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1. RAPD Objectives and characteristics: The Revista Andaluza de Patología Digestiva is the official publication of the Andalusian Society of Digestive Pathology (SAPD), which since 2007 has been published in electronic format only, under the name RAPD Online. Its purpose is to disseminate all epidemiological, clinical, basic and sociological aspects of digestive diseases, through the contributions sent to the journal from Andalusia and from the entire scientific community. The official language for the publication of this journal is Spanish, but some contributions may be accepted in the author's original language in English, French or Italian. RAPD Online is published bimonthly, with one of the issues being specially dedicated to the Annual Meeting of the SAPD and the Editorial Board deciding to reserve one or more issues per year for the monographic development of a topic related to the speciality.

All submitted contributions must be original and not be simultaneously under review for publication in another journal. The publication of abstracts or posters is not considered duplicate publication. Manuscripts will be evaluated by expert reviewers, appointed by the editorial board, before being accepted for publication, in a process that will take less than 30 days.

2. RAPD Contents: *regular numbers of RAPD Online include defined sections such as:*

- *Original articles on clinical or basic research.*
- *Thematic reviews on specific aspects of Gastroenterology.*
- *Consensus documents.*
- *Clinical cases.*
- *Clinical cases with videos or Videoforum.*
- *Images of the month.*
- *News and updates on gastroenterology and hepatology.*
- *Letters to the Editor.*

Other contributions that are considered of interest by the Editorial Board, relating to different aspects of clinical practice in the recent past, biographical comments, or other contents of a cultural nature, or related to scientific activities in any territorial area, will be inserted in RAPD Online in sections designed specifically for this purpose.

3.Submission of manuscripts: *The preferred way to submit manuscripts is through the SAPD website (https://www.sapd. es), by accessing the RAPD Online page and clicking on the "Submit an original" button located on the same access page to the journal. This will take you to the Manuscript Centre, from where you will be able to send manuscripts and all the required documentation. To use this tool you must be previously registered, access requires a username and password. If you are a member of the SAPD, you can use your usual username. If you are not a member, you can request a username for access to the Manuscript Centre using the form on the website. You can write to sulime@ sulime.net or RAPDonline@sapd.es, for the solution of any problem in the submission of manuscripts.*

4. Writing standard for manuscripts: *monographic numbers, thematic reviews, updates and annotated articles will be commissioned by the Editorial Board, but the submission of any of these contributions at the request of an author will be considered by the RAPD Online Management and evaluated with great interest for inclusion in the journal.*

All manuscripts will be subject to specific rules, depending on the type of contribution, and to common ethical and legal standards.

A) Specific standard for manuscripts writing

They refer to the recommended length and structure of each type of manuscript. As a basic unit of length for the text, in any of the contributions, a page of 30-31 lines, spaced 1.5 lines apart, with a font size of 12, with 75-80 characters without spaces per line and a total of 400-450 words per page is considered. Texts should be sent spell-checked and in editable format in all their applications (main text, figures, legends or figure captions, tables, graphs, drawings).

Originals: *originals can be up to 12 pages long (5,100 words), excluding bibliographical references and captions to figures and tables. It is not advisable to insert more than 10 images, including tables and figures. Colour illustrations and videos will not represent an economic charge for the authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. However, the editing method of RAPD Online allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. It is not advisable to have more than 9 authors, except in the case of collaborative works. In these originals, the first nine participants will be listed at the head of the paper and the rest of the participants will be listed at the end of the first page of the manuscript.*

Through the Manuscript Centre, the following information will be required for the submission of an original:

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a) Introduction and objectives
b) Material and methods
c) Results
d) Conclusions

2° List of abbreviations used in the text.

3° Text: it will include the following sections:
a) Introduction
b) Material and methods
c) Results
d) Discussion
e) Conclusions; each of them appropriately headed.

4° Bibliography: according to the specifications established in the group of common standards (See common standards and other supporting documents).

5° Acknowledgements.

6° Figure captions.

7° Tables and figures in text.

Thematic Reviews: *texts on Thematic Reviews can be up to 15 pages long (6,375 words), excluding bibliographical references and captions to figures and tables, and chapters corresponding to Update series up to 20 pages (8,500 words). In both cases the number of inserted images should not exceed 15, including tables and figures. However, the RAPD Online editing method allows, in specific cases, for manuscripts of greater length, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Illustrations in colour will not be charged to the authors. Exceptionally, the inclusion of videos will be accepted. It is not advisable to include more than 4 authors per chapter.*

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- Main body of the manuscript, containing:

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2° Text: Structured according to the criteria of the author(s), for a better understanding of the topic developed.
3° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
4° Acknowledgements.
5° Figure captions
6° Tables and Figures in the text.

Consensus documents: texts on Consensus documents are not limited in length in terms of text or images and tables. Exceptionally, the inclusion of videos is allowed. It is not advisable to have more than 10 authors per chapter.

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2° Surnames and first names of all authors.
3° Centre(s) of origin (department, institution, city and country).
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5° Declaration on the existence or non-existence of a source of funding for the work, or conflicts of interest.

- Main body of the manuscript, containing:

1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 350 words, emphasising the most important aspects of the manuscript.
2° Text: Structured according to the criteria of the author(s), for a better understanding of the topic developed.
3° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
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6° Tables and Figures in the text.

Clinical Cases: *the manuscripts included in this section will include 1-5 clinical cases, which due to their infrequent or unusual clinical behaviour, or because they provide some diagnostic or therapeutic novelty, deserve to be reported.*

The length of the texts in the Clinical Cases section should not exceed 5 pages (2,125 words), excluding bibliographical references and captions to figures and tables, and the number of inserted images should not exceed 5, including tables and figures. However, the RAPD Online editing method allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the

characteristics of the material presented so require. Colour illustrations and videos will not represent a financial charge for authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. No more than 5 authors will be admitted, except in specific and reasoned cases.

Through the Manuscript Centre, and for the submission of Clinical Cases, the following information will be required:

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- Main body of the manuscript, containing:

1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 250 words.
2° Introduction. To present the clinical problem reported.
3° Description of the clinical case.
4° Discussion. To highlight the peculiarities of the case and its consequences.
5° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
6°Acknowledgements.7° Figure captions.
8° Tables and text figures.

Clinical Cases with Videos or Videoforum: *the manuscripts included in this section will include 1-5 clinical cases, which due to their infrequent or unusual clinical behaviour, or because they provide some diagnostic or therapeutic novelty, deserve to be communicated.*
The length of the texts in the Videoforum section should not exceed 5 pages (2,125 words), excluding bibliographical references and captions to figures and tables, and the number of images inserted should not exceed 5, including tables and figures. However, the RAPD Online editing method allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Colour illustrations and videos will not represent a financial charge for authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. No more than 5 authors will be admitted, except in specific and reasoned cases.

Videos should be submitted in AVI, MPEG, MP4 OR MOV format, and at a recommended high quality resolution (720p or 1080p). They must not contain personal data of the patients. It is recommended that they be edited to minimise editing time, which should not exceed 10 minutes. If the video includes sound, it must be processed in MP3 format. If the videos to be included are in other formats, please contact the publisher to verify their validity. They should not exceed 2GB.
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3° Centre(s) of origin (department, institution, city and country).
4° Full postal address of the responsible author, to whom correspondence should be addressed, including telephone, fax and email address.

- Main body of the manuscript, containing:

1° Structured abstract in Spanish and English. 3-5 key words. The abstract will have a maximum length of 250 words.
2° Introduction. To present the clinical problem reported. 3° Description of the clinical case.
4° Discussion. To highlight the peculiarities of the case and its consequences.
5° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
6°Acknowledgements.7° Figure captions.
8° Tables and figures in text.
9° Videos.

Link tutorial videos: https://www.sapd.es/videoteca/varios/ tutoriales/

Images of the month: *the manuscripts included in this section can take two formats, depending on the authors' preference.*

- Format A. Images with educational value: these shall include images of any kind, clinical, radiological, endoscopic, anatomopathological, macro and microscopic, which contribute to postgraduate training and therefore deserve to be shown because of their peculiarity, or because they represent a characteristic example.
- Format B. Key images for a diagnosis: These will include images of any kind, clinical, radiological, endoscopic, anatomopathological, macro and microscopic, together with a summarised clinical history, which will provide the possible final diagnostic resolution. This will be presented in a separate section in the same issue of the journal.

The length of the texts in the Images of the Month section must not exceed 1 page (425 words) in the clinical approach to the image presented and 2 pages (850 words), excluding bibliographical references and captions to figures and tables, in the commentary on the image (Format A) or in the diagnostic resolution of the case (Format B). However, the RAPD Online editing method allows, in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the material presented so require. Colour illustrations and videos will not represent a financial charge for authors, but the insertion of videos, for technical reasons, will be previously agreed with the editor. No more than 3 authors will be accepted, except in specific and reasoned cases.

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2° Description of the image.
3° Comments on the image.
4° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents).
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New developments and updates in gastroenterology and hepatology: this section will be devoted to commenting on the scientific and medical developments that have occurred in recent years in the speciality of Gastroenterology and Hepatology.

This section will systematically and periodically analyse all facets of the speciality.

Texts on " New developments in Gastroenterology" may be up to 5 pages long (2,125 words), excluding bibliographical references and captions to added figures and tables. In both cases the number of inserted images must not exceed 5, including tables and figures. However, the RAPD Online editing method allows,

in specific cases, the acceptance of longer manuscripts, or the inclusion of a greater number of images, provided that the characteristics of the

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1° Name of the bibliographic area reviewed and period analysed 2° Surname and first name of all authors. It is advisable to place a hyphen between the first and second surname.
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- Main body of the manuscript, containing:

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2° Description of the bibliographic material analysed.
3° Critical comments on the results contained in the selected works.
4° Bibliography: According to the specifications established in the group of common standards (See common standards and other supporting documents). If two or more originals have been chosen for the analysis, it is advisable to divide the section into sections at the authors' discretion.
5° Figure captions.
6° Tables and Figures in text.

Letters to the Editor: *this section will be dedicated to comments on any manuscript published in RAPD Online. This section may also include comments of a more general nature, establishing the authors' own hypotheses and suggestions, within the scientific field of Gastroenterology. The length of the texts in this section of Letters to the Editor should not exceed 2 pages (850 words), including bibliographical references. Two figures or tables may be included and the number of authors should not exceed four.*

Through the Manuscript Centre, and for the submission of a Letter to the Editor, the following information will be required:

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3° Centre(s) of origin (department, institution, city and country).
4° Full postal address of the responsible author, to whom correspondence should be addressed, including telephone, fax and e-mail address.
5° Declaration on the existence or non-existence of a source of funding for the work, or conflicts of interest.

- Basic body of the manuscript, containing:

1° Text of the manuscript.
2° Bibliography: According to the specifications set out in the common standards group (See common standards and other supporting documents).

B)Common standards and other supporting documents

This refers to the set of mandatory standards, both for uniformity in the presentation of manuscripts and for compliance with current legal regulations. In general, the style of manuscripts should follow the guidelines set out in the Vancouver Agreement of the International Committee of Medical Journal Editors. (http://www.ICMJE.org).

Units, generic names and abbreviations:

- Units. Biochemical and haematological parameters shall be expressed in International Units (SI), except haemoglobin which shall be expressed in g/dL. Length, height and weight measurements shall be expressed in decimal metric units and temperatures in degrees Celsius. Blood pressure shall be measured in millimetres of mercury.
There is an aid for the conversion of non-international (non-SI) units into international (SI) units. (http://www.techexpo.com/techdata/techcntr.html).

- Generic names. The generic names of medicinal products, clinical instruments and tools and software shall be used. When a brand name is the subject of research, the brand name and the name of the manufacturer, city and country shall be included in parentheses the first time the generic name is mentioned in the Methods section.

- Abbreviations. Abbreviations should be avoided, but if they have to be used, in order not to repeat long technical names, the full word should appear the first time in the text, followed by the abbreviation in brackets, which will already be used in the manuscript.

Bibliographical references: bibliographical references should be presented in the order in which they appear in the manuscript, with a sequential number, which will appear in the appropriate place in the text, in brackets. This numbering will be maintained and will serve to order the list of all references at the end of the manuscript, as normal text and never as a footnote. Personal communications and unpublished data will not be included in the final list of bibliographical references, although they will be mentioned in the appropriate place in the text, in brackets, as appropriate, i.e. personal communication or unpublished data. When the bibliographic citation includes more than 6 authors, the first 6 authors should be cited, followed by the abbreviation et al.

The style of bibliographic references will depend on the type and format of the source cited:

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- Article already published in print and online journals Internet:
The authors (surname and initial of the first name, comma separation between authors), the full name of the manuscript, the abbreviation of the journal, the year of publication and after a semicolon the volume of the journal and after a colon the complete numbers of the first and last page of the paper.

Kandulsky A, Selgras M, Malfertheiner P. Helicobacter pylori infection: A Clinical Overview. Dig Liver Dis 2008; 40:619-626.

Alvarez F, Berg PA, Bianchi FB, Bianchi L, Burroughs AK,Cancado EL, et al. International Autoimmune Hepatitis Group Report: review of criteria for diagnosis of autoimmune hepatitis. J Hepatol 1999; 31:929-938.

- Admitted article, published only on the Internet, but not yet included in a regular number of the journal: the authors, the full name of the manuscript, the abbreviation of the journal, the year and month since the article is available on the Internet and DOI will be noted. The original paper to which reference is made usually details how to cite the manuscript.
Stamatakos M, Sargedi C, Stefanaki C, Safi oleas C, Matthaiopoulou I, Safi oleas M. Anthelminthic treatment: An adjuvant therapeuticstrategy against Echinococcus granulosus. Parasitol Int (2009), doi:10.1016/j.parint.2009.01.002

Inadomi JM, Somsouk M, Madanick RD, Thomas JP, Shaheen NJ. A cost-utility analysis of ablative therapy for Barrett'sesophagus, Gastroenterology (2009), doi: 10.1053/j.gastro.2009.02.062.

- Article from a journal that is published only on the Internet, but arranged in a conventional way: the authors, the full name of the manuscript, the abbreviation of the journal (can be added in brackets online), the year of publication and after a semicolon the volume of the journal and after a colon the complete numbers of the first and last page of the paper. If the original work being referenced provides the DOI and Internet address (URL), these can be added at the end of the reference.

Gurbulak B, Kabul E, Dural C, Citlak G, Yanar H,Gulluoglu M, et al. Heterotopic pancreas as a leading point for small-bowel intussusception in a pregnant woman. JOP (Online) 2007; 8:584-587.

Fishman DS, Tarnasky PR, Patel SN, Raijman I. Managementof pancreaticobiliary disease using a new intra-ductal endoscope: The Texas experience. World J Gastroenterol 2009; 15:1353-1358. Available from: URL: http://www.wjgnet.com/1007-9327/15/1353.asp. DOI: http://dx.doi.org/10.3748/wjg.15.1353

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REVIEW ARTICLE

CARBOHYDRATE MALABSORPTION. INTERPRETATION OF THE BREATH TEST.

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Abstract

Carbohydrate malabsorption, especially of lactose and fructose, is a common condition in clinical practice. Accurate diagnosis is essential to avoid unnecessary dietary restrictions that could compromise bone and cardiovascular health. The breath test with hydrogen (H_2) and methane (CH_4) determination is becoming the preferred technique due to its non-invasive nature and high sensitivity. In this review, we will focus on lactose and fructose malabsorption, as these are the most frequent types.

Keywords: carbohydrate malabsorption, breath test.

Lactose Malabsorption

Lactose is a disaccharide composed of galactose and glucose, linked by a β-1,4-glucosidic bond. It is the primary sugar in mammalian milk and is widely used as an additive in the food industry (cold cuts, sauces, medications, etc.)[1]. In addition to providing energy, it facilitates calcium absorption and promotes a bifidogenic microbiota[2].

The hydrolysis of lactose depends on lactase, a disaccharidase enzyme located at the brush border of the enterocyte, encoded by the LCT gene (chromosome 2). Its activity is highest in the jejunum and is absent in the colon and stomach. After hydrolysis, glucose and galactose enter the enterocyte via the SGLT1 transporter and exit into the interstitial space via GLUT2. When more glucose is needed, GLUT2 migrates to the apex of the enterocyte and assists SGLT1 in taking up glucose.

The loss of this enzyme is called "lactase non-persistence." This decline exhibits marked epidemiological variations globally. In East Asian populations, lactase non-persistence affects over 90% of individuals, with enzyme activity declining progressively from childhood onwards. Conversely, in Europe, there is a pronounced latitudinal gradient driven by natural selection: northern and north-western European populations display high rates of lactase persistence, with malabsorption prevalence ranging between only 2% and 15%, whereas in southern Europe this figure rises progressively, reaching values between 15% and 55%.

The types of lactose malabsorption include:

1. **Primary (late-onset) hypolactasia:** This is the most common form (non-persistence). It is genetically mediated and associated with the CC or CG

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polymorphisms. Persistence is associated with the TT and CT genotypes.

2. **Secondary form:** Resulting from damage to the intestinal mucosa (acute gastroenteritis, celiac disease, small intestinal bacterial overgrowth (SIBO), inflammatory bowel disease, etc.). It is usually transien (Table 1).

Intestinal diseases	Multisystem disorders	Iatrogenic causes
SIBO/IMO	Carcinoid syndrome	Aspirin
HIV enteropathy	Cystic fibrosis	NSAIDs
Regional enteritis	Diabetic gastropathy	Antibiotics
Coeliac disease	Kwashiorkor	Alcohol
Whipple's disease	Zollinger–Ellison syndrome	Radiation-induced enteritis
Severe gastroenteritis		
Crohn's disease		

Table 1. ***Secondary causes of lactose malabsorption.***

3. **Congenital:** An extremely rare autosomal recessive disorder (cases have only been reported in Finland). It presents with severe diarrhea from birth and requires a strict diet for life.

Recent evidence[3-5] suggests that consumption of dairy products, especially fermented ones, is associated with a reduced risk of cardiovascular disease and improved bone mineral density. Furthermore, the implementation of restrictive dietary regimens adversely affects other facets, including health-related quality of life, social interactions, and psychological well-being.

Fructose and Sorbitol Malabsorption

Fructose is a monosaccharide found in fruits and processed sweeteners. Unlike lactose, its absorption is limited and occurs by diffusion, facilitated by the GLUT5 transporter. Its prevalence is estimated at around 30% in Europe.

The presence of glucose stimulates the GLUT2 transporter, which migrates to the apical membrane, facilitating fructose absorption. In contrast, sorbitol competes for GLUT5, hindering its absorption. Likewise, rapid intestinal transit impedes the absorption of this sugar.

Types of fructose malabsorption include:

1. **Congenital or Fructosemia:** Hepatic aldolase B deficiency (Hereditary Fructose Intolerance). This is a serious condition with systemic toxicity[6].

2. **Primary:** GLUT5 deficiency (SLC2A5 gene), with a genetic basis that has not yet been fully elucidated.

3. **Secondary:** The most common type. Caused by excessive fructose consumption or damage to enterocytes (celiac disease, dysbiosis, SIBO, etc.).

Diagnosis of Lactose Malabsorption

We have several diagnostic tools at our disposal; however, table 2 shows the most commonly used ones. The breath test for sugar malabsorption is currently the test of choice because it is noninvasive, reproducible, and low-cost, with a sensitivity of 78–98% and a specificity of 98%[7].

Diagnosis of Fructose/Sorbitol Malabsorption

The diagnosis of fructose and sorbitol malabsorption presents particular challenges, since, unlike lactose, these substrates have a saturable absorption capacity even in healthy individuals.

A critical issue in the medical literature is the relationship between the administered substrate dose and the positivity rate. According to the study by Rao *et al.*[8], fructose absorption is a process with limited capacity. In healthy subjects, doses of 25 g of fructose have been observed to be absorbed properly by the majority of the population, whereas doses of 50 g cause malabsorption (detected by exhaled H_2) in up to 80% of healthy subjects.

This dose-response relationship was confirmed in subsequent reviews, which found a significant correlation ($r = 0.86$, $P < 0.001$) between fructose load and the percentage of positive test results[9]. This variability engenders controversy regarding the clinical utility of carbohydrate challenge tests, as malabsorption induced by high substrate loads may merely reflect an intrinsic physiological absorption threshold rather than an underlying pathological disorder. Due to the high rate of false positives with 50-gram doses, the Rome Consensus[2] and subsequent documents have questioned the clinical relevance

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Method	Description	Remarks
Intestinal biopsy	Measurement of enzyme activity	Gold standard, but invasive; the enzyme shows an uneven distribution throughout the intestine
Oral load	Blood glucose measurement (an increase of < 20 mg/dL indicates malabsorption)	Sensitivity 76–94%. Unsuitable for patients with diabetes mellitus and requires repeated venepuncture
Gaxilose test	Hydrolysis of a lactose analogue measured in urine/blood	Poorer concordance with breath testing; risk of false-negative results
Hydrogen/methane breath test (H_2/CH_4)	Measurement of gases produced by colonic bacterial fermentation	Investigation of choice. Non-invasive and cost-effective

Table 2. ***Diagnostic tests for lactose malabsorption.***

of fructose malabsorption as an isolated entity. It is suggested that fructose malabsorption could be considered a variant of normality when it occurs at high doses. Therefore, the European Consensus[10] recommends reducing the substrate dose to 20–25 g for the diagnostic test, with the aim of identifying those patients who truly have a pathologically reduced absorption capacity.

We recommend performing a fructose test in combination with a sorbitol test (both substrates together), since in current clinical practice this is more representative of "real-life" conditions. In foods (fruits, processed foods, etc.), both substrates typically coexist. Since sorbitol competes for the GLUT5 transporter, performing the combined test increases diagnostic sensitivity by better simulating the carbohydrate load of a standard diet.

Symptoms of Carbohydrate Malabsorption

The symptoms resulting from carbohydrate malabsorption do not depend solely on the presence of the unabsorbed substrate, but rather on the interaction between the substrate and the colonic microbiota. When carbohydrates reach the colon, they are fermented by bacteria, producing short-chain fatty acids (SCFAs), lactic acid (which acidifies the luminal pH), and gases (H_2, CH_4, CO_2).

This process triggers a clinical cascade characterized by:

- Osmotic Effect: Undigested sugar draws water into the intestinal lumen, causing explosive diarrhea and borborygmi.

- Luminal Distension: Gas production leads to bloating, flatulence, and colicky abdominal pain.

It is estimated that symptoms appear when enzymatic activity (in the case of lactose) drops below 50%. However, the severity of symptoms is strongly influenced by the patient's visceral sensitivity and the speed of intestinal transit.

Indications for the Breath Test (H_2/CH_4)

The breath test is a versatile diagnostic tool that allows for the evaluation not only of absorptive capacity but also of the state of the intestinal bacterial ecosystem.

Main Clinical Indications:

1. Evaluation of Specific Intolerances: Differential diagnosis in patients with nonspecific digestive symptoms (pain, bloating, diarrhea) following the consumption of dairy products, fruits, or processed foods containing lactose, fructose, or sorbitol.

2. Evaluation of Functional Disorders: Complementary assessment in patients with Irritable Bowel Syndrome (IBS) or functional dyspepsia to identify dietary triggers[10].

History of the Breath Test

The history of the breath test for the study of gastrointestinal disorders spans more than half a century, evolving from pioneering studies to current international consensus guidelines aimed at standardizing its use.

The first scientific studies were published approximately 50 years ago. In 1970, Levitt and Donaldson laid the initial groundwork in their publication[11]. In 1975, Newcomer *et al*[12] published a prospective comparison of indirect methods for detecting lactase deficiency, solidifying clinical interest in the technique; in 1983[13], the test's application was expanded to the study of fructose malabsorption. Despite its promising beginnings, the breath test's subsequent development was uneven. For decades, the technique was hampered by inconsistent methodology, characterized by a lack of consensus regarding the doses of substrate administered, the duration of

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the tests, and the criteria for defining a result as positive or negative. Over the past fifteen years, the scientific community has made significant efforts to ensure the test's rigor and reproducibility. In 2009, the Rome Consensus[2] rrepresented the first major standardization effort in Europe, establishing basic protocols for the diagnosis of malabsorption and SIBO. In 2017, the North American Consensus[14], updated the diagnostic criteria, standardized substrate doses, and formally introduced the inclusion of methane in the measurement, in addition to establishing the 90-minute criterion for the diagnosis of SIBO. And the most recent guideline, published in 2022—the European Guideline (UEG/ESNM/ESPGHAN)[10]—, refined the methodology and emphasized the distinction between malabsorption and intolerance. Its key contribution was the recommendation to use validated symptom questionnaires (such as the aCPQ: Carbohydrate Perception Questionnaire for adults) in conjunction with gas measurements to ensure accurate clinical interpretation.

Breath Test Protocol

Proper preparation is essential to minimize false-positive and false-negative results in the diagnosis of carbohydrate malabsorption [2,10,14]. The most important guidelines to follow are detailed below:

-Fasting: A strict 12-hour fast is required before the test.

-Pre-test Diet: For the 24 hours prior to the test, the patient must follow a residue-free diet (avoiding fiber and slow-absorbing carbohydrates).

-Avoid: One month prior: The patient must not have taken antibiotics or undergone a colonoscopy. One week prior: The patient must discontinue the use of probiotics, laxatives, prokinetics, and opioids.

-Oral hygiene: The patient must rinse their teeth (with 1% chlorhexidine) prior to the baseline sample collection.

-During the procedure: Smoking, chewing gum, and physical exercise are not permitted before or during the procedure, as these factors can alter exhaled gas levels.

Performing the Test[2,10,14]

Regarding the dose of the administered substrate, the amount of sugar varies depending on the type of test and the patient:

·Lactose: 25 g.

·Fructose: 25 g.

·Fructose/Sorbitol: 25 g and 5 g, respectively.

·Pediatric population: Adjusted to 1 g per kg of body weight, with a maximum limit of 25 g.

To ensure that the analyzed air is of alveolar origin, the patient must follow three strict steps:

1. Take a deep breath.
2. Hold your breath for 15 seconds.
3. Blow into the collection device.

The recommended total duration is 3 hours, with samples collected every 30 minutes.

Breath samples were analysed using either a Quintron analyser (BreathTracker)—based on gas chromatography with solid-state detection, which quantifies H_2, CH_4, and CO_2 whilst correcting values for alveolar dilution—or a portable Gastrolyzer monitor (Bedfont), equipped with a dedicated electrochemical sensor for H_2. In parallel with the gas measurements, it is essential to record the patient's subjective experience using the aCPQ questionnaire[15], which employs a visual analog scale (0–10). The symptoms to be recorded are: abdominal pain, nausea, abdominal distension (if early-onset, dyspepsia or SIBO should be ruled out), flatulence, and diarrhea. Symptoms are assessed before the test, every 30 minutes during the test, and again 3 to 6 hours after the test ends. A positive result is considered when there is an increase of more than 2 points above the baseline value on the visual scale.

Interpretation of Results

For a correct interpretation, it is essential to simultaneously measure H_2, CH_4, CO_2, with H_2S, also gaining increasing importance, whilst accurately evaluating the time point at which any gas rise occurs, given that increments in exhaled hydrogen recorded from the 90-minute mark onwards predominantly reflect colonic bacterial fermentation, alongside assessing the presence of symptoms throughout the test (Figure 1). The interpretation must always distinguish between malabsorption and intolerance.

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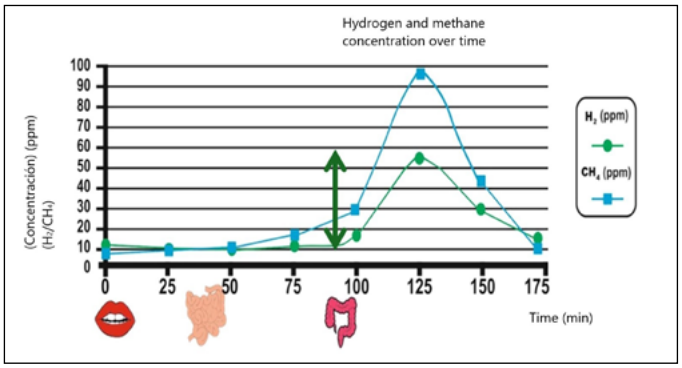


Figure 1. ***Increments in gas concentrations subsequent to the 90-minute time point (vertical arrow) are attributed to colonic bacterial fermentation. A rise of > 20 ppm for H_2 or > 10 ppm for CH_4 above baseline is considered positive, H_2: hydrogen; CH_4: methane; ppm, parts per million.***

Once we have the curve, we must first measure the baseline value. The optimal value is considered adequate when it is ≤10 ppm. An elevated baseline > 10–20 ppm may indicate poor adherence to the pre-test diet, fermentation by oropharyngeal flora, or nocturnal hypoventilation; nocturnal hypoventilation can cause slightly elevated fasting H_2 levels, produced by persistent fermentable substrates in the colon. A recent Spanish study found that light walking for one hour before the test can help reduce high levels of H_2 and CH_4 [16] allowing the test to be performed without having to repeat it. However, according to the European consensus[10], if the baseline is >10 ppm, a doubling of the initial value in three consecutive samples could be considered positive.

Subsequently, the excretion curve is analysed on the premise that any increase in hydrogen following the 90-minute time point predominantly reflects colonic bacterial fermentation; therefore, a positive test is defined as an increase of more than 20 ppm above baseline for H_2 or more than 10 ppm above baseline for CH_4 from minute 90 onwards.

Based on these results, there are four possible clinical scenarios[10]:

- Positive test result associated with symptoms: Diagnosis of intolerance.
- Positive test result with no symptoms: Carbohydrate malabsorption.
- Negative test result associated with symptoms: No malabsorption, but symptoms are the primary clinical indicator.
- Negative test result with no symptoms: Normal result.

Regarding early peaks—a rise before the 90-minute mark—this could suggest SIBO or rapid intestinal transit[17]. In a 2021 article by Piero Vierna[18], the authors analyzed whether early peaks are associated with SIBO, concluding that in most cases they are due to rapid intestinal transit. In another article published by the Laserna group[19] in 2024, they evaluated carbohydrate malabsorption curves that suggested SIBO (when an increase of ≥20 ppm in H_2 was observed relative to baseline at 90 minutes or when IMO (Intestinal Methanogen Overgrowth) (when CH4 values were ≥10 ppm at any point on the curve), and they concluded that the lactose test had high specificity for detecting SIBO and IMO, whereas the fructose test did not (false positives for SIBO: 27%, false negatives for IMO: 27%). Regarding suspected IMO in a breath test for sugar malabsorption, according to the published literature[20], CH_4 is not detected in breath until there are $>10^8$ methanogens per gram of dry stool (>1 ppm), and in Western countries, it is estimated that around 20% of the Central European population may even be classified as high-methane producers (> 5 ppm); therefore, we recommend ruling out IMO in these tests when CH_4 > 10 ppm at any point on the graph. However, according to the American consensus, SIBO should be ruled out before performing malabsorption tests to avoid false positives, and the presence of two peaks in the breath test is not diagnostic of SIBO.

Conclusions

Carbohydrate malabsorption is a common clinical condition whose significance lies in its impact on quality of life and long-term nutritional health. The H_2 and CH_4 breath test has established itself as the diagnostic tool of choice due to its safety, low cost, and ability to distinguish between malabsorption and intolerance. It is essential that the interpretation of results not be limited exclusively to exhaled gas levels but be integrated with a thorough medical history and the use of validated symptom scales. An accurate diagnosis helps avoid unnecessary dietary restrictions, ensuring that treatment is focused on those patients who will truly benefit from a reduction in substrate intake—always with a view toward maintaining nutritional balance and preventing associated risks, such as impaired bone health in the case of dairy exclusion.

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CLINICAL CASE

HERPETIC ESOPHAGITIS IN A YOUNG IMMUNOCOMPETENT PATIENT: AN UNUSUAL CAUSE OF SEVERE ODYNOPHAGIA. A CASE REPORT.

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Abstract

Introduction: Herpetic esophagitis is a rare cause of severe odynophagia associated with immunocompromised patients, although cases have also been reported in young immunocompetent individuals.

Case Presentation: A 19-year-old woman presented with a five-day history of retrosternal pain and odynophagia, with near-complete inability to tolerate oral intake. She was initially treated for tonsillitis without improvement. Examination revealed a mildly hyperemic oropharynx, and laboratory tests showed elevated acute-phase reactants. Upper gastrointestinal endoscopy revealed multiple superficial serpentine ulcers in the middle and proximal esophagus, and fibrinous erosions at the esophagogastric junction. Biopsies were taken from the margins and base of the ulcers. Empirical treatment with oral acyclovir was initiated, resulting in complete clinical resolution after seven days. Histological examination and detection of HSV-1 in the biopsy confirmed the diagnosis of herpetic esophagitis in an immunocompetent patient.

Discussion: Herpetic esophagitis should be considered in the differential diagnosis of severe odynophagia and retrosternal pain in immunocompetent young adults. The typical endoscopic pattern of small ulcers with preserved adjacent mucosa guides the diagnosis, which must be confirmed by histopathological examination and viral detection techniques. Early treatment with acyclovir accelerates symptom resolution and reduces the risk of complications, with an excellent prognosis in immunocompetent patients.

Keywords: herpetic esophagitis, odynophagia, herpes simplex virus, immunocompetent, gastrointestinal endoscopy.

Introduction

Infectious esophagitis is a rare condition in clinical practice, generally associated with immunocompromised patients, such as those with HIV infection, transplant recipients, or patients on immunosuppressive therapy. Notable causes

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include herpes simplex virus type 1 (HSV-1), cytomegalovirus (CMV), and Candida albicans. Of these, HSV-1 accounts for less than 10 % of cases, usually in the context of immunosuppression, although cases have been reported in immunocompetent individuals, particularly young adults.

Herpetic esophagitis typically presents with severe retrosternal pain and odynophagia that limits food intake and may be accompanied by dysphagia, fever, or general malaise. It is usually caused by direct contact of the virus with the esophageal mucosa following an acute oropharyngeal infection or reactivation of a latent viral infection in the vagus nerve or esophageal plexus. Diagnosis is based on endoscopy and histological confirmation or PCR detection of the virus in a biopsy specimen. Treatment with acyclovir accelerates clinical resolution and prevents complications.

The following is a case report of herpetic esophagitis diagnosed in an immunocompetent female patient, whose clinical presentation initially mimicked an otolaryngological condition. Informed consent was obtained from the patient for the publication of the case and the endoscopic images, ensuring that the data were anonymized.

Case presentation

A 19-year-old woman with no medical history or clinical findings suggestive of known immunosuppression presented to the emergency department three times in the past 24 hours with low retrosternal pain that had been present for 5 days. The patient described the pain as a continuous, burning sensation that worsened after eating and progressively increased in intensity, eventually preventing her from eating solids. She did not experience episodes of choking, excessive salivation, a foreign body sensation, or oropharyngeal dysphagia. Additionally, her symptoms were accompanied by an isolated fever spike of 38°C the previous day. One week earlier, the patient had begun antibiotic and corticosteroid therapy (40 mg of prednisone daily for 5 days) for suspected bacterial tonsillitis after being evaluated at her local health center for odynophagia; however, she showed no clinical improvement.

On physical examination, the patient appeared in good general condition, with mild oropharyngeal hyperemia but no tonsillar hypertrophy or exudate. No palpable lymphadenopathy was noted. Cardiopulmonary auscultation and abdominal examination were unremarkable.

Laboratory findings revealed mild leukocytosis with neutrophilia, along with elevated C-reactive protein (70 mg/L). The chest X-ray showed no significant findings. Given the persistence of retrosternal pain and the exclusion of otolaryngological or pulmonary causes, it was decided to complete the evaluation with an urgent upper gastrointestinal endoscopy.

The examination was performed up to the second portion of the duodenum, revealing, upon retraction, two circular fibrinous erosions measuring 3–4 mm, with preserved adjacent mucosa, at the esophagogastric junction (see Figure 1). In addition, the patient also presented with several superficial ulcerated lesions arranged in a linear pattern with a serpiginous appearance in the middle and proximal esophagus, suggestive of a viral etiology (see Figure 2). Samples were taken from the edge and base of the ulcers for histopathological and microbiological examination.

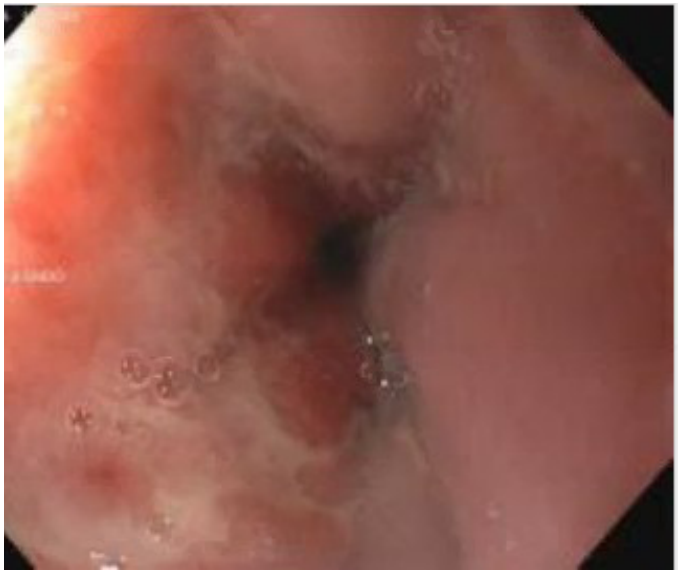


*Figure 1. **Upper gastrointestinal endoscopy: Two circular fibrinous erosions, 3–4 mm in diameter, are visible at the esophagogastric mucosal junction, with the surrounding mucosa appearing normal.***

Following the endoscopic findings of esophagitis of probable infectious origin, empirical outpatient treatment was initiated with oral acyclovir 400 mg every 8 hours for 7 days, given the suspicion of herpetic esophagitis.

Finally, the patient was re-evaluated during a follow-up visit 4 weeks later, showing complete resolution of her symptoms following completion of antiviral treatment. Microbiological testing using polymerase chain reaction (PCR) yielded a positive result for HSV-1, while she tested negative for HSV-2 and CMV. In addition, histopathological examination of the biopsies revealed ballooning degeneration of epithelial cells, the presence of characteristic intranuclear eosinophilic inclusion bodies, and a cytopathic effect consistent with HSV-1 infection;

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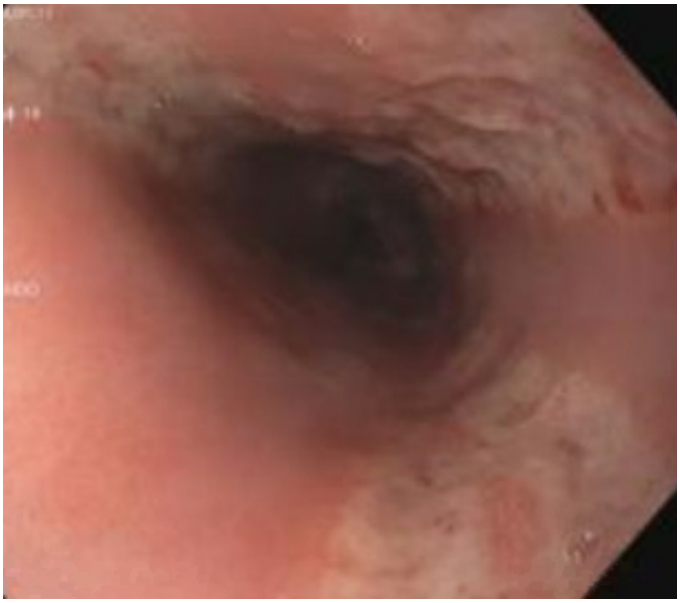


Figure 2. ***Upper gastrointestinal endoscopy: Several superficial, serpiginous-appearing ulcers are observed in the middle and proximal esophagus.***

the diagnosis was confirmed by immunohistochemistry, which was positive for HSV-1 and negative for CMV.

Discussion

Herpetic esophagitis is an acute infection of the esophageal mucosa usually caused by herpes simplex virus type 1 (HSV-1), although type 2 may also be involved to a lesser extent[1]. Its overall incidence is low and it has been described primarily in immunocompromised patients; however, in recent years, numerous cases have been reported in immunocompetent individuals, particularly young adults[2,3]. In this group, the infection usually presents as an acute, self-limiting condition, although the severity of symptoms can be striking and lead to repeated visits to the emergency department[1].

The most widely accepted pathogenic mechanism in immunocompetent patients is local spread from an oropharyngeal focus, usually in the context of primary herpesvirus infection, although reactivation of latent infection in the vagal plexus or oesophageal mucosa has also been proposed[4-6]. Local factors, such as microtrauma, acid reflux or short courses of corticosteroid therapy, may facilitate viral replication and initial epithelial damage[5,6]. In our case, the history of a brief course of systemic corticosteroid therapy probably acted as a predisposing factor in an otherwise healthy mucosa.

From a clinical standpoint, the classic triad of odynophagia (60–76%), retrosternal pain (46–50%), and fever (44–52%) characterizes the presentation of herpetic esophagitis in immunocompetent individuals; other symptoms, such as dysphagia or general malaise, may occur less frequently[1-3]. Oropharyngeal examination may be normal or show only mild inflammatory changes, and herpetic lesions on the lips or in the mouth are observed in only a minority of cases, which contributes to the initial consideration of alternative diagnoses such as pharyngotonsillitis or functional disorders[1,3]. This clinical pattern is consistent with the case described here, in which retrosternal pain and progressive odynophagia were the predominant symptoms and led to several visits to the emergency department before an esophageal cause was suspected.

Upper gastrointestinal endoscopy is the essential tool for diagnosing suspected cases[1-3]. Typical findings include multiple small, superficial, rounded, or "geographic-appearing" ulcers with well-defined margins and relatively intact adjacent mucosa, located primarily in the middle and distal thirds of the esophagus[7-9]. This pattern allows herpetic esophagitis

Aetiology	Characteristic endoscopic findings	Key features
Candida albicans	·Adherent whitish or yellowish plaques with a cotton-wool appearance ·Plaques may coalesce, leaving erythematous or friable mucosa when dislodged.	·The most typical form of infectious oesophagitis. ·Plaques do not usually come away with simple irrigation.
Herpes simplex virus (HSV)	·Multiple small, round, superficial ulcers with a volcano-like appearance, sometimes with a necrotic base. ·Ulcers may coalesce into larger lesions.	·Usually affects the mid-to-distal oesophagus. ·Ulcers tend to be small and superficial.
Cytomegalovirus (CMV)	·Large, deep, linear or longitudinal ulcers. ·Solitary or few in number, with well-defined margins.	Lesions tend to be deeper and more extensive than those caused by HSV.
Human immunodeficiency virus (HIV)	·Any of the above patterns may be observed, depending on the causative pathogen. ·Mixed or non-specific lesions may occur in some cases.	Endoscopic findings alone cannot identify the causative agent; biopsy is essential.

Tabla 1. ***Differential endoscopic findings in infectious esophagitis.***

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to be distinguished from other infectious causes (see Table 1), such as candidal esophagitis, which is characterized by confluent whitish plaques, or cytomegalovirus esophagitis, in which larger and deeper ulcers predominate, usually in the distal thir [7,8]. In the case presented, the presence of superficial serpentine ulcers in the upper-middle esophagus and fibrinous erosions at the esophagogastric junction was highly suggestive of infectious esophagitis of probable herpetic origin.

However, a definitive diagnosis requires confirmation through histopathological examination and/or viral detection techniques on biopsy specimens[10]. Characteristically, ballooning degeneration of squamous cells, multinucleation, and type A Cowdry intranuclear inclusion bodies are observed, which are considered pathognomonic findings of herpes infection[1,2,10]. Detection of HSV-1 via immunohistochemistry or PCR in the biopsy specimen increases diagnostic sensitivity and allows differentiation from other viral infections[10]. In our patient, the histopathological finding of typical cytopathic changes and a positive immunohistochemical result for HSV-1, together with the detection of HSV-1 in the biopsy via PCR, confirmed the endoscopic suspicion.

The standard treatment for herpetic esophagitis is based on the use of acyclovir, a nucleoside analog that inhibits viral DNA polymerase[5,6]. In immunocompetent patients with uncomplicated disease, the most commonly used regimen is oral acyclovir 400 mg every 8 hours for 7 to 10 days, with rapid improvement in odynophagia and retrosternal pain in most cases[2-4]. In immunocompromised patients, those with severe disease, or those who cannot tolerate oral administration, intravenous administration of the drug is recommended[11]. Although cases of spontaneous resolution without antiviral treatment have been reported, several studies suggest that early initiation of acyclovir shortens the duration of symptoms by reducing viral replication and the occurrence of complications resulting from poor oral tolerance, such as dehydration or nutritional deterioration; therefore, its use is considered reasonable even in immunocompetent patients with severe clinical presentation[2,4,11].

The course of herpetic esophagitis in immunocompetent individuals is generally favorable, with complete resolution of symptoms within one or two weeks and a low recurrence rate[1-3,5]. Nevertheless, during the initial evaluation, it is advisable to rule out underlying immunosuppressive conditions, such as HIV infection, neoplasms, or immunomodulatory treatments, especially if the presentation is atypical or the course is prolonged[1,4]. In our case, the absence of clinical and laboratory findings suggestive of immunodeficiency, along with the rapid response to treatment, support the self-limiting nature of the condition.

The case presented illustrates several issues relevant to daily clinical practice. First, it highlights that herpetic esophagitis should be included in the differential diagnosis of severe odynophagia and retrosternal pain in previously healthy young adults, especially when the ENT examination is normal and there is no response to conventional treatments[1-3]. Second, it highlights the key role of early endoscopy in identifying the characteristic ulcerated lesions and obtaining targeted biopsies[1-3,7,10]. Finally, it underscores that treatment with oral acyclovir leads to rapid clinical improvement and complete resolution of symptoms in most immunocompetent patients, minimizing the risk of complications and avoiding unnecessary additional investigations[2-4].

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CLINICAL CASE

CHRONIC DIARRHEA AND INTESTINAL SPIROCHETOSIS: A CASE HIGHLIGHTING THE IMPORTANCE OF HISTOLOGICAL DIAGNOSIS. A CASE REPORT.

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Abstract

Human intestinal spirochetosis is an uncommon cause of chronic diarrhea caused by colonic colonization by *Brachyspira* species. We report the case of a 56-year-old man with chronic watery diarrhea, weight loss, and occasional fecal incontinence. Laboratory tests and colonoscopy were unremarkable. Colonic biopsies and immunohistochemical analysis confirmed intestinal spirochetosis. Treatment with metronidazole led to complete symptom resolution. This case highlights the importance of considering intestinal spirochetosis in the differential diagnosis of chronic diarrhea, even in patients without risk factors or endoscopic abnormalities.

Keywords: Intestinal spirochetosis, chronic diarrhea, *Brachyspira*, immunohistochemistry, colonoscopy.

Introduction

Chronic diarrhea, defined as the emission of loose stools for more than four weeks, is one of the most common reasons for referral to gastroenterology clinics and poses a diagnostic challenge due to the wide variety of potential etiologies, including inflammatory, infectious, functional, malabsorptive, endocrine, and neoplastic causes. Clinical guidelines recommend a systematic approach based on the medical history, physical examination, and targeted laboratory and microbiological tests, with the goal of distinguishing between organic and functional causes and determining the need for further diagnostic tests[1,3].

Despite advances in diagnostic techniques, a proportion of patients continue to present with an inconclusive initial

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evaluation, especially when endoscopic findings are macroscopically normal. In this context, it is necessary to consider less common conditions within the differential diagnosis. Among these, human intestinal spirochetosis is a rare and likely underdiagnosed cause of chronic watery diarrhea, the diagnosis of which typically depends on histopathological examination due to the absence of specific endoscopic findings[2,4].

Intestinal spirochetosis is defined by the colonization of the colonic mucosa by anaerobic spirochetes of the genus Brachyspira, primarily Brachyspira aalborgi and Brachyspira pilosicoli[5]. Although it is a well-recognized disease in veterinary medicine, especially in poultry and swine, its clinical significance in humans remains a subject of debate. It was first described in 1967 by Harland and Lee, and to date, only a few cases have been reported in the literature. In the largest series published to date in our setting, the prevalence of ID was estimated at 0.7% (8/1,174) among patients with chronic watery diarrhea[10]. Transmission appears to occur primarily via the fecal-oral route, although the exact mechanism of transmission is unknown[2].

The reported prevalence varies depending on the population studied and the geographic area, being higher in developing countries and among certain at-risk groups, particularly people with human immunodeficiency virus (HIV) infection and men who have sex with men (MSM). However, cases have also been reported in immunocompetent individuals with no apparent epidemiological risk factors, which makes clinical suspicion even more difficult[6-8].

From a clinical standpoint, intestinal spirochetosis may be asymptomatic or present with nonspecific symptoms such as chronic watery diarrhea, abdominal pain, bloating, or weight loss[9]. Endoscopically, the mucosa is usually normal; therefore, the diagnosis depends largely on histological examination, in which a filamentous basophilic band adherent to the colonic epithelium ("*false brush border*") is classically observed and confirmed by special stains or immunohistochemistry[8].

We present the case of an immunocompetent patient with long-standing chronic watery diarrhea and a macroscopically normal colonoscopy, whose definitive diagnosis of intestinal spirochetosis was established through histopathological examination.

Clinical case

We present the case of a 56-year-old man with no significant medical or surgical history who was referred to the Gastroenterology department for chronic diarrhea that had persisted for more than one year. He presented with predominantly watery, liquid stools—occasionally explosive—accompanied by episodes of fecal incontinence and intermittent abdominal pain unrelated to bowel movements. He also reported a weight loss of approximately 6 kg since the onset of symptoms, with no fever or emissions of pathological material.

Regarding epidemiological history, the patient reported that his wife had had a *Clostridioides difficile* infection more than one year before the onset of his symptoms. He denied recent travel, consumption of non-potable water, risky sexual practices, relevant epidemiological exposure, or use of toxic substances, supplements, or medications. The physical examination was entirely normal, with no abnormal abdominal findings.

A complete laboratory workup was performed, including a complete blood count, biochemical panel, C-reactive protein, thyroid panel, and serology tests, all of which were normal. Celiac disease was ruled out based on normal IgA levels and negative antitransglutaminase antibodies.

The microbiological stool analysis revealed a positive PCR result for *Blastocystis hominis*, this finding was considered of uncertain significance given the debated pathogenicity of the organism and the patient's clinical persistence.

Given the persistence of symptoms and the absence of conclusive findings, a colonoscopy was performed with serial biopsies to rule out microscopic colitis. During the examination, the colonic mucosa appeared macroscopically normal, with no inflammatory lesions, ulcerations, or vascular abnormalities. Histological examination of the colonic biopsies revealed the presence of a basophilic filamentous band adherent to the surface epithelium, consistent with intestinal spirochetosis, which was subsequently confirmed by a positive immunohistochemical test for spirochetes (Figure 1).

Following the diagnosis, treatment was initiated with metronidazole 500 mg every 8 hours for 10 days, resulting in complete resolution of the diarrhea and disappearance of the gastrointestinal symptoms upon completion of treatment.

Discussion

Human intestinal spirochetosis is a rare condition and is likely underdiagnosed, especially in immunocompetent patients without classic risk factors. Although it has traditionally been associated with HIV infection and MSM, there are an

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increasing number of case reports in the general population, suggesting that its actual prevalence may be underestimated[6-8].

The true pathogenic significance of intestinal spirochetosis remains controversial, as in some individuals it may present as an incidental finding. However, various studies have demonstrated an association between colonization by *Brachyspira spp.* and chronic gastrointestinal symptoms—particularly watery diarrhea, abdominal pain, and weight loss—with clinical improvement following antibiotic treatment, as was the case in our patient[9,10].

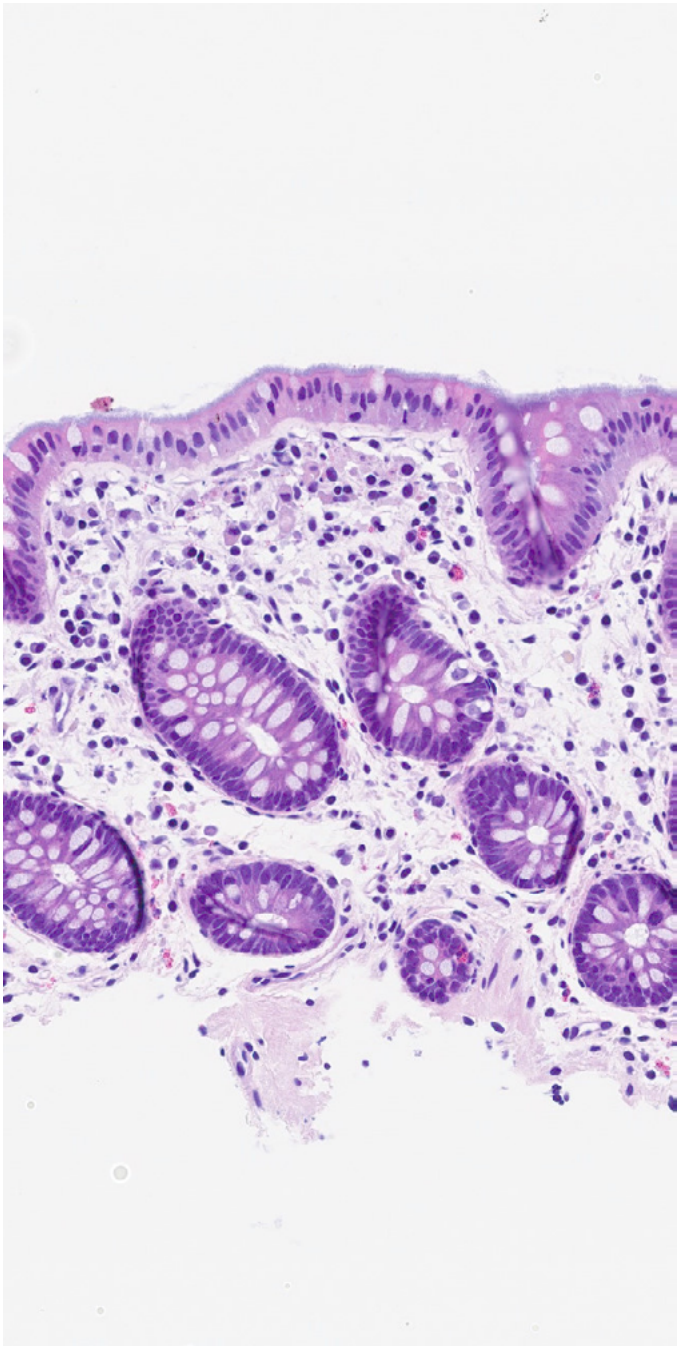


Figure 1. ***Large intestine mucosa showing a bluish, feathery band on the surface of the epithelium (H&E).***

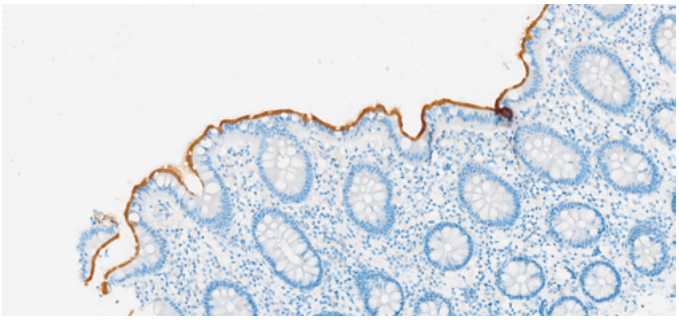


Figure 2. ***Immunohistochemical staining for spirochetes showing positive expression on the colonic surface (spirochete IHC).***

One of the most clinically significant aspects is the difficulty in diagnosis. Most patients have normal endoscopic findings; therefore, the diagnosis depends primarily on histopathological examination[8]. The characteristic lesion consists of a basophilic pseudo-brushed band on the colonic epithelium, corresponding to the adhesion of spirochetes to the mucosal surface. Confirmation can be achieved using special stains such as Warthin-Starry or through immunohistochemical and molecular techniques[4].

In our case, the diagnosis was reached after ruling out the most common causes of chronic diarrhea and thanks to the systematic collection of biopsies despite the macroscopically normal appearance of the mucosa, which highlights the importance of maintaining a broad, multidisciplinary diagnostic approach.

Another point of interest is the concomitant detection of Blastocystis hominis in stool. Although this protozoan has been linked to gastrointestinal symptoms in certain studies, its pathogenic role remains controversial, and current guidelines do not consider a causal relationship to be proven in all immunocompetent patients; therefore, its detection must be interpreted within the context of the individual clinical presentation[3,10,11].

Clinical resolution following metronidazole administration is consistent with a possible etiological role for intestinal spirochetosis; however, this association should be interpreted with caution. The available evidence remains insufficient to establish an unequivocal causal relationship between colonization by *Brachyspira spp.* and gastrointestinal symptoms, as most published studies are retrospective or consist of case series. A recent meta-analysis confirmed the association between intestinal spirochetosis and gastrointestinal symptoms, although it highlighted the low quality of the evidence and the inability to establish causality[13].Furthermore, metronidazole is active against various anaerobic microorganisms and protozoa and is also one of the therapeutic options for patients with small intestinal

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bacterial overgrowth (SIBO); therefore, it cannot be ruled out that the clinical improvement was influenced, at least in part, by mechanisms other than the treatment of *Brachyspira spp.* colonization[12].

Furthermore, the lack of specific tests to rule out SIBO constitutes a limitation of our case. Similarly, it cannot be completely ruled out that the response to metronidazole reflected the simultaneous treatment of another condition sensitive to this antibiotic. However, the pathologic demonstration of intestinal spirochetosis, the exclusion of the most common causes of chronic diarrhea, and the complete resolution of symptoms following treatment support the notion that this condition may have played a clinically relevant role in the presentation of the case. In any case, given the observational nature of this isolated clinical case and the currently available evidence, it is not possible to establish a definitive causal relationship between the pathologic finding and clinical improvement[4,10,13,14].

Metronidazole remains the most frequently used antibiotic in published symptomatic cases, although the available evidence comes primarily from retrospective series and case reports, with no randomized clinical trials or specific guidelines defining the therapeutic indication. Consequently, the decision to initiate treatment must be individualized based on symptoms, the clinical context, and the reasonable exclusion of other causes of chronic diarrhea[4,13,14].

This case illustrates the need to consider intestinal spirochetosis as part of the differential diagnosis of chronic watery diarrhea, even in the absence of classic risk factors or endoscopic findings, and highlights the fundamental role of histopathological examination in the diagnosis of rare conditions. It also highlights the importance of critically interpreting the response to antibiotic treatment, avoiding unequivocally attributing clinical improvement to the histopathological finding in the absence of studies that establish a causal relationship.

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CLINICAL CASE

NOT EVERYTHING THAT OBSTRUCTS IS A TUMOR: THE BEZOAR AS A GREAT COLONIC SIMULATOR. A CASE REPORT.

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Abstract

Bezoars are accumulations of indigestible material within the gastrointestinal tract and represent an uncommon cause of intestinal obstruction. Colonic obstruction due to bezoars is exceptionally rare and may mimic colorectal malignancy, making preoperative diagnosis challenging. We report the case of a 66-year-old man with no previous abdominal surgery who presented with abdominal distension, nausea, and a two-day history of obstipation. Contrast-enhanced abdominal computed tomography demonstrated diffuse colonic dilatation with an abrupt transition point and mural thickening at the sigmoid colon, initially suggesting an obstructing colorectal neoplasm. Retrospective review of the images identified two heterogeneous intraluminal masses consistent with bezoars. Flexible sigmoidoscopy was unsuccessful because of abundant fecaloid material obstructing endoscopic progression. Owing to persistent bowel obstruction, urgent exploratory laparoscopy was performed, revealing two intraluminal bezoars, one impacted in the sigmoid colon and the other located in the descending colon. Both bezoars were removed by colotomy, and a segmental sigmoid colectomy with primary anastomosis was performed. Histopathological examination identified both masses as trichobezoars. The postoperative course was uneventful. Trichobezoars are exceptionally uncommon in older adults, particularly when presenting as colonic obstruction without a history suggestive of trichophagia. This case highlights the importance of considering bezoars in the differential diagnosis of large bowel obstruction and emphasizes the role of contrast-enhanced computed tomography in guiding diagnosis and surgical management.

Keywords: bezoar, colonic obstruction, impaction.

Introduction

Bezoars are masses of undigested ingested material that accumulate in the gastrointestinal tract. Depending on their composition, they are classified as phytobezoars (plant material), trichobezoars (hair), pharmacobezoars, and other less common types. They are a rare cause of intestinal obstruction, and their occurrence in the colon is exceptional.

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Peña Tomey L, Alonso Bilbao N, Martínez Alcalá García S, Gascón Meléndez NJ, Martínez Rodenas M. Not everything that obstructs is a tumor: the bezoar as a great colonic simulator. A case report. RAPD 2026;49(5):174-177. DOI: 10.37352/2026495.4

Their clinical presentation is nonspecific, and radiological findings may mimic neoplastic or inflammatory processes, making diagnosis difficult. We present the case of a colonic obstruction secondary to the impaction of two trichobezoars.

Clinical case

A 66-year-old man, originally from Colombia, with a history of hypertension and a previous hospitalization for intestinal obstruction treated conservatively, