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Hereditary angioedema with normal C1 inhibitor due to FXII mutation: report of the first case confirmed with genetic diagnostic in Chile

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Rationale: HAE with a factor XII mutation (HAE-FXII) is one of the 6 subtypes of HAE with normal C1-INH. Mainly affecting young women with estrogens as the main trigger, HAE-FXII affects quality of life, specially while diagnostic remains unknown. We present the first case of HAE-FXII with genetic diagnostic in Chile.

Method: Review of a patient's clinical history, after obtaining informed consent.

Results: 38 year-old female, without personal or familiar clinical history, at age 20 presents with hands and face swelling, abdominal pain and vomiting during a dental procedure, associated to recent initiation of combined oral contraceptives (COC). She developed recurrent 3 day-long attacks of facial swelling, triggered by trauma and emotional stress. Hospitalized during an attack, intestinal edema and ascites were demonstrated.

HAE workup resulted negative, including C4, C1q and C1INH, therefore genetic studies were performed identifying a pathogenic variant of FXII, c.938C>A (p.Thr328Lys).

Following unsuccessful treatment with tranexamic acid, her COC were changed to a levonorgestrel intrauterin device, now the patient remains asymptomatic.

Conclusions: HAE-FXII primarily affects women (10:1), usually manifesting during the 2nd decade of life with estrogens as the main trigger. It usually affects face, digestive system and upper airways, has long symptom free periods and rarely prodromes. Around 500 cases of HAE-FXII have been reported, with p.Thr328Lys as the main mutation. Attacks are treated with C1INH, icatibant or ecallantide and long term profilaxis includes avoiding estrogens while using progestins, antifibrinolytics, C1INH and danazol. We present the 1st known case of HAE-FXII in Chile with genetic confirmation. Due to the clinical implications and impact on quality of life, completing specific study is relevant when clinical history suggests it, even if familiar history is abscent. Nowadays availability of genetic diagnostic is limited, mostly meaning to study samples abroad.