An uncommon case of postpartum venous thrombosis in a patient with hereditary angioedema. Patient from the ITACA Cohort (Italian Network for Hereditary and Acquired Angioedema)

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ABSTRACT

Hereditary angioedema (HAE) is a rare genetic condition characterized by episodes of cutaneous or submucosal edema, most commonly affecting the skin, the abdomen, and the upper respiratory tract. The most common cause of HAE is either a deficiency (type 1) or dysfunction (type 2) of the C1-inhibitor, leading to the overproduction of bradykinin and activation of bradykinin B2 receptors. This increases vascular permeability and results in angioedema attacks. Anatomic, physiological, and hormonal changes during pregnancy can have an impact on the manifestations of the disease and therefore its treatment. Here, we describe the case of a 30-year-old woman who experienced a significant worsening in both the number and severity of angioedema attacks during pregnancy. The cesarean section was complicated by thrombosis of the ovarian vein and inferior vena cava.

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Introduction

Hereditary angioedema (HAE) is a rare genetic disease that manifests with episodes of cutaneous or submucosal edema, most commonly affecting the skin, the abdomen, and the upper respiratory tract. The most common cause of HAE involves either a deficiency (type 1) or dysfunction (type 2) of C1-inhibitor (C1-INH), which leads to the overproduction of bradykinin and activation of bradykinin B2 receptors. This increases vascular permeability and results in angioedema attacks.[1] Anatomic, physiological, and hormonal changes during pregnancy can influence the manifestations of the disease and therefore its treatment.[2-4]

Case Report

We describe the case of a 30-year-old woman with HAE type 1, who, since the age of 12, had about 1-2 attacks per month, treated on demand with Icatibant and Berinert with good disease control.

During pregnancy, the number and severity of angioedema attacks worsened, with about 10 attacks per month, one of which, due to glottis edema, required access to the emergency department.

For this reason, we decided to start long-term prophylaxis with Cinryze 1000 I.U. intravenously every 4 days. After 2 months of reported well-being and disease control, she began experiencing angioedema attacks again, mainly in the evening/night before the next administration.

For this reason, we decided to reduce the administration interval from 4 to 3 days (Cinryze 1000 I.U. intravenous every 3 days) until delivery. The obstetrician and anesthesiologist scheduled a cesarean section with spinal anesthesia, and a few hours before delivery, Cinzyre 1000 I.U. intravenous was administered.

The day after delivery, during hospitalization in the gyne-

cology ward, the patient presented significant pain in the right flank. An abdominal ultrasound was immediately performed, showing the presence of a floating thrombus in the inferior vena cava (Figure 1). Subsequently, an abdominal computed tomography scan with and without contrast confirmed the thrombosis of the inferior vena cava and identified a thrombosis of the right ovarian vein (Figures 2 and 3). Following this finding, therapy with Fondaparinux 7.5 mg subcutaneous injection per day was initiated. During pregnancy, the patient underwent thrombophilia tests with negative results.

The patient decided not to breastfeed, so she took a prolactin inhibitor to prevent physiological lactation, and after a few days, she was discharged home.

Considering the cessation of triggers such as pregnancy and breastfeeding, and after the diagnosis of thrombosis, we decided to suspend long-term prophylaxis with Cinryze and manage the attacks with on-demand therapy.

The patient was treated with anticoagulants for 6 months until resolution of the thrombosis. She also began to experience about 1-2 angioedema attacks per month, easily manageable with on-demand therapy with Berinert or Icatibant.

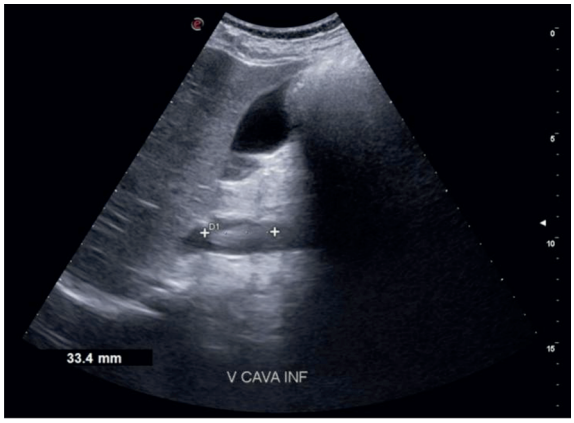

Figure 1. Floating thrombus in inferior cava vein.

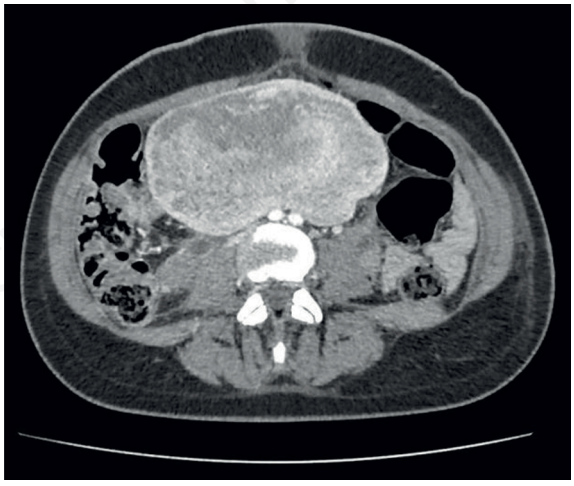

Figure 2. Right ovarian vein thrombosis.

