*South Health and Policy.* 2025; 4:352
doi: 10.56294/shp2025352

CASE REPORT

# Two patients diagnosed with hereditary angioedema in Pinar del Río

## Dos pacientes con diagnóstico de angioedema hereditario en Pinar del Río

Mayelín García García[1], Lidia Morejón Gamboa[2], Luis Alexis Peláez Yáñez[1], Odalys Orraca Castillo[3]

[1]Hospital Pediátrico Provincial Docente Pepe Portilla, Pinar del Río, Cuba.
[2]Instituto de Ciencias Básicas y preclínicas Victoria de Girón, La Habana, Cuba.
[3]Clínica Central Cira García, La Habana, Cuba.

**Cite as:** García García M, Morejón Gamboa L, Peláez Yáñez LA, Orraca Castillo O. Two patients diagnosed with hereditary angioedema in Pinar del Río. South Health and Policy. 2025; 4:352. https://doi.org/10.56294/shp2025352

**Submitted:** 05-02-2025 **Revised:** 16-05-2025 **Accepted:** 27-07-2025 **Published:** 28-07-2025

**Editor:** Dr. Telmo Raúl Aveiro-Róbalo

**Corresponding author:** Odalys Orraca Castillo

## ABSTRACT

**Introduction:** hereditary angioedema (HAE) is a rare autosomal dominant disease that can be fatal if not treated promptly. It is caused by a deficiency in the synthesis of the inhibitory complement C1.
**Objective:** to describe The clinical presentation, diagnosis, and treatment of two patients with hereditary angioedema in Pinar del Río.
**Method:** two patients are reported with a definitive diagnosis of hereditary angioedema treated at the Pepe Portilla Pediatric Hospital from November 2011 to January 2023. The following are included: Classification, family tree, personal and family history, description, laboratory diagnosis, evolution, and treatment of the disease.
**Results:** the patients presented recurrent episodes of edema in various regions of the body, both spontaneously and due to trauma, affecting the gastrointestinal mucosa with vomiting and diarrhea. Laboratory tests showed a severe decrease in C4 levels. Both received preventive treatment with danazol. Berinert was used in severe attacks in the patient with hereditary angioedema type I. One case showed an absence of family history, suggesting a new mutation; while the other had a family history, demonstrating an autosomal dominant pattern and milder symptoms.
**Conclusions:** there is a delay in the diagnosis of this disease due to its rarity. The family tree contributes to early diagnosis. Although the clinical picture was similar in both cases, the greater severity and complications were related to the quantitative deficiency of C1 inhibitor.

**Keywords:** Hereditary Angioedema; C1 Inhibitor Protein; Genetics; Pathophysiology.

## RESUMEN

**Introducción:** el angioedema hereditario (AEH) es una enfermedad rara con herencia autosómica dominante que puede llegar a ser mortal si no es tratada a tiempo. Es provocado por una deficiencia en la síntesis del complemento C1 inhibidor.
**Objetivo:** describir la presentación clínica, diagnóstico y tratamiento de dos pacientes con angioedema hereditario en Pinar del Río.
**Método:** se reportan dos pacientes con diagnóstico definitivo de angioedema hereditario atendidos en el Hospital Pediátrico Pepe Portilla durante el período de noviembre de 2011 hasta enero de 2023. Se incluye clasificación, árbol genealógico, antecedentes personales, familiares, descripción, diagnóstico de laboratorio, evolución y tratamiento de la enfermedad.
**Resultados:** los pacientes presentaron episodios recurrentes de edemas en varias regiones del organismo

© 2025; Los autores. Este es un artículo en acceso abierto, distribuido bajo los términos de una licencia Creative Commons (https://creativecommons.org/licenses/by/4.0) que permite el uso, distribución y reproducción en cualquier medio siempre que la obra original sea correctamente citada

de forma espontánea y por traumas, que afectaron mucosa gastrointestinal con vómitos y diarreas. Los exámenes de laboratorio mostraron disminución severa de los niveles de C4. Ambos recibieron tratamiento con danazol de forma preventiva. El berinert fue usado en crisis severas en el paciente con angioedema hereditario tipo I. Se evidenció ausencia de antecedentes familiares en uno de los casos, que sugiere una nueva mutación; mientras en el otro sí estuvieron presente estos antecedentes, evidenciando el patrón autosómico dominante, así como sintomatología más leve.
**Conclusiones:** existe retraso en el diagnóstico de esta enfermedad por su rareza. El árbol genealógico contribuye al diagnóstico precoz. Aunque el cuadro clínico fue similar en ambos casos, la mayor severidad y complicaciones se relacionó con la deficiencia cuantitativa de C1 inhibidor.

