Immune thrombocytopenia (ITP) in the setting of hereditary angioedema with C1 inhibitor deficiency (HAE C1 INH): a possible consequence of low C4

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BACKGROUND

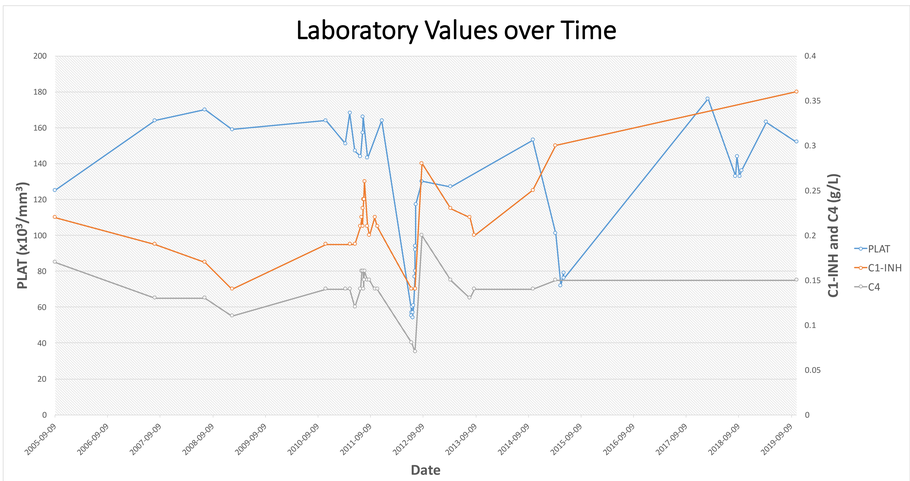
- Hereditary angioedema (HAE) is a rare autosomal dominant disorder that is defined by a deficiency of complement component 1 (C1) esterase inhibitor (C1-INH), a glycosylated serine protease inhibitor, that plays a regulatory role in the complement cascade and the intrinsic coagulation
- One of the most important functions of C1-INH is the inhibition of kallikrein, which in turn limits the production of the vasoactive mediator bradykinin. Deficiency of C1-INH results in the hyper-activation of kallikrein and the overproduction of bradykinin and development of angioedema.
- HAE patients have unregulated activation of the early steps of the classic complement pathway with decreased (but not absent) levels of C4 and C2. Decreased or dysfunctional complement may promote the tissue deposition of immune complexes and autoimmnue disease because complement proteins play an important role in the clearance of immune complexes or autoantibodies.
- C4 levels may be falsely high since HAE patients make a nonfunctional chain detected by the assay

CASE

- We present a 37 year old female who was diagnosed with HAE type 1 after she had recurrent swelling since childhood and was found to have a low C4 of <0.11 g/L (0.13-0.52 g/L) and a low C1 inhibitor level at <0.14 (0.21-0.39 g/L) She was diagnosed with HAE at age of 23 years.
- She started taking C1inhibitor IV in 2010 but only infrequently about once every 3 months for severe attacks.
- When she was 30 years old in 2012 and again in 2015, she developed ITP with the lowest platelet count of 55 in 2012 (normal 150-400 x 10 9/L); at that time her C4 level was as low as (0.07). She was treated with prednisone, IVIG and platelet transfusions. Her platelets improved and her C4 level came up.
- She began using C1INH more frequently in 2016 taking 20 U/kg IV on demand about once per week to treat attacks. She has had no recurrence of ITP. Her C1 inhibitor levels have normalized since 2014 while her C4 level remains low but not as low as previously

DISCUSSION

- It has been reported that patients with HAE have an increased incidence of immunoregulatory or autoimmune diseases. In 1986, 157 patients with HAE-C1-INH were systematically evaluated for manifestations of autoimmunity and reported an increased frequency of autoimmune disease[1] .
- In 2012, it was found that 47.5% of HAE patients had at least one of the autoantibodies tested versus a prevalence of 10% in the healthy controls[2]
- In 2014, medical record review of 143 patients with HAE C1INH demonstrated enhanced production of autoantibodies. Time between HAE diagnosis and the detection of the autoimmune conditions was 9–30 years[3].



Normal levels: PLAT 150-400 x 10^3/mL C1-INH 0.21-0.39 g/L C4 0.13-0.52 g/L

CONCLUSION

- To our knowledge, this is the first case of ITP reported in an HAE patient.
- Future consideration to treating HAE with low C4 with C1-INH replacement at doses which restore C4 levels versus treatments, which only prevent kallikrein activation, but do not restore C4 levels, may need to be given.
- Long term studies are needed to understand the risk of low C4 levels in HAE patients

REFRENCES

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