauma center. *J Pediatr Surg*. 2015;50(5):864-868. doi:10.1016/j.jpedsurg.2014.08.022

5. Juyia RF, Kerr HA. Return to play after liver and spleen trauma. *Sports Health.* 2014;6(3):239-245. doi:10.1177/1941738114528468

6. Becker JA, Smith JA. Return to play after infectious mononucleosis. *Sports Health.* 2014;6(3):232-238. doi:10.1177/1941738114521984

7. Sergent SR, Johnson SM, Ashurst J, Johnston G. Epstein-Barr virus-associated atraumatic spleen laceration presenting with neck and shoulder pain. *Am J Case Rep.* 2015;16:774-777. doi:10.12659/ajcr.893919

8. Baker CR, Kona S. Spontaneous splenic rupture in a patient with infectious mononucleosis. *BMJ Case Rep*. 2019;12(9):e230259. doi:10.1136/bcr-2019-230259

9. Lu Q, Fu W, Ouyang G, Xu Q, Huang D. A case of infectious mononucleosis complicated with spontaneous atraumatic splenic rapture caused by Epstein-Barr virus infection. *J Med Virol.* 2022;94(12):6127-6132. doi:10.1002/jmv.28083

10. Bryarly M, Phillips LT, Fu Q, Vernino S, Levine BD. Postural orthostatic tachycardia syndrome: JACC Focus Seminar. *J Am Coll Cardiol*. 2019;73(10):1207-1228. doi:10.1016/j.jacc.2018.11.059

11. Kamalanathan KC, Barnacle AM, Holbrook C, Rees C. Splenic rupture secondary to vascular Ehlers-Danlos syndrome managed by coil embolization of the splenic artery. *European J Pediatr Surg Rep.* 2019;7(1):e83-e85. doi:10.1055/s-0039-3399555

12. Khalife H, Muwakkit S, Al-Moussawi H, et al. Spontaneous splenic rupture in a patient with factor XIII deficiency and a novel mutation. *Pediatr Blood Cancer.* 2008;50(1):113-114. doi:10.1002/pbc.20786

13. Malfait F, De Paepe A. Bleeding in the heritable connective tissue disorders: mechanisms, diagnosis and treatment. *Blood Rev.* 2009;23(5):191-197. doi:10.1016/j.blre.2009.06.001

14. Kumskova M, Flora GD, Staber J, Lentz SR, Chauhan AK. Characterization of bleeding symptoms in Ehlers-Danlos syndrome. *J Thromb Haemos*t. 2023;21(7):1824-1830. doi:10.1016/j.jtha.2023.04.004

15. Privitera A, Milkhu C, Datta V, Sayegh M, Cohen R, Windsor A. Spontaneous rupture of the spleen in type IV Ehlers-Danlos syndrome: report of a case. *Surg Today.* 2009;39(1):52-54. doi:10.1007/s00595-007-3782-3

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 2379-3961) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.