**Palabras clave:** Angioedema Hereditario; Proteína Inhibidora de C1; Genética; Fisiopatología.

## INTRODUCTION

HAE is a rare disease with autosomal dominant inheritance that can be fatal if not treated in time.[1,2,3,4] It is clinically characterized by recurrent episodes of inflammation affecting the subcutaneous tissues, the gastrointestinal tract, and the oropharyngeal area.[5,6] Genetic mutations are the most common genetic cause of HAE and are observed in more than 90 % of patients. To date, more than 700 mutation variants have been described.[2,3,4]

Three types are recognized: HAE types I and II, which involve mutations in the *C1NH* (*SERPING1*) gene,[7] which encodes the C1 inhibitor protein, while in HAE type III, several mutations have been described, the best known of which involves mutations in the *F12 gene*, which encodes coagulation factor XII (Hageman factor).

The three types of HAE share a common final pathway that leads to increased bradykinin formation.[6,8,9] It is estimated that one in every 10 000 to 50 000 individuals is affected, although the number of unknown cases is probably much higher. In Europe, it is estimated that there were around 75 000 people affected in 2009, of whom only 45 % were correctly diagnosed.

When episodes are not diagnosed, they lead to suspected diagnoses such as acute abdomen, and patients undergo unnecessary surgical procedures. Upper airway edema, which frequently affects the pharynx, uvula, and larynx, is less common but is the most dramatic event for these patients.

It was initially called Quincke's edema, after Heinrich I. Quincke, who published the first detailed description in 1882, after observing the condition in two generations of the same family. Three years later, Strubing first used the term angioedema to refer to this disorder, and by 1888, Osler demonstrated its hereditary nature.[11]

It has also traditionally been called angioneurotic edema, because one of the manifestations of the disease, unexplained abdominal pain, led to the assumption that it was caused by a nervous disorder.[11,12]

More than 125 years after Osler recognized the hereditary nature of HAE, the heterogeneity of its clinical manifestations, the genetics of this disorder, and the genotype-phenotype relationships still represent a challenge for the attending physician.[9]

With the aim of reviewing the clinical presentation, diagnosis, and treatment of two patients with hereditary angioedema in Pinar del Río, we intend to provide essential tools that contribute to improving clinical diagnosis and knowledge of the disease, and allow for improved prognosis and evolution of these patients, as well as a reduction in the risk of death, in an approach to personalized medicine and evidence-based medicine.

## CASE REPORT

*Patient 1*

A 31-year-old male patient with a history of recurrent edema beginning at the age of 4, presenting with abdominal colic attacks accompanied by vomiting lasting approximately 4 days, as well as edema in the upper and lower limbs treated with steroids and antihistamines with clinical improvement after 72 hours. He had two episodes of glottis edema. He was treated by several specialists, including gastroenterologists and allergists, and almost underwent surgery due to signs of acute abdomen.

There was no family history of angioedema symptoms.

Diagnostic tests showed decreased plasma C4 levels (0,063 g/L) and low C1-INH antigen, confirming the diagnosis of type 1 HAE.

He was treated with danazol and tranexamic acid.

