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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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A CASE OF REFRACTORY IRON DEFICIENCY ANEMIA REVEALING HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Abstract.

Background: Hereditary Hemorrhagic Telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is a rare autosomal dominant vascular disorder. It is characterized by abnormal blood vessel formation, leading to arteriovenous malformations (AVMs) and telangiectasias, which can cause chronic or acute bleeding. This report presents the case of a 44-year-old Saudi female with severe recurrent iron deficiency anemia (IDA) of an unknown etiology, highlighting the diagnostic challenges and the importance of a thorough clinical and family history.

Objective: The primary objective of this case study is to present the clinical presentation, diagnostic approach, and definitive diagnosis of HHT in a patient with recurrent, severe IDA secondary to chronic blood loss. The case emphasizes the classic triad of recurrent epistaxis, a strong family history, and the presence of mucocutaneous telangiectasias as key indicators for this diagnosis.

Methods: A systematic diagnostic approach was undertaken to investigate the underlying cause of the patient's chronic anemia. This included consultations with gastroenterology and hematology, upper and lower endoscopies to exclude occult gastrointestinal bleeding, and specific laboratory tests such as platelet function and von Willebrand factor assays to rule out other hereditary bleeding disorders. A fiber optic nasopharyngoscopy was performed to visualize the nasopharyngeal mucosa. The diagnosis was ultimately confirmed by fulfilling the Curaçao diagnostic criteria for HHT, based on a comprehensive evaluation of her clinical and family history.

Conclusion: This case underscores the importance of considering HHT in the differential diagnosis of patients with severe, chronic iron deficiency anemia, particularly when accompanied by recurrent epistaxis and a positive family history. The successful diagnosis was contingent upon a high index of suspicion and a systematic investigation that fulfilled the established clinical criteria.

Key words. Hereditary hemorrhagic telangiectasia, Osler-Weber-Rendu syndrome, Iron deficiency anemia, Epistaxis.

Introduction.

Osler-Weber-Rendu syndrome (OWRS) is a genetic disorder that runs in families. It is characterized by key features: recurring epistaxis, small red spots on the skin, mucocutaneous telangiectasias, and arteriovenous malformations that can be noticed in various organs, most commonly the lungs, liver, gastrointestinal tract, and brain [1-3]. OWRS has several other names, including Babington's disease, Goldstein's hematemesis, Goldstein heredofamilial angiomatosis, Goldstein syndrome, Osler's disease, Osler-Rendu-Weber syndrome, and hereditary hemorrhagic telangiectasia (HHT) [4]. It is a rare disorder with an estimated prevalence of 1 in 5,000 to 1 in 8,000 people. Diagnosis often shows a gender-based difference in timing: it is frequently identified in males during infancy and childhood, whereas in females, diagnosis typically occurs later, in the third or fourth decade of life [1].

In 1864, Henry Gawen Sutton first described the constellation of symptoms, which included epistaxis, telangiectasias, and internal bleeding. This was followed by Benjamin Guy Babington's report in 1865, which documented the familial pattern of epistaxis across five generations. A pivotal description came in 1896 from Henri Jules Louis Marie Rendu, who correctly identified the recurrent epistaxis in a 52-year-old male as being caused by telangiectasias rather than hemophilia. He also highlighted the hereditary nature of the condition by noting similar manifestations in the patient's mother and brother. The syndrome was further characterized by Sir William Osler in 1901, who noted the potential for visceral organ involvement and its hereditary transmission. Subsequently, in 1907, Frederick Parkes Weber added the finding of a distinct red, angiomatous appearance of the nails to the clinical picture [5]. Currently, this inherited disorder is known as hereditary hemorrhagic telangiectasia (HHT) or OWRS.

Hereditary hemorrhagic telangiectasia (HHT) is a genetic vascular disorder that affects approximately 1 in 5,000 to 8,000 people and is passed down through families in an autosomal-dominant pattern [6,7].

The clinical diagnosis of hereditary hemorrhagic telangiectasia is established by the presence of at least three of the four main diagnostic criteria: recurrent epistaxis, cutaneous or mucosal telangiectasias, evidence of visceral involvement, and a family history of the disease [8]

Internal organ involvement is a hallmark of HHT, with arteriovenous malformations being a common finding. These malformations are prevalent in the lungs (affecting approximately 33% of patients), the gastrointestinal (GI) tract (around 44%), and the liver (about 17%). Cerebral involvement is also seen in up to 15% of patients [9,10].

