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## Short communication

# Retinal venous thrombosis in a young patient with coagulation factor XII deficiency<sup>☆</sup>

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### ABSTRACT

**Case report:** A 35-year-old woman, with no relevant medical history, was referred for sudden vision loss in the left eye. Ophthalmological examination showed best corrected visual acuity of 1.0 in the right eye and 0.3 in left eye, with normal anterior pole and intraocular pressure. Fundus examination of the left eye revealed a venous thrombosis in the superior temporal branch, with dilated and tortuous retinal veins. The patient was referred to the hematology unit for thrombophilia study, and was diagnosed with a coagulation XII or Hageman factor deficiency.

**Discussion:** The development of retinal vessel occlusions, in patients under 50 years of age, is frequently associated with thrombophilia or hypercoagulability disorders. Factor XII deficiency is a rare condition, and its presence could contribute to a higher risk of thromboembolic events.

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## Trombosis venosa retiniana en paciente joven con déficit de factor XII de la coagulación

### RESUMEN

**Caso clínico:** Mujer de 35 años enviada a la consulta por disminución de la visión en ojo izquierdo. En la oftalmoscopia se apreció una trombosis venosa de rama en ese mismo ojo. La paciente fue derivada a la unidad de hematología para estudio de trombofilia, siendo diagnosticada de déficit de factor XII de la coagulación o factor de Hageman.

**Discusión:** El desarrollo de fenómenos trombóticos oculares en pacientes sanos menores de 50 años debe hacer sospechar la presencia de trombofilia o estados de hipercoagulabilidad. El déficit de factor XII es poco frecuente y su presencia contribuye al desarrollo de procesos trombóticos.

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#### Palabras clave:

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## Introduction

Thromboembolic disease is a multifactorial disorder favored by decreased blood flow or blood stasis, due to vascular disorder factors and blood dyscrasias leading to hypercoagulable states. This is known as Virchow's triad.<sup>1</sup>

Various conditions may favor its aspect, such as surgeries, long periods of immobilization or pregnancy, and also alcohol and tobacco, obesity or old age. Furthermore, malignancies and certain medications, such as estrogen or erythropoietin, contribute to this situation.

Moreover, there are thrombotic risk primary situations known as thrombophilia, which are a genetic or hereditary disorder in the coagulation system.<sup>1-3</sup>

Factor XII, also known as Hageman factor, is a plasma protein (serine endopeptidase) forming part of the intrinsic coagulation pathway, activating the XIII factor and prekallikrein. Kallikrein, synthesized with kininogen, boosts factor XII activation, which in turn activates XI.<sup>4</sup>

The gene agent known to cause thrombophilia in this factor is C46T mutation in the gene for factor XII. Its deficiency has been detected in 1.5-3% of the healthy population.<sup>5</sup>

## Case report

A 35-year-old woman, with no relevant history, referred to our unit due to decreased vision in her left eye (OS).

Visual acuity in her right eye (OD) was 1.0, and 0.3 in the OS.

Left eye (OS) ophthalmoscopy examination revealed an area with intraretinal bleeding in the path of the superior temporal arcade, some vascular tortuosity and cottony exudation (Figs. 1 and 2). FA confirmed venous thrombosis in the left branch. OCT revealed mild macular edema measuring 350  $\mu$ m.

Given the unusual presentation of thrombosis in a healthy young patient, we suspected a coagulation disorder or thrombophilia.

The patient was referred to the hematology unit and was diagnosed with coagulation factor XII (Hageman factor) deficiency.



**Fig. 1 – Normal right eye retinography.**



**Fig. 2 – Retinography showing flame-shaped hemorrhage in left eye temporal arcade path and superior macular arcade after venous branch occlusion, along with some vascular tortuosity.**

Patient developed deep vein thrombosis during the examination, compromising one ileofemoral vessel of the right lower limb, diagnosed with echo-Doppler (Color Doppler Ultrasound KR-800, Jiangsu, China).

After starting therapy with low-molecular-weight heparin, at present the patient is stable, asymptomatic and undergoing prophylactic treatment with oral anticoagulants.

From the ophthalmologic point of view, the macular edema was resolved with a single injection of Lucentis® (Ranibizumab Novartis, Basel, Switzerland). Patient did not need photocoagulation; bleeding was fully resolved and no complications associated with retinal ischemia have been observed so far. At one year, visual acuity was 0.8.

## Discussion

Hypercoagulable states produce an increased risk of developing venous thrombosis in different organs. At the ocular level, venous branch or central retinal vein obstructions are diseases related to hypercoagulable states.<sup>1,2,4</sup> They should be studied in specific patients, as they may be related to various hematological disorders.

The role of factor XII is controversial, as its deficiency causes asymptomatic aPTT enlargement, which should increase bleeding; when it decreases, other clotting factors tend to compensate for its absence, possibly leading to thrombotic disorders<sup>5</sup> (Figs. 1 and 2).

Mostly, this deficiency is asymptomatic and is an incidental finding; however, its study must not be overlooked in patients who are seen frequently for thrombotic events. Additionally, a correlation has been reported between factor XII deficiency and repeated miscarriages in young women, and on this factor being involved in the placenta's microvascular system; thus, its deficiency causes uteroplacental circulation disorders.<sup>6</sup>

Although factor V Leiden had been commonly accepted as the thrombophilic defect responsible for most retinal

occlusion cases in patients under 45 years old, a recent study showed that up to 18% of these patients were factor XII<sup>6</sup> deficient.

The few cases reported in the literature show characteristics similar to ours, i.e., early age of onset and the frequent development of thrombotic events associated with it. Therefore, all cases were treated with oral anticoagulants; however, so far no standardized criteria exist regarding its onset and duration, or whether it is necessary to perform antithrombotic prophylaxis before surgery or obstetrical procedures in these patients.<sup>6,7</sup> Likewise, no therapies have been reported to correct this factor's deficiency.

Close monitoring of retinal involvement is needed because normal progression may result in ischemia and secondary neovascularization causing severe visual deficiencies.

The above stresses the importance of differential diagnosis and a complete blood count, including screening for factor XII deficiency in young patients with retinal vascular disorders not showing apparent risk factors.

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### Conflicts of interest

The authors declare that they have no conflicts of interest.

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