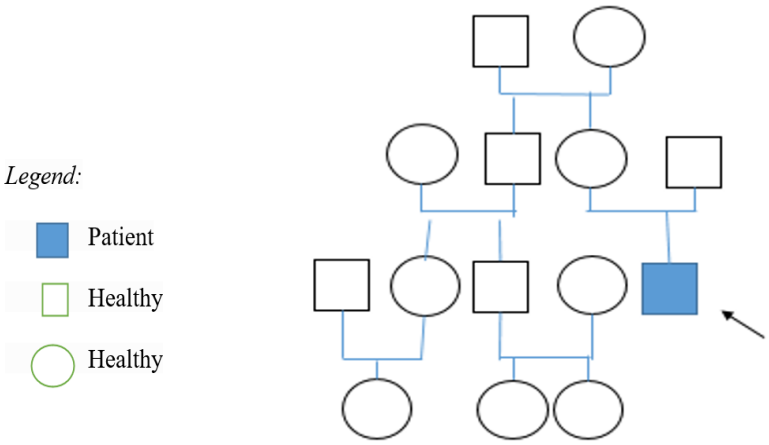


**Figure 1.** Family tree. Patient 1

*Patient 2*

28-year-old male patient with a history of recurrent edema on the soles of the feet and toes, beginning in childhood, accompanied by episodes of pain. At age 18, he began to develop edema in his knees, testicles, upper and lower limbs, for which he was treated by several specialists, including gastroenterology, orthopedics, rheumatology, and urology, without obtaining a definitive diagnosis.

He has a family history of angioedema symptoms.

Diagnostic tests showed decreased plasma C4 levels, confirming the diagnosis of HAE.

He received treatment with danazol.

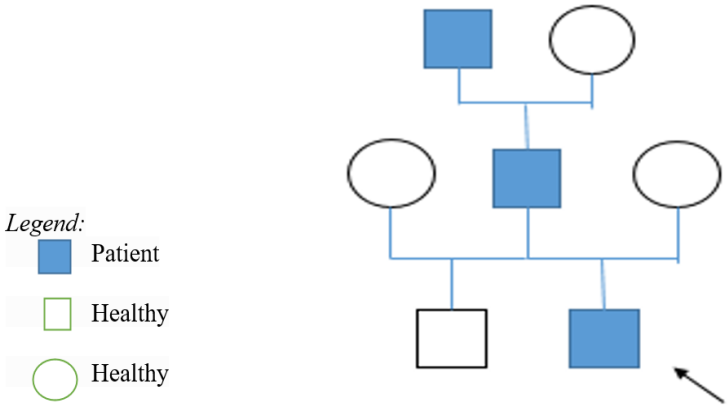


**Figure 2.** Family tree. Patient 2

## DISCUSSION

Hereditary angioedema is commonly subclassified into three types, all of which are virtually indistinguishable clinically and largely driven by bradykinin.[13]

Type I HAE presents with a C1-INH deficiency and accounts for 85 % of cases, type II presents with a dysfunctional C1-INH and accounts for 15 %, and type III is generally estrogen-dependent or hereditary angioedema with normal C1-INH activity and accounts for a very small percentage of cases. The three types of HAE behave similarly and present with similar symptoms.[14]

HAE is largely mediated by the proinflammatory mediator bradykinin and results from a deficiency in the acute phase reactive C1 inhibitor protein produced in the liver.[13] The C1 inhibitor protein minimizes the activation of C1r, C1s, MASP 1, and MASP 2, thereby inhibiting the complement system. Low or non-functional levels of C1 inhibitor protein allow unrestricted complement activity, facilitating vascular permeability and edema.[3,13,16]

In addition, C1 inhibitor protein inhibits plasma kallikrein, the enzyme involved in the conversion of high molecular weight kininogen (HMWK) to bradykinin. Low levels of C1 inhibitor allow plasma kallikrein levels to rise, subsequently increasing bradykinin levels.[15] Plasma kallikrein increases the active form of factor XII, factor XIIa, which feeds back positively to facilitate the conversion of prekallikrein to kallikrein, facilitating the production of bradykinin, which is responsible for many of the symptoms in patients with HAE, as it acts on

endothelial contraction, nociceptor activation, and bronchoconstriction, explaining the edema, pain, and dry cough typical of HAE presentation.[3,13,16]

The third type of angioedema is an extremely rare subclass that was only described at the beginning of the second millennium. Although the pathophysiological mechanism has not been fully elucidated, it is strongly associated with increases in estrogen levels and, consequently, is called estrogen-dependent HAE. It occurs more frequently in women and has been shown to initiate the onset and/or exacerbate symptoms in pregnant patients or users of hormonal contraceptives.[1]

