Mesenteric Thrombosis Complicating Influenza B Infection

To the Editor:

A 44-year-old healthy, active man presented to an outside hospital complaining of a 1-day history of fever up to 39°C, muscle aches, sinus pressure, nausea, vomiting, and diarrhea in April 2015. Review of systems was negative for abdominal pain, hematochezia, or melena. A chest radiograph was negative for infiltration, consolidation, edema, or other pathology. Lipase level was 37 U/L (within normal limits). A nasopharyngeal swab antigen test was positive for influenza B, and the patient was discharged on oseltamivir. Three days later, intermittent fevers persisted with chills, nausea, vomiting, and severe abdominal pain. Anorexia developed, and the patient described "something twisting and pulling at [his] insides." An abdominal computed tomography scan showed extensive superior mesenteric vein thrombosis, which extended into the main portal vein and proximal splenic vein. He was transferred to our facility for transhepatic thrombolysis, which was complicated by intrahepatic hematoma requiring subselective hepatic artery embolization. He recovered completely and was discharged with rivaroxaban. Hematology evaluation was negative for predisposing hypercoagulable conditions including factor II mutation, factor V Leiden, and lupus anticoagulant. Of note, his past medical, surgical, and family history were unrevealing for malignancy, coagulopathy, cirrhosis, pancreatitis, or other prothrombotic states.

Infection is not prominent among etiologies of acute mesenteric venous thrombosis, but any local inflammation may be predisposing.[1] One case of influenza A with coincident mesenteric venous thrombosis has been reported, although the patient also had protein S deficiency.[2] Epidemiologic data have indicated that prior infection is a risk factor for venous thromboembolism,[3] and studies with vascular devices have shown that infectious and thrombotic complications may coincide.[4] Interestingly, influenza infection has specifically been hypothesized, but not confirmed, as a contributing, if not causative, factor in thrombotic events.[5,6]

Recent research in influenza pathogenesis offers potential links between influenza infection and thrombosis. Highly pathogenic avian influenza infects endothelial cells, promoting vascular pathology in some species, but evidence of direct human endothelial cells infection is lacking.[7] However, endothelial activation may be indirect. In ferrets, influenza infection causes increased D-dimer levels, von Willebrand factor activity, prothrombin time, and intravascular thrombin deposition. These findings have been more pronounced in pandemic H1N1 and highly pathogenic avian influenza H5N1, compared with seasonal H3N2.[8] Influenza may further promote thrombosis and vascular disease by inducing cytokines such as interleukin-6, interleukin-1β, and tumor necrosis factor-α, signals known to activate endothelial cells and platelets and modulate macrophage survival.[7]

Perhaps underappreciated, Influenza B accounts for a substantial portion of influenza infections in the US.[9] It accounted for 13.5% of influenza admissions and the majority of influenza cases occurring after mid-March during the 2014-2015 season at our institution. Although there is similar mortality among hospitalized influenza A- and B-infected adults, there are many fewer clinical and epidemiologic data regarding influenza B and its complications.[9,10] While its virology and host tropism make a pandemic unlikely, Influenza B can be responsible for a high proportion of incidence, morbidity, and cost of total influenza illness.[9]

Although this patient with a complicated course of Influenza B infection had a favorable outcome, this case illustrates the increasingly appreciated clinical pearl that Influenza B can be as pathogenic as Influenza A. Further epidemiologic and basic research may discern the relationship between influenza infection and pathologic vascular events. Finally, clinicians should bear in mind that patients with any strain of influenza, including seemingly mild cases, may still suffer complications of thromboembolic disease, which can be effectively treated when diagnosed promptly.

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References

1. Singal AK, Kamath PS, Tefferi A. Mesenteric venous thrombosis. *Mayo Clin Proc*. 2013;88(3):285-295.
2. Hayakawa T, Morimoto A, Nozaki Y, et al. Mesenteric venous thrombosis in a child with type 2 protein S deficiency. *J Pediatr Hematol Oncol*. 2011;33(2):141-143.
3. Schmidt M, Horvath-Puho E, Thomsen RW, Smeeth L, Sørensen HT. Acute infections and venous thromboembolism. *J Intern Med*. 2012;271(6):608-618.
4. Thakarar K, Collins M, Kwong L, Sulis C, Korn C, Bhadelia N. The role of tissue plasminogen activator use and systemic hypercoagulability in central line associated blood stream infections (CLABSIs). *Am J Infect Control*. 2014;42(4):417-420.
5. Bunce PE, High SM, Nadjafi M, Stanley K, Liles WC, Christian MD. Pandemic H1N1 influenza infection and vascular thrombosis. *Clin Infect Dis*. 2011;52(2):e14-e17.
6. Ludwig A, Lucero-Obusan C, Schirmer P, Winston C, Holodniy M. Acute cardiac injury events ≤30 days after laboratory-confirmed influenza virus infection among U.S. veterans, 2010-2012. *BMC Cardiovasc Disord*. 2015;15(1):109.
7. Short KR, Veldhuis Kroeze EJ, Reperant LA, Richard M, Kuiken T. Influenza virus and endothelial cells: a species specific relationship. *Front Microbiol*. 2014;5:653.
8. Goeijenbier M, van Gorp EC, Van den Brand JM, et al. Activation of coagulation and tissue fibrin deposition in experimental influenza in ferrets. *BMC Microbiol*. 2014;14(1):1-12.
9. Su S, Chaves SS, Perez A, et al. Comparing clinical characteristics between hospitalized adults with laboratory-confirmed influenza A and B virus infection. *Clin Infect Dis*. 2014;59(2):252-255.
10. Glezen WP, Schmier JK, Kuehn CM, Ryan KJ, Oxford J. The burden of influenza B: a structured literature review. *Am J Public Health*. 2013;103(3):43-52.