Hemarthrosis in a pediatric patient with idiopathic thrombocytopenic purpura and Lyme arthritis

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Abstract

Presentation of idiopathic thrombocytopenic purpura (ITP) is dependent on degree of thrombocytopenia with no to mild bleeding symptoms, primarily mucocutaneous bleeding. Severe bleeding of other organ systems is a rare complication. Spontaneous hemarthrosis is rare in patients without hemophilia. We report a child presenting with oral and cutaneous petechial lesions and left knee hemarthrosis without trauma. Laboratory findings showed severe thrombocytopenia consistent with ITP. Serologic tests were consistent with Lyme disease. Hemarthrosis was presumed secondary to Lyme disease monoarticular joint inflammation with bleeding exacerbated by severe thrombocytopenia. Hemarthrosis resolved and platelet counts normalized following immunoglobulin infusion, steroid course, and antibiotics.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is a blood disorder characterized by immune-mediated antibody platelet destruction[1,2] . ITP is categorized into primary, or idiopathic, and secondary if a cause is identified such as a preceding viral illness or an underlying immunodeficiency[3]. The incidence rate of 1-6.4 cases per 100,000 children shows a biphasic age distribution: toddlers and adolescents[4]. The result is a quantitative platelet deficiency available for primary hemostasis manifesting as mucocutaneous bleeding (e.g., petechiae, bruising, oral/buccal purpura, epistaxis). Severe presentations including internal bleeding are rare in children and occur less frequently than in adults[5].

A comparative prospective registry of 1,784 children newly diagnosed with ITP reported the incidence of joint bleeding involvement as the lowest of all organ systems[6]. Factors predictive for severe bleeding include severe thrombocytopenia (platelet count $<$ 20 x 10*3/uL, Ref. range and units: 142 – 508 x 10*3/uL), newly diagnosed ITP, and previous minor bleeding[6]. Hemarthrosis is defined as bleeding into a joint and can cause monoarticular swelling and pain. The most common cause is trauma where bleeding develops due to bone, soft tissue, or ligamentous injury. Non-traumatic etiologies include bleeding disorders, osteoarthritis, septic arthritis, bursitis, intra-articular vascular anomalies or tumors such as synovial hemangiomas[7,8,9]. While prevalence rates of hemarthrosis in children with severe hemophilia A or B can be as high as 33-47%[10], acute hemarthrosis in children without hemophilia is rare and typically follows traumatic injury[8]. While imaging findings can be suggestive, definitive diagnosis is via arthrocentesis for synovial fluid analysis. We present a case of non-traumatic hemarthrosis in the setting of ITP where the patient was found to have positive serologies for Lyme Disease.

Lyme Disease was first described as an arthritis in children that could be monoarticular or oligoarticular. Typical presentation occurs in stages with localized skin lesions followed by disseminated infection days to weeks later with migratory joint pain[11]. Without antibiotic treatment, 60% of patients with Lyme Disease develop arthritis involving one or many joints[12]. Progression to arthritis is a late disease manifestation

resulting from strains of *Borrelia burgdorferi* disseminating into the joint space causing immune response with resultant inflammation[12]. Following antibiotics, spirochetes are destroyed, and inflammation of the affected joints typically resolves[12].

RESULTS & CASE DESCRIPTION

A 7-year-old male presented with left knee swelling, generalized petechiae, and severe thrombocytopenia. The patient was previously healthy with no recent illnesses, medications, or trauma. Two weeks before presentation, he developed petechiae that progressed to cover his torso and extremities. Three days before presentation, he developed swelling of the left knee with restricted range of motion and limping. A complete blood count (CBC) performed on the day of presentation showed platelets of 6 x 10*3/uL with otherwise normal hemoglobin, red blood cell indices, and white blood cell count. There was no known tick exposure but Lyme serologies were obtained. The patient was sent to the emergency department.