The presence of these AVMs can lead to severe complications. For instance, pulmonary AVMs can bypass the normal capillary

filter in the lungs, allowing bacteria and clots to enter the systemic circulation, potentially causing cerebral abscesses or emboli. Gastrointestinal bleeding, which often begins in a patient's fifties, can be severe enough to necessitate frequent blood transfusions and may, in some cases, be fatal [11].

HHT, or OWR syndrome, is caused by mutations in specific genes that are crucial components of the transforming growth factor beta (TGF-β) signaling pathway. This pathway is vital for the proper formation and maintenance of blood vessels, specifically for distinguishing arteries from veins. Disruptions in this pathway lead to angiogenesis and the development of the characteristic arteriovenous malformations (AVMs) [12]. HHT is categorized into two main subtypes based on the gene mutation: HHT1, which is more common, is linked to mutations in the ENG gene and HHT2 is linked to mutations in the ACVRL-1 gene. Clinically, a key distinction between these subtypes is the prevalence of pulmonary AVMs, which are observed at a higher rate in patients with HHT1. Consequently, the prognosis for patients with HHT2 is generally considered to be better [12,13].

Epistaxis and gastrointestinal bleeding are frequent clinical findings in patients with HHT. The risk of severe, life-threatening bleeding from telangiectasias is known to increase with age Recurrent epistaxis can significantly impact a patient's daily life [14].

Arteriovenous malformations, which can develop in major organs like the liver, lungs, and brain, pose a risk of serious complications [15,16]. These include high-output heart failure, portal hypertension, and liver failure. Pulmonary AVMs can lead to hemoptysis and polycythemia while cerebral AVMs can cause cerebral abscesses and stroke.

The diagnosis of HHT is typically guided by the Curaçao diagnostic criteria [17]. Treatment strategies are customized based on the patient's specific clinical presentation and the location and nature of their vascular abnormalities.

Given the systemic nature of HHT, a multidisciplinary team approach is essential for patient care. This team typically includes specialists such as an otolaryngologist, pulmonologist, interventional radiologist, neurologist, geneticist, cardiologist, gastroenterologist, dermatologist, hepatologist, and hematologist. Thus, treatment for HHT is customized to the patient's specific symptoms and vascular abnormalities. Options range from local interventions for nosebleeds and GI bleeding to more intensive procedures, such as a liver transplant, for severe cases of hepatic AVMs [18]

Case Presentation.

A 44-year-old Saudi female presented to the emergency department with chief complaints of palpitation and dyspnea on exertion (DOE). Her medical history is significant for recurrent anemia, with a prior admission six months ago for the same condition, during which she received blood transfusions and intravenous iron.

The patient has a long-standing history of recurrent epistaxis (nosebleeds), which have been bilateral but more frequent from the left nostril. She has undergone multiple cauterization procedures to control the bleeding. There are no other bleeding symptoms reported, such as menorrhagia, melena, or bleeding from other orifices. She denies any skin bruising or gastrointestinal symptoms. A crucial aspect of her history is a strong family history of similar bleeding issues, with her father having passed away from this condition after a surgical procedure on his nose. Other first-degree relatives, including her sisters and daughter, are also affected.

On examination, the patient was conscious, oriented, and had a GCS of 15/15. She appeared pale and had scattered areas of lividoreticularis on her right arm. A key finding was the presence of reddish spots, described as telangiectasias, on her tongue and within the oral cavity. Vital signs were stable (Figure 1).

Laboratory results show a microcytic hypochromic anemia (MHA) with a current hemoglobin (Hb) of 6.5 g/dL, compared to a previous low of 6.9 g/dL. Her iron studies indicate iron deficiency, with low serum iron and ferritin levels. Other labs showed low vitamin D and B12 levels. Her platelet count and coagulation profile (PT, PTT) were normal.

The initial impression was severe iron deficiency anemia (IDA) due to chronic blood loss, with a high suspicion for an underlying hereditary bleeding disorder. Given the classic triad of recurrent epistaxis, positive family history, and visible telangiectasias, the presumptive diagnosis is Hereditary Hemorrhagic Telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome.

Given the patient's strong family history and the inadequacy of her previous treatment, a systemic investigation was initiated. To rule out other potential causes of bleeding, consultations were requested for gastroenterology and hematology. An upper and lower endoscopy was performed to exclude occult gastrointestinal (GI) bleeding or vascular malformations, despite the absence of GI symptoms. Findings included mild gastritis, hyperemia, duodenitis, and a hiatal hernia; however, no active bleeding sites were identified. Following these findings, the patient was initiated on a course of Proton Pump Inhibitor (PPI) therapy for the treatment of her gastritis and duodenitis.