The clinical manifestations of HAE include sudden onset of swelling around the eyes, face, and extremities; abdominal pain (as a result of intestinal edema); and laryngeal edema causing hoarseness, difficulty breathing, and occasionally death.[16,17]

In addition to clinical symptoms, the age of onset of symptoms is also taken into account when diagnosing the disease. Most patients with HAE present symptomatic cases before the age of 20. However, it is rare for the disease to present in young children, as they are often asymptomatic.[18]

In 50 % of cases, clinical manifestations generally begin before the age of 10, with symptoms increasing during puberty and then again in the third decade of life. In 20-25 % of patients with HAE, there is no family history.[6]

In most cases, episodes of acute angioedema last between 2 and 5 days and resolve spontaneously without medical intervention.[18]

Cutaneous edema is characterized by recurrent inflammation without urticaria, i.e., it does not cause hives, is not itchy or painful, and does not cause a rise in temperature.[19]

An increase in the incidence of autoimmune diseases (12 %) has been reported in patients with HAE, the most common being arthritis, glomerulonephritis, and inflammatory bone diseases.[6,20]

Some attacks may have a previous trigger, but often many attacks have no trigger.[9]

While triggers vary for each patient, the most common may include trauma, medical procedures, stress, oral contraceptives (estrogens), infectious processes, and ACE inhibitors. In addition, patients have different levels of disease response to the same triggers.[21]

Several disorders can manifest with subcutaneous or submucosal swelling. The presence of severe swelling can be confused with an allergic reaction or an acute abdominal condition. Misdiagnosis can lead to ineffective therapies and unnecessary surgery.[22,23]

Since the symptoms of acute episodes are similar to those of more common diseases, such as allergic angioedema or, in the case of abdominal attacks, appendicitis, an important clue is the lack of response of edema to antihistamines or cortisone preparations, which allows for a differential diagnosis from allergic reactions. The diagnosis is most difficult in patients who experience episodes exclusively in the digestive tract.[20]

It would also be important to differentiate the diagnosis from other causes of acquired angioedema, such as immune complex diseases.[6]

To diagnose HAE, a thorough interview and physical examination must be performed. The necessary complementary tests will be carried out for a definitive diagnosis, including quantification of C1-INH, C2, and C4, as well as determination of the functional activity of C1-INH proteins in cases excluded from the diagnosis of type I HAE. To diagnose type II, if the possibility of acquired angioedema (AEA) is reconsidered, it is necessary to quantify C1q, as this is only altered in these cases.[20]

Treatment must be defined according to the patient's clinical condition. In the chronic phase of the disease, i.e., between attacks, it is necessary to know whether or not the patient is using prophylactic medication to prevent attacks.[6]

In the prophylaxis phase, the basic treatment is mainly the use of attenuated androgens such as Danazol or Stazonolol and antifibrinolytics such as tranexamic acid and epsilon aminocaproic acid, all taken orally. In the case of acute attacks, it is necessary to individualize and personalize each case, as well as to define the use of one or another medication according to the intensity and location of the angioedema; in severe cases, the use of plasma C1 inhibitor, marketed under the name Berinert-500, is required. Subcutaneous epinephrine in divided doses may be used, but its effect is limited.[24]

The age of onset for both patients was in childhood with characteristic clinical manifestations; however, the most severe case was patient 1, who developed laryngeal edema on two occasions.

The course of the disease tends to be more severe in patients with early onset of symptoms.[16] The literature suggests that in a subset of HAE, which is more dependent on the patient's clinical presentation, there are identifiable clinical symptoms, normal laboratory values (including C1-INH), a positive family history, and a known failure of treatment with chronic high-dose antihistamines; clinical findings are more predictive and diagnostic for the disease, and the combination of these different factors may help establish a diagnosis of HAE with normal C1-INH levels.[25] However, despite the typology of the disease, the clinical manifestations are practically identical in all of its variants, and no correlation has been found between the different genetic and clinical forms of the disease, as it is characterized by great allelic heterogeneity, demonstrating that each

carrier family has its own genetic defect, as well as poor genotype-phenotype correlation,[26] There are more than 500 different alterations of SERPING 1, distributed throughout all the exons of the gene.[18]

The diagnosis was based on the determination of C4 and C1 INH antigenic and functional levels.

- C4 (Patient 1 (0,063 g/L), Patient 2 (0,053 g/L))
- C1-INH was low in patient 1 and not tested in patient 2.

C4 levels correlate with quantitative and qualitative values of C1-INH, so they are a good diagnostic test for HAE on their own, but not for the type of angioedema where it is essential to determine antigenic and functional C1-INH levels. Therefore, patient 1 was diagnosed with type 1 hereditary angioedema, and it was not possible to classify the type of angioedema in patient 2.[20,21,27]

The diagnosis is commonly confused with allergies, appendicitis, stress disorders, reactions to insect bites, gastroenteritis, and gastric ulcers. In certain cases, the presentation of the disease with exclusive abdominal involvement, together with limited knowledge of the disease, means that this deficiency is underdiagnosed, with an average delay in diagnosis of 13 years.[12,28] In both patients, there was a delay in diagnosis of approximately 20 years, and the long time between the onset of symptoms and diagnosis, as well as access to therapy, increases the morbidity related to the disease, affecting the quality of life of patients and their families. Patients who are not treated properly have an estimated mortality rate of 25 % to 40 % due to laryngeal angioedema, resulting in asphyxia.[10]

This disease has a major impact on patients' quality of life, both due to the recurrence of symptoms and the risk to life. The importance of a correct diagnosis can never be underestimated and is essential to avoid potentially fatal consequences such as airway obstruction or unnecessary abdominal surgery.[29]

A family tree is a chart that represents the inheritance of a trait or condition through generations of a family. It shows the relationships between family members and, when the information is available, indicates which individuals have a trait of interest. Although it has traditionally been used to recognize the pattern of inheritance of hereditary diseases with a specific genetic trait, its clinical use goes beyond this. Following the sequencing of the human genome, it has gained greater interest, partly because of the possibility of identifying the hereditary component of many diseases and, on the other hand, because of the proliferation of preventive clinical practice guidelines where the evaluation of heritable factors and personalization are of interest, contributing to the diagnosis and prevention of risks in family members,[30] This was evidenced in patient 2, where C1-INH antigen and function testing was not performed, but the information provided by this tool, together with clinical manifestations and laboratory results, allowed the diagnosis of the disease.

The treatment of hereditary angioedema consists of several pillars: treatment of acute attacks or on demand, short-term prophylaxis, and long-term prophylaxis.[23]

The first group includes human C1-INH plasma concentrate (pdC1-INH) or Berinert, recombinant human C1-INH concentrate (rhC1-INH, Ruconest®), fresh frozen plasma, and plasma with solvent or detergent. The second group includes therapies such as icatibant (Firazyr®) and ecalantide (Kalbitor®). Long-term prophylaxis includes intravenous phC1INH, subcutaneous phC1INH, lanadelumab (Takhzyro®) or berotralstat (Orladeyo®), attenuated androgens, or antifibrinolytics such as tranexamic acid (Anchafibrin®).[15]

Both patients were treated with danazol (attenuated androgen). Berinert was used in severe crises in the patient with type I hereditary angioedema, and tranexamic acid was used for prophylaxis, with good subsequent evolution in both cases.

**Table 1.** Clinical and laboratory characteristics and treatment of two patients diagnosed with HAE in Pinar del Río

| HAE | Patient 1 | Patient 2 |
|---|---|---|
| Classification | HAE type I | AEH |
| Age at onset of symptoms | 4 | Childhood |
| Family history | No | Yes |
| Gastrointestinal edema | Abdominal colic | no |
| Subcutaneous edema on the face, eyes, and extremities | yes | Yes |
| Laryngeal edema | Yes (two episodes of glottis edema) | no |
| Presence of prodromal symptoms | no | No |
| Laboratory diagnosis | C4 (0,063 g/L) (decreased)<br>Low C1-INH antigen. | C4 decreased |
| Treatment | Danazol, tranexamic acid, berinet | Danazol |

Treating patients with different phenotypes in a personalized, evidence-based manner is an art.

Evidence-based medicine and personalized medicine are crucial in the study of hereditary angioedema. Evidence-based medicine ensures that clinical decisions are based on the results of rigorous research, allowing for the evaluation of the efficacy and safety of existing and emerging treatments for HAE, which is characterized by its clinical variability.

At the same time, personalized medicine is essential for understanding the genetic and phenotypic heterogeneity of HAE, adapting management to the particularities of each patient, optimizing crisis prevention and therapeutic choice, considering factors such as age, gender, medical history, and individual response to medications, thus maximizing effectiveness and minimizing risks.

## CONCLUSIONS

There is a delay in the diagnosis of this disease due to its rarity.

The family tree contributes to early diagnosis in cases with a family history of angioedema.

Although the clinical picture was similar in both cases, the greater severity and complications are related to the quantitative deficiency of C1 inhibitor (type I) in one of the patients. However, the lack of correlation between the different genetic and clinical forms of the disease and the high allelic heterogeneity do not allow patient 2 to be classified as having any of the specific types of the disease.

HAE is a potentially fatal disease, so it is very important to be aware of it for early diagnosis to ensure improved quality of life for patients and the prevention of complications, based on personalized, evidence-based medicine.

## BIBLIOGRAPHIC REFERENCES

1. López AL, Crespo CJO, Romero DSF. Hereditary angioedema: diagnosis in an asymptomatic elderly woman. Medicina (B Aires). 2021;81(4):645-8.

2. Sharma J, Jindal AK, Banday AZ, et al. Pathophysiology of hereditary angioedema (HAE) beyond the SERPING1 gene. Allergy Immunol. 2021;60:305-15.

3. Busse P, Kaplan A. Specific targeting of plasma kallikrein for treatment of hereditary angioedema: a revolutionary decade. J Allergy Clin Immunol Pract. 2022;10(3):716-22. https://doi.org/10.1016/j.jaip.2021.11.011

4. J DT, López-Trascasa M. Angioedema hereditario: un trastorno poco frecuente pero potencialmente mortal. Med Gen Fam. 2012;1(7):321-32.

5. Vives R, Vicente J, Guerola S. Un paciente con angioedema hereditario. Rev Clin Med Fam. 2015;8(1):62-5.

6. Ustariz García CR. Angioedema hereditario. Rev Cuba Hematol Inmunol Hemoter. 2016;32(2):176-89.

7. Drouet C, López-Lera A, Ghannam A, et al. SERPING1 variants and C1-INH biological function: a close relationship with C1-INH-HAE. Front Allergy. 2022;3:1-17. https://doi.org/10.3389/falgy.2022.835503

8. Giavina-Bianchi P, Arruda LK, Aun MV, et al. Brazilian guidelines for hereditary angioedema management - 2017 update part 1: definition, classification and diagnosis. Clinics (Sao Paulo). 2017;72(7):391-5. https://doi.org/10.6061/clinics/2017(07)01

9. Santacroce R, D'Andrea G, Maffione AB, Margaglione M, Apolito M. The genetics of hereditary angioedema: a review. J Clin Med. 2023;12(1):1-9. https://doi.org/10.3390/jcm12010001

10. Titericz T. Abordagem das características clínicas e laboratoriais de pacientes com angioedema hereditário atendidos em um centro de referência no sul do Brasil [dissertation]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2021.

11. Francisca A, Peralta M, Vigueira EB, Pulido JC. Angioedema type I: a case report. Medwave. 2016;16(1):e6368. https://doi.org/10.5867/medwave.2016.01.6368

12. Sil A, Jindal AK. Hereditary angioedema. Indian J Pract Pediatr. 2021;23(2):183-90.

13. López-Lera A. Pathophysiology and underlying mechanisms in hereditary angioedema. Balkan Med J. 2021;38(2):82-8. https://doi.org/10.5152/balkanmedj.2021.21030

14. Nzeako UC, Frigas E, Tremaine WJ. Hereditary angioedema. Arch Intern Med. 2001;161(20):2417-29. https://doi.org/10.1001/archinte.161.20.2417

15. Nicola S, Rolla G, Brussino L. Breakthroughs in hereditary angioedema management: a systematic review of approved drugs and those under research. Drugs Context. 2019;8:212580. https://doi.org/10.7573/dic.212580

16. Contreras MB. Actuación en el angioedema hereditario: tratamiento del ataque agudo y prevención de las crisis: una revisión sistemática [dissertation]. Madrid: Universidad Complutense de Madrid; 2022.