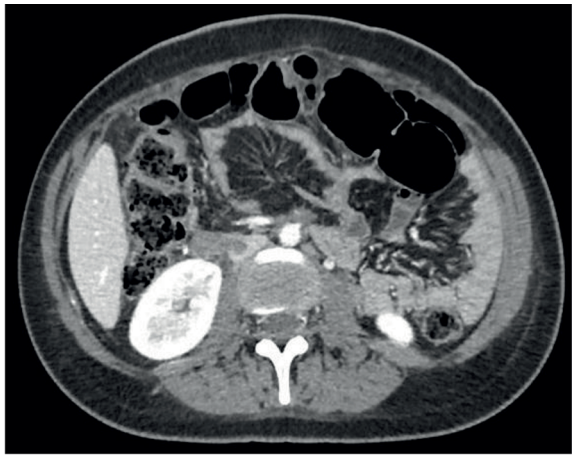

Figure 3. Inferior cava vein thrombosis.

Discussion

HAE is a rare genetic disease characterized by episodes of skin and submucosal edema, predominantly affecting the skin, abdomen, and upper airways. Common causes of HAE include both deficiency (type 1) and dysfunction (type 2) of C1-INH, resulting in the release of bradykinin and binding to B2 receptors. These result in vasodilation and increased capillary permeability, causing angioedema attacks.[1]

Pregnancy in women affected by HAE can modify the course of the disease unpredictably. It can influence the manifestations and, therefore, its treatment. The frequency of attacks before pregnancy partially predicts how the disease will progress during pregnancy.[2-4]

These patients require close attention and monitoring by an experienced angioedema specialist. Pregnancy and labor can rarely induce an attack, and close follow-up is recommended for at least 72 hours after delivery. Breastfeeding may also increase the number of attacks.

Long-term prophylaxis during pregnancy is indicated for patients with an increased number of attacks. In these women, C1-INH is considered safe and effective, while other therapeutic options are not currently recommended.[1,5]

Postpartum thrombosis of the ovarian vein is a rare complication, with an incidence of 1 in every 600-1200 births. The reported percentage is approximately 0.01-0.18% for vaginal delivery and 2% for cesarean section. The main complication is pulmonary embolism (25%), which in 5% of cases can be fatal. If ovarian vein thrombosis is not promptly diagnosed, it can extend to the ileofemoral vein and the inferior vena cava and cause pulmonary embolism.

Ovarian vein thrombosis may resolve spontaneously, but given the catastrophic complications, anticoagulation therapy is always recommended.[6]

Our patient also received high doses of C1-INH to prevent angioedema attacks, which have been associated with cases of thrombosis, but related to the vascular access left in place (port-a-catch).[7] In our case, ovarian vein thrombosis seemed to be more related to pregnancy and especially to cesarean section.[6]

Conclusions

Pregnancy in women affected by HAE can modify the course of the disease in an unpredictable manner. Thrombosis episodes can complicate the postpartum period, requiring close monitoring to detect them early and initiate anticoagulant treatment promptly. C1-INH is currently considered the safest and most effective treatment.

To our knowledge, this is the first description of an ovarian vein and vena cava thrombosis postpartum in a patient with HAE in long-term prophylaxis with C1-INH.

References

1. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema - the 2021 revision and update. Allergy 2022;77:1961-90.
2. Triggianese P, Senter R, Petraroli A, et al. Pregnancy in women with hereditary angioedema due to C1-inhibitor deficiency: results from the ITACA cohort study on outcome of mothers and children with in utero exposure to plasma-derived C1-inhibitor. Front Med 2022;9:930403.
3. Czaller I, Visy B, Csuka D, et al. The natural history of hereditary angioedema and the impact of treatment with human C1-inhibitor concentrate during pregnancy: a long-term survey. Eur J Obstet Gynecol Reprod Biol 2010;152:44-9.
4. Caballero T., H. Farkas, L. Bouillet, et al. International consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency. J Allergy Clin Immunol 2012;129:308-20.
5. Longhurst H, Cicardi M, Craig T, et al. Prevention of hereditary angioedema attacks with a subcutaneous C1 inhibitor. N Engl J Med 2017;376:1131-40.
6. Riva N, Calleja-Agius J. Ovarian vein thrombosis: a narrative review. Hamostaseologie 2021;41:257-66.
7. Yoo SM, Khan DA. Implantable venous access device associated complications in patients with hereditary angioedema. J Allergy Clin Immunol Pract 2013;1:524-5.