Furthermore, platelet function tests and von Willebrand factor (VWF) assays were performed to rule out other hereditary bleeding disorders. These tests returned normal results, effectively ruling out common platelet and coagulation defects. A fiber optic nasopharyngoscopy was performed, which revealed multiple telangiectasias on the nasal septum extending into the pharynx. The combined clinical and endoscopic findings fulfilled the Curaçao diagnostic criteria for HHT: Recurrent epistaxis, Positive family history in first-degree relatives and Presence of mucocutaneous telangiectasias on the tongue and in the nasal cavity.

The planned workup includes addressing her vitamin D and B12 deficiencies. Other radiological scanning to rule out A-V malformations and Genetic testing are required to confirm the diagnosis; unfortunately, it is not available in our institution. This case highlights a complex and often undiagnosed genetic disorder as the cause of her chronic anemia.

Discussion.

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is an inherited disorder with an autosomal dominant pattern, leading to the formation of abnormal blood vessels [19]. It is a rare disease, affecting an

estimated 1 to 20 out of every 100,000 people. Due to its rarity, HHT is frequently misdiagnosed or improperly treated before the correct diagnosis is made [20]. The patient presented in this case was also undiagnosed the first time she was admitted. A retrospective study conducted in Italy revealed a significant diagnostic delay of 25.7 years for HHT. This delay was primarily attributed to the heterogeneous clinical presentation of the disease, the absence of reliable biochemical diagnostic tests, and limited public awareness [21].

The clinical presentation of HHT is characterized by recurrent epistaxis, gastrointestinal bleeding, and the development of iron deficiency anemia. Patients also exhibit mucocutaneous telangiectasias, which are commonly found on the lips, oral mucosa, and fingertips. Approximately one-third of HHT patients have been found to have hepatic arteriovenous malformations (AVMs), which is an increasingly significant clinical concern [22].

The location of AVMs often varies with age. Most AVMs that manifest during childhood are found in the hepatic circulation, followed by the pulmonary and cerebral vasculature in descending order [23]. The bleeding diathesis, particularly from the gastrointestinal tract, typically presents in adulthood, most often after the age of 40. It has been reported that for roughly one-third of these patients, the initial symptom is anemia [24]. The same holds true for the present case.

Following a presumptive or confirmed diagnosis of HHT, genetic testing is typically performed to identify mutations in the endoglin and ALK-1 (ACVRL-1) genes. This confirms the diagnosis and helps to guide a patient's screening protocol for internal organ lesions. Screening for internal organ involvement is a critical step in managing HHT. The recommended screening methods for specific arteriovenous malformations (AVMs) include hepatic AVMs (Doppler ultrasound), pulmonary AVMs (transthoracic echocardiography with contrast and agitated saline), gastrointestinal AVMs (endoscopy, and cerebral AVMs) and Brain MRI. In addition to these screenings, all patients with HHT should have their hemoglobin levels monitored annually to assess for chronic blood loss [25].

For patients diagnosed with HHT, treatment options are determined by the severity of the disease's manifestations. Pharmacologic therapies include systemic antifibrinolytics, estrogen receptor modulators, vascular endothelial growth factor (VEGF) inhibitors, and immunomodulators. Localized physical treatments are also available for specific sites, such as sclerotherapy and laser ablation, while more invasive procedures like radiologic-guided embolization and surgical removal of arteriovenous malformations (AVMs) are reserved for more severe cases [17,19,26,27].

Hormone therapy has shown a reduction in the number of blood transfusions required for several HHT patients experiencing gastrointestinal bleeding. However, this treatment is problematic for male patients due to pronounced side effects such as gynecomastia, feminization, as well as edema. Consequently, hormone therapy is generally reserved for postmenopausal women who have undergone a hysterectomy [28].

Epistaxis, or nosebleeds, is typically the first and most common symptom of HHT, occurring in 90% of patients. In this particular case, the patient's telangiectasias were observed on her tongue, and oral and nasal mucosa (Figures 1 and 2) [16].

Based on multiple clinical trials, several systemic and local therapies have shown promise in managing epistaxis severity. Anti-estrogen medications like tamoxifen and antifibrinolytics such as tranexamic acid have been effective in reducing bleeding. Additionally, antiangiogenic agents like bevacizumab, administered either systemically or locally, have been shown to lessen the severity of epistaxis. While immunomodulators like thalidomide can also reduce bleeding episodes, their use is limited by significant side effects [18].

