Spontaneous Spinal Subdural Hematoma Secondary to Hemophilia A and Zanubrutinib

John Lynes1 Sebastian Rubino1 Andrea Rogers1 Sameh Gaballa3 Hien D. Liu4 John A. Arrington2 Edwin Peguero1 James K. C. Liu1,5

1Department of Neuro-Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States
2Department of Radiology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States
3Department of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States
4Department of Bone Marrow Transplant and Cellular Immunotherapy, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, United States
5Department of Oncologic Sciences, University of South Florida Morsani College of Medicine, Tampa, Florida, United States

Abstract

Spontaneous spinal subdural hematomas (SSH) are rare occurrences that can occur most commonly secondary to vascular malformations or coagulopathies. Only a small fraction of spontaneous SSHs are caused by acquired coagulation disorders such as leukemia, hemophilia, and thrombocytopenia. This case report describes a patient with a history of Guillain–Barré syndrome (GBS), hemophilia A, and mantle cell lymphoma, on zanubrutinib therapy, a Bruton tyrosine kinase inhibitor associated with a risk of spontaneous hemorrhage. This patient developed a spontaneous spinal subdural hematoma, most likely due to the zanubrutinib therapy and exacerbated due to hemophilia. Treatment was delayed due to the patient’s history of GBS that confounded the clinical diagnosis. This case is the first report of a spontaneous SSH in a patient on zanubrutinib, highlighting the need for a high index of suspicion for CNS hemorrhage in patients on Bruton’s tyrosine kinase (BTK) inhibitor therapy.

Keywords
► hemophilia
► zanubrutinib
► spinal subdural hematoma
► hemorrhage
► mantle cell lymphoma

Introduction

Spinal subdural hematomas (SSH) are a rare entity. Etiologies for SSH most often involve posttraumatic or iatrogenic causes although a subset of SSH are spontaneous secondary to vascular malformations or coagulopathies.1 Previous reviews have demonstrated that 10 to 35% of spontaneous SSH are secondary to anti-coagulation therapy, while 4 to 19% are secondary to acquired coagulation disorders such as leukemia, hemophilia, thrombocytopenia, polycythemia vera, and cryoglobulinemia.1–3

This case is the first reported spontaneous spinal subdural hematoma in a patient with a history of hemophilia A and mantle cell lymphoma on zanubrutinib treatment. The case was also unique in that in addition to the patient’s acquired coagulation issues, the patient had a history of Guillain–Barré syndrome that resulted in an initial misdiagnosis before appropriate imaging was received November 17, 2021 accepted January 11, 2022

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obtained and the patient was transferred for surgical intervention.

Case Report

A 76-year-old man with a history of hemophilia A and mantle cell lymphoma presented to an outside hospital for abdominal pain. He was initially diagnosed with mantle cell lymphoma (MCL) (TP53 mutated) 2 years ago by tissue biopsy, with CD5-positive monoclonal B cells identified by flow cytometry and t11:14 by fluorescence in situ hybridization (FISH). His hemophilia was mild with baseline factor VIII activity of 16% without inhibitor. His mantle cell lymphoma was diagnosed 2 years prior, with CD5-positive monoclonal B cells with 11:14 translocation identified by FISH. He underwent six cycles of rituximab–bendamustine, but was complicated by prolonged neutropenia requiring growth factor administration. Two months after completing bendamustine, he was admitted for neutropenic fever and diarrhea and diagnosed with Campylobacter colitis and bacteremia. Following this, he experienced ascending weakness involving all extremities, and was diagnosed with Guillain–Barré syndrome confirmed by EMG, requiring plasmapheresis and IVIG with one episode of relapse and ultimate complete neurological recovery. Twenty-two months following his initial diagnosis, he developed recurrence of his MCL and was started on zanubrutinib, at half dose due to his hemophilia A.

He had been on zanubrutinib for 4 months when he presented to the outside hospital, at which time he was diagnosed with gallstones with bile duct dilation and underwent endoscopic retrograde cholangiopancreatography. For-
Although the etiology for the spontaneous SSH in this case is likely a combination of hemophilia and zanubrutinib, it is unclear as to whether there may have been an inciting event that led to the hemorrhage 48 hours following admission to the outside hospital and an ERCP procedure. Possibilities may include an occult trauma to the spine or a hypertensive episode secondary to pain following the procedure. In this case, diagnosis was delayed due to the confounding history of Guillain–Barré syndrome although the presentation was not consistent in that both motor and sensory functions were impaired. This scenario highlights the need for awareness of acute central nervous system-related hemorrhages in a patient with an underlying acquired coagulation disorder while on a medication with a risk for hemorrhage. Acute onset of these symptoms should raise suspicion for an acute neurological event that warrants immediate work-up that should include MRI of the spine.

In addition to spontaneous SSH, the risk of iatrogenic SSH is elevated as a nearly half of previously spontaneous SSH are secondary to iatrogenic causes, such as lumbar puncture, with an underlying coagulopathy. Therefore, the risk of a
SSH needs to be accounted for when considering invasive procedures on these patients.

**Conclusion**

Spontaneous spinal subdural hematomas can occur in the presence of acquired coagulation disorders, such as hemophilia and BTK inhibitor therapy. This case highlights the need for maintaining a high index of suspicion of spontaneous hemorrhage in the central nervous system while on this type of therapy.

Conflict of Interest
None declared.

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