Initial exams showed petechiae on the palate, torso, and all four extremities with swelling of the left knee (Image 1) leading to decreased range of motion and weight bearing. The family denied patient or family history of easy bleeding or bruising disorders. Laboratory evaluation was significant for platelet count of 4 x 10*3/uL, immature platelet fraction of 22.2% (Ref. range and units: 1.1% – 8.5%), prolonged activated partial thromboplastin time (aPTT) of 47s. (Ref. range and units: 24 – 36 seconds), normal prothrombin time (PT) of 14.7s. (Ref. range and units: 12.4 – 14.7 seconds), fibrinogen 460 mg/dL (Ref. range and units: 170 – 410 mg/dL). Due to prolonged aPTT, mixing studies were completed to rule out a coagulation factor deficiency or inhibitor. Quantitative Factor XII, XI, VIII, and IX levels were normal. An ultrasound showed an echogenic joint effusion distending the knee capsule (Image 2) consistent with left knee hemarthrosis. Patient was admitted for further management.

On hospital day one, peripheral blood smear showed findings consistent with ITP. X-rays showed no fracture or traumatic findings. Intravenous immunoglobulin (IVIG) and steroids were initiated due to severe thrombocytopenia with hemarthrosis. On hospital day two, the patient demonstrated improved knee swelling and range of motion along with improved platelet count to 29 x 10*3/uL. Arthrocentesis and additional imaging were deferred given clinical improvement. The Lyme Disease screening assay resulted positive (Ref. range and units: Negative, a positive screen result is considered presumptive positive for Lyme Disease with confirmatory immunoblot sent). Repeat screening assay and confirmatory immunoblot were obtained but empiric antibiotics were not started.

Two days following hospital discharge, repeat Lyme Disease screening resulted positive for IgM and IgG and a 28-day course of doxycycline was prescribed. Patient was seen by infectious diseases and hematology five days after hospital discharge. He had no ongoing bleeding symptoms and near resolution of knee swelling and pain. Initial immunoblot testing resulted in positive IgM bands 3/3 and IgG bands 9/10 (Ref. range and units: Lyme Disease IgM immunoblot requires reactivity to 2 of 3 specific borrelial proteins to be considered positive, Lyme Disease IgG immunoblot must show reactivity to at least 5 of 10 specific borrelial proteins to be considered positive). Stronger consideration was given to Lyme arthritis as contributive to clinical presentation. At final follow up, evaluation showed a robust platelet response to 738 x 10*3/uL without evidence of recurrent symptoms.

DISCUSSION

In the setting of positive serologic Lyme Disease testing, hemarthrosis was thought to be secondary to Lyme arthritis causing joint inflammation and bleeding symptoms exacerbated by concurrent ITP. Spontaneous hemarthrosis in ITP is an atypical presentation with the most common bleeding symptoms being mucocutaneous. It is of utmost importance to expedite therapy for hemarthrosis to prevent further joint damage. Initial differential was broad and included ITP, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, hemolytic uremic syndrome, hemophilia, septic or inflammatory arthritis, bursitis, intra-articular venous malformations, or trauma[7,9,13]. Upon reflection, a unifying explanation for the presentation is Lyme Disease with resultant inflammatory arthritis and severe thrombocytopenia as causative of the hemarthrosis. The initial symptom improvement was thought to be due to the anti-inflammatory effects

of the steroid regimen without treatment of additional underlying disease. Realizing an additional contributing etiology, oligoarticular or monoarticular joint inflammation must be considered as an unrecognized cause for spontaneous hemarthrosis in a child with severe ITP.

This provides an example for clinicians to consider when evaluating abnormal bleeding presentations of ITP. It is important to keep a high index of suspicion for other treatable conditions. Limitations of this report include the inability to establish a causal relationship between the various disease processes occurring in this patient. A single case report limits generalizability, especially given the geographic distribution of Lyme Disease in the northeastern and north central United States[11]. Also, further diagnostic testing via magnetic resonance imaging or arthroscopy was not pursued to rule out additional pathology[8,9]. In conclusion, this report depicts a rare complication of ITP and suggests that additional underlying pathology may contribute to abnormal presentations with severe bleeding symptoms. Providers should be mindful of additional precipitating causes and consider appropriate testing to reduce overall morbidity and improve long-term outcomes.

IMAGES

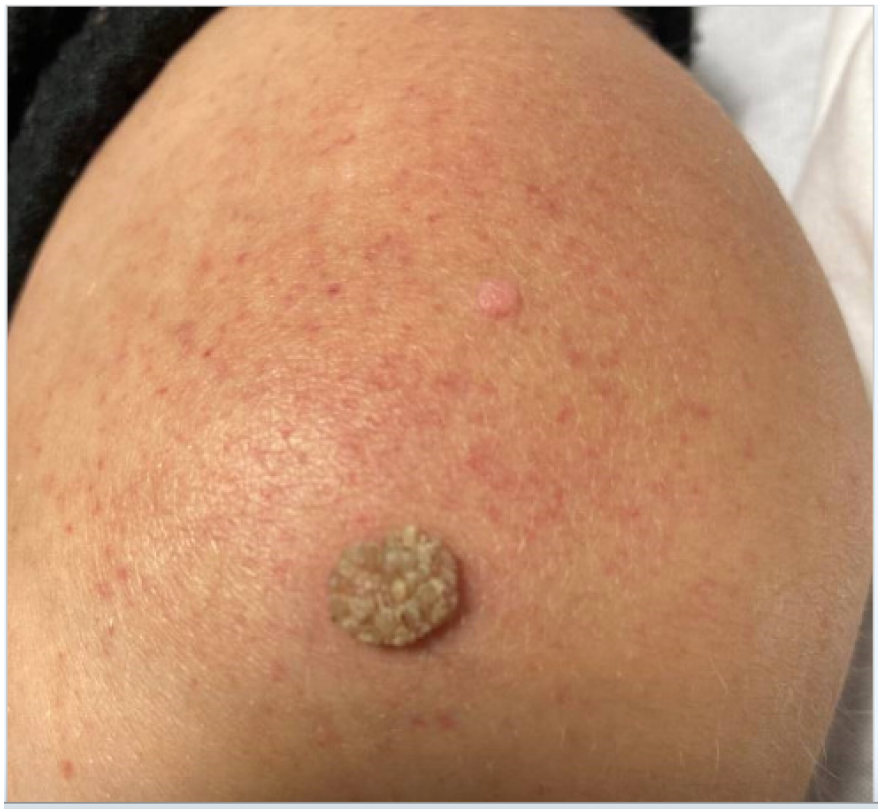

Image 1: Generalized soft tissue swelling of the left knee and demonstration of petechial cutaneous lesions.

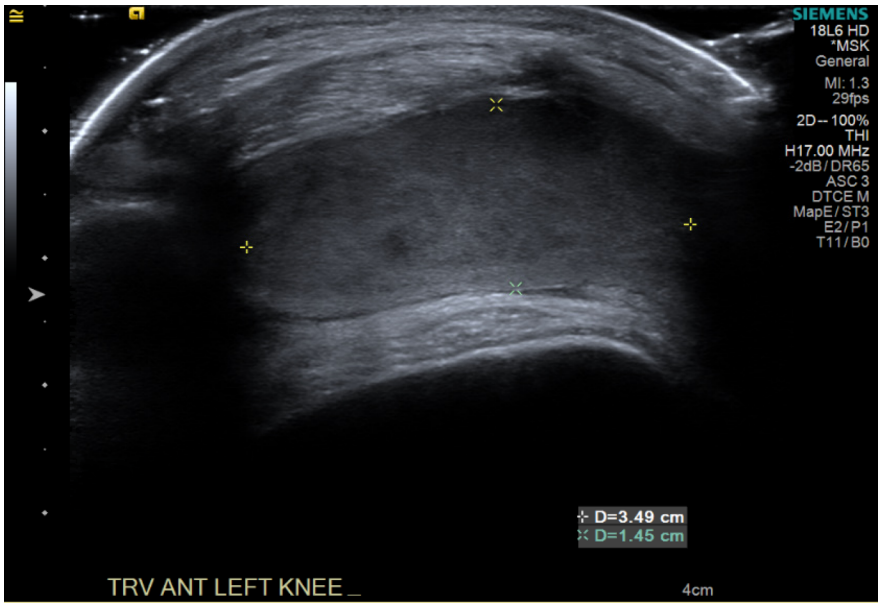

Image 2: High-resolution linear grayscale and color doppler sonography of the left knee. Imaging showed an echogenic joint effusion distending the joint capsule measuring 3.49cm x 1.45cm in the transverse anterior view. Findings consistent with left knee hemarthrosis.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interests to disclose.

ETHICS STATEMENT

Informed consent was obtained from patient's guardian to allow us to use deidentified images of his petechiae/hemarthrosis as well as pictures of his ultrasound imaging.

REFERENCES

1. D'Orazio JA, Neely J, Farhoudi N. ITP in children: pathophysiology and current treatment approaches. *J Pediatr Hematol Oncol* . 2013;35(1):1-13. doi:10.1097/MPH.0b013e318271f457
2. Semple JW, Rebetz J, Maouia A, Kapur R. An update on the pathophysiology of immune thrombocytopenia. *Curr Opin Hematol* . 2020;27(6):423-429. doi:10.1097/MOH.0000000000000612
3. Elalfy MS, Nugent D. Viruses, anti-viral therapy, and viral vaccines in children with immune thrombocytopenia. *Semin Hematol* . 2016;53 Suppl 1:S70-S72. doi:10.1053/j.seminhematol.2016.04.021
4. Saeidi S, Jaseb K, Asnafi AA, et al. Immune Thrombocytopenic Purpura in Children and Adults: A Comparative Retrospective Study in IRAN.*Int J Hematol Oncol Stem Cell Res* . 2014;8(3):30-36.
5. Neunert C, Noroozi N, Norman G, et al. Severe bleeding events in adults and children with primary immune thrombocytopenia: a systematic review. *J Thromb Haemost* . 2015;13(3):457-464. doi:10.1111/jth.12813
6. Kühne T, Berchtold W, Michaels LA, et al. Newly diagnosed immune thrombocytopenia in children and adults: a comparative prospective observational registry of the Intercontinental

Cooperative Immune Thrombocytopenia Study Group. *Haematologica* . 2011;96(12):1831-1837. doi:10.3324/haematol.2011.050799

7. Lin HK, Wang JD, Fu LS. Recurrent hemarthrosis in a boy with synovial hemangioma: a case report. *J Pediatr Orthop B* . 2011;20(2):81-83. doi:10.1097/BPB.0b013e328341bcf9
8. Matelic TM, Aronsson DD, Boyd DW Jr, LaMont RL. Acute hemarthrosis of the knee in children. *Am J Sports Med* . 1995;23(6):668-671. doi:10.1177/036354659502300605
9. Mattila KA, Aronniemi J, Salminen P, Rintala RJ, Kyrklund K. Intra-articular venous malformation of the knee in children: magnetic resonance imaging findings and significance of synovial involvement.*Pediatr Radiol* . 2020;50(4):509-515. doi:10.1007/s00247-019-04580-5
10. Wilkins RA, Stephensen D, Siddle H, et al. Twelve-month prevalence of haemarthrosis and joint disease using the Haemophilia Joint Health score: evaluation of the UK National Haemophilia Database and Haemtrack patient reported data: an observational study. *BMJ Open* . 2022;12(1):e052358. Published 2022 Jan 12. doi:10.1136/bmjopen-2021-052358
11. Steere AC, Coburn J, Glickstein L. The emergence of Lyme disease.*J Clin Invest* . 2004;113(8):1093-1101. doi:10.1172/JCI21681
12. Steere AC, Schoen RT, Taylor E. The clinical evolution of Lyme arthritis. *Ann Intern Med* . 1987;107(5):725-731. doi:10.7326/0003-4819-107-5-725
13. Aldin Z, Obaid H, Abdelsalam H, Bolia A. Case report: Spontaneous recurrent idiopathic knee haemarthrosis in a paediatric patient: successful transcatheter embolization. *Clin Radiol* . 2010;65(1):82-84. doi:10.1016/j.crad.2009.07.016