17. Bork K, Meng G, Staubach P, Hardt J. Hereditary angioedema: new findings concerning symptoms, affected organs, and course. Am J Med. 2006;119(3):267-74. https://doi.org/10.1016/j.amjmed.2005.09.064

18. Giavina-Bianchi P, França AT, Grumach AS. Diretrizes do diagnóstico e tratamento do angioedema hereditário. Rev Bras Alerg Imunopatol. 2011;33(6):241-52.

19. Manning ME. Hereditary angioedema: differential diagnosis, diagnostic tests, and family screening. Allergy Asthma Proc. 2020;41(Suppl 1):S22-5. https://doi.org/10.2500/aap.2020.41.200063

20. Khan DA. Hereditary angioedema: historical aspects, classification, pathophysiology, clinical presentation, and laboratory diagnosis. Allergy Asthma Proc. 2011;32(1):1-10. https://doi.org/10.2500/aap.2011.32.3412

21. Johnston DT, Smith RC. Hereditary angioedema: special considerations in children. Allergy Asthma Proc. 2020;41(Suppl 1):S43-6. https://doi.org/10.2500/aap.2020.41.200066

22. Andrási N, Veszeli N, Kőhalmi KV, et al. Idiopathic nonhistaminergic acquired angioedema versus hereditary angioedema. J Allergy Clin Immunol Pract. 2018;6(4):1205-8. https://doi.org/10.1016/j.jaip.2017.09.032

23. Ruiz AN, Diz CC, Andrés JLP, Cebollero A. Algoritmo de diagnóstico y tratamiento del angioedema hereditario como herramienta para su manejo. Farm Hosp. 2013;37(6):521-9. https://doi.org/10.7399/FH.2013.37.6.744

24. Cicardi M, Suffritti C, Perego F, Caccia S. Novelties in the diagnosis and treatment of angioedema. J Investig Allergol Clin Immunol. 2016;26(4):212-21. https://doi.org/10.18176/jiaci.0082

25. Sinnathamby ES, Issa PP, Roberts L, et al. Hereditary angioedema: diagnosis, clinical implications, and pathophysiology. Adv Ther. 2023;40(3):814-27. https://doi.org/10.1007/s12325-022-02401-0

26. Banday AZ, Kaur A, Jindal AK, Rawat A, Singh S. An update on the genetics and pathogenesis of hereditary angioedema. Genes Dis. 2020;7(1):75-83. https://doi.org/10.1016/j.gendis.2019.07.002

27. Farkas H, Harmat G, Farkas H, Fu G. Clinical management of hereditary angio-oedema in children. Pediatr Allergy Immunol. 2002;13(3):153-61. https://doi.org/10.1034/j.1399-3038.2002.00029.x

28. López A, Ortune Crespo CJ, Fernández Romero DS. Angioedema hereditario: diagnóstico en una mujer anciana asintomática. Medicina (B Aires). 2021;81(4):645-6.

29. Lumry WR, Settipane RA. Hereditary angioedema: epidemiology and burden of disease. Allergy Asthma Proc. 2020;41(Suppl 1):S8-13. https://doi.org/10.2500/aap.2020.41.200061

30. Yanes Rodríguez M, Cruz Cánovas MC, Gamero de Luna EJ. Genograma y árbol genealógico. Med Fam. 2022;48(3):200-7.

**FUNDING**

The authors did not receive funding for the development of this research.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## AUTHORS' CONTRIBUTIONS

*Conceptualization:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Data curation:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Formal analysis:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Research:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Methodology:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Project management:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Resources:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Software:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Supervision:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Validation:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Presentation:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Original draft:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.

*Writing, correction, and editing:* Mayelín García García, Lidia Morejón Gamboa, Luis Alexis Peláez Yáñez, Odalys Orraca Castillo.