A Case of Late-Onset Hereditary Angioedema in a Patient with Non-Hodgkin's Lymphoma, Common Variable Immunodeficiency, and Antiphospholipid Antibody Syndrome

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Background

Hereditary angioedema (HAE) with C1q deficiency is a rare hereditary condition characterized by repeated attacks of angioedema. This condition most frequently affects the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. HAE can be associated with lymphoproliferative disorders such as splenic marginal zone non-Hodgkin's lymphoma and should be considered in the differential for patients with recurrent attacks of angioedema or abdominal pain that is unresponsive to treatment.

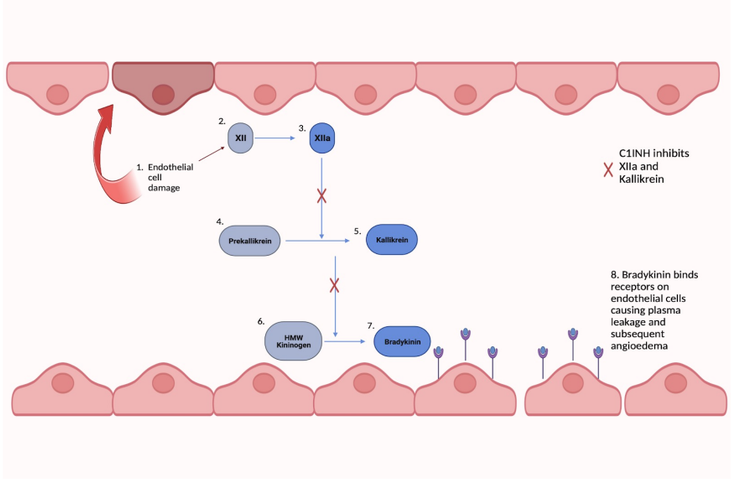

Figure 1. Pathogenesis of HAE.[4] Endothelial cell damage activated factor XII activates prekallkrein to kallkrein. Kallikrein cleaves high-molecular weight kininogen to produce bradykinin. Bradykinin binds receptors on endothelial cells which causes plasma leakage and subsequent angioedema. C1INH functions to inhibit activated factor XII (XIIa) and kallikrein.

Case Report

A 71-year-old woman presented to the emergency department (ED) with a complaint of abdominal pain in January of 2022. Her symptoms included cramping, constipation, diarrhea, nausea, and severe vomiting despite avoidance of food sensitivities. The episodes were preceded by constipation for 24-36 hours and began in the evening with diarrhea, leading to vomiting, pain, and abdominal swelling. No facial or upper extremity edema was observed on physical exam.

The patient had a history of several similar attacks in 2017 and 2018 that varied in frequency. The episodes were symptomatically treated with Pepto Bismol which gradually became ineffective. Initially, her symptoms were attributed to *C. diff*.

In the ED in January of 2022, the patient underwent CT imaging which showed large segments of duodenal wall thickening from the second through the fourth portions with adjacent inflammatory change and splenomegaly with a spleen size of 17.5 cm. The patient's previous medical history consists of splenic marginal zone non-Hodgkin's lymphoma, treated successfully with chemotherapy; common variable immunodeficiency with ongoing IVIG treatment; positive anticardiolipin antibody testing with daily 81 mg of aspirin and no thrombotic events to date.

Due to several visits to the ED while in Utah, and prior discussion of possible HAE, a trial of Berinant proved to successfully resolve the patient's symptoms. Subsequent immunological testing of the patient's C4 complement component, C1 esterase inhibitor, C1 esterase inhibitor functional, and C1Q complement component affirmed a diagnosis of late-onset C1q deficient HAE.

Conclusions

HAE due to acquired C1-INH deficiency is difficult to identify and is most commonly diagnosed after many years of recurring attacks. Currently, HAE treatment relies on short- and long-term prevention and treatment for acute attacks. The goal of HAE therapy is to reduce the frequency and severity of angioedema and improve patient quality of life. Due to the variable clinical presentation and severity of the disease, if untreated, it is essential to recognize and initiate appropriate treatment for HAE.

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