Multiple studies have investigated the use of bevacizumab, with many utilizing a dose ranging from 5–10 mg/kg of body weight [29-31]. A non-comparative study found that a monthly regimen of 5 mg/kg was particularly effective at controlling

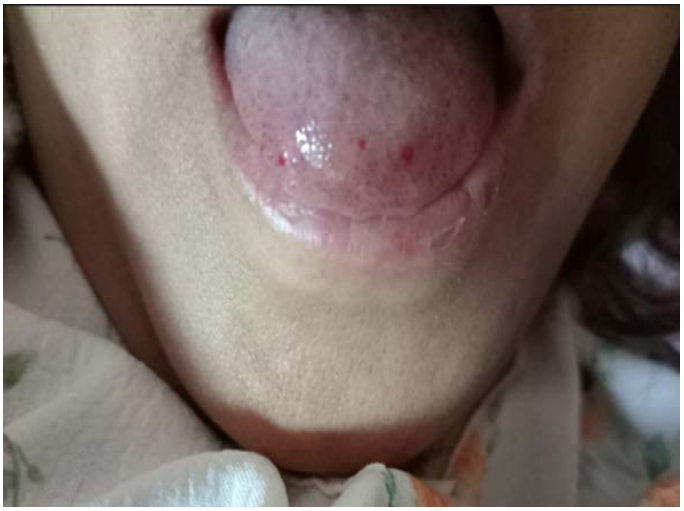

Figure 1. *A photo showing tongue telangiectases, a key clinical sign of HHT.*

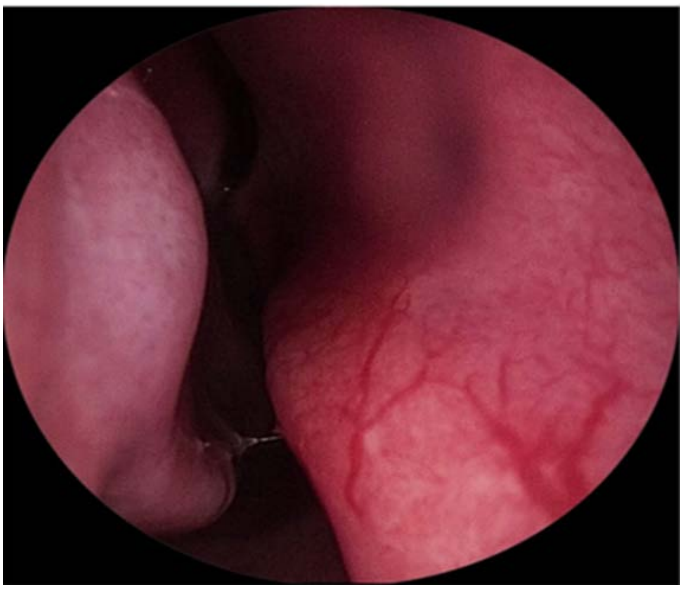

Figure 2. *An endoscopic view of the nasal cavity. The image shows a mucosal surface with visible, delicate, reddish blood vessels that are dilated and tortuous. This appearance is consistent with nasal telangiectasias, which are characteristic findings in HHT.*

epistaxis and improving cardiac function [32]. Conversely, other research has suggested that much lower doses—such as 1 mg/kg every two weeks or 0.125 mg/kg monthly—may also be effective in reducing the frequency and duration of epistaxis [33].

In fact, most HHT treatments are largely palliative, offering temporary relief rather than a cure, and often require repeated interventions. A notable exception is nasal closure, which provides a more definitive solution for severe, recurrent epistaxis [34].

For gastrointestinal bleeding, repeated endoscopic ablations are used for short-term control, though outcomes are generally less effective than in non-HHT patients. Iron-deficiency anemia is managed conservatively with daily iron supplementation. The treatment for pulmonary arteriovenous malformations (AVMs) is typically embolotherapy, which has been shown to reduce mortality and disease severity. If embolotherapy isn't an option, surgical intervention is considered. In cases of end-stage liver disease due to complex hepatic AVMs, a liver transplant is the definitive treatment. For patients with end-stage hepatic failure who are not candidates for transplantation, the drug bevacizumab may be considered as an alternative [18].

While the life expectancy of patients with HHT can be reduced, it is highly dependent on the disease's severity. Patients who do not develop internal arteriovenous malformations (AVMs) in the liver, lungs, or brain often have a normal or near-normal life expectancy. However, approximately 10% of all HHT patients experience severe morbidity or death due to vascular complications [18].

Despite the lack of genetic testing, the diagnosis was soundly established using the Curaçao criteria. Reiterate that these criteria are the widely accepted international standard for diagnosing (HHT), specifically noting the number of criteria met by the patient such as recurrent epistaxis, a strong family history, and the presence of mucocutaneous telangiectasias fulfilled the requirements for a definite HHT diagnosis based on the Curaçao criteria. Furthermore, in resource-limited settings or when genetic testing is not immediately available, the Curaçao criteria remain essential and highly effective for guiding immediate patient management and screening for common HHT organ involvement [35,36].

Beyond the clinical findings assessed by the Curaçao criteria, molecular diagnostics are routinely employed for HHT diagnosis. A pathogenic mutation in either the ENG or ACVRL1 gene is responsible for approximately 90% of all HHT cases. Less frequently, pathogenic variants linked to HHT have been reported in genes including MADH4, GDF2, and RASA-1 [37-39]. Other studies found out that (HHT) is caused by mutations in either the endoglin (ENG) or activin A receptor type-like kinase 1 (ACVRL1, also known as ALK-1) genes [38,39].

Hereditary Hemorrhagic Telangiectasia (HHT) is a genetically diverse disorder resulting from mutations in several genes that are integral to the TGF-β/ BMP signaling pathway. A key component of this pathway is the ligand BMP9, which initiates signaling by binding to a receptor complex on the cell surface. This complex includes the type I receptor ALK1 and a type II receptor (R-II), as well as the auxiliary receptor endoglin. Following ligand binding, the R-II receptor transphosphorylates ALK1, which then propagates the signal intracellularly [40].

Two studies reached the conclusion that Two genes, PTPN14 and ADAM17, have recently been identified as genetic modifiers that influence both angiogenesis and HHT [41,42].

While the ongoing discovery of additional HHT-associated genes is anticipated, these new genes will, by nature, represent only a small fraction of total HHT cases. Crucially, these new genes can be readily integrated into existing NGS diagnostic panels, thereby improving the overall clinical sensitivity and diagnostic yield [43].

In terms of organs, Liver involvement in HHT is typically asymptomatic. However, in the few patients who do develop symptoms, the associated morbidity and mortality can be significant. It is notable that focal nodular hyperplasia occurs much more frequently in patients with hepatic HHT than in the general population. Invasive therapies, such as liver transplantation, are reserved only for patients whose condition has failed to improve with intensive medical therapy [44].

Another study concluded that In HHT patients, increased mortality is associated with chronic gastrointestinal (GI) bleeding, anemia, and symptomatic liver vascular malformations (VMs), a risk that holds true across all ages due to limited effective treatment options for these conditions. In contrast, mortality rates do not appear to be elevated by the presence of pulmonary AVMs or brain VMs, likely because these lesions are routinely and successfully managed through preventative screening and treatment at specialized HHT Centers [45].

Conclusion.

This case highlights the importance of considering rare genetic disorders in patients with chronic, unexplained IDA, particularly when a strong family history of bleeding is present. Although the patient's presentation initially seemed to be a simple case of IDA from nosebleeds, the persistent nature of her anemia and the familial pattern of bleeding pointed toward an underlying hereditary vascular malformation.

The diagnosis of HHT has significant implications for long-term management, as it is a systemic disease. It is characterized by the presence of arteriovenous malformations (AVMs) in various organs, with common sites including the lungs, liver, brain, and gastrointestinal tract. Complications can include high-output heart failure, stroke, and pulmonary hemorrhage.

This case underscores that recurrent IDA secondary to chronic epistaxis, especially in the context of a positive family history, should prompt a thorough investigation for HHT. An accurate and timely diagnosis is crucial for appropriate screening for systemic AVMs and for implementing a comprehensive, multidisciplinary management plan to prevent life-threatening complications.

Moreover, this case report confirms the utility of the Curaçao criteria in establishing a definite HHT diagnosis and guiding timely clinical intervention for symptomatic patients. We candidly acknowledge the limitation that genetic testing was not accessible at this location. Future efforts should prioritize molecular diagnostics, as identifying the specific pathogenic variant offers the highest level of academic rigor and provides an indispensable tool for public health efforts. Genetic subtyping facilitates precise prognostic prediction for

the patient and is vital for implementing cascade screening programs among asymptomatic first-degree relatives, allowing for earlier identification and life-saving prophylactic treatment of silent organ AVMs. The treatment strategy for this patient focused on preventing complications and providing supportive care. Medical management for gastritis was administered, while the patient's epistaxis resolved spontaneously without requiring active treatment.

Conflict of Interest.

The authors declare no conflicts of interest related to this manuscript.

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Ethical approval.

This case report did not necessitate formal ethical approval from the institutional review board, as it constitutes retrospective documentation of standard clinical care devoid of research interventions or experimental procedures. The patient provided written informed consent for the publication of this case report, which includes clinical images. The patient's identity has been kept secret, and the case report was written following ethical rules for medical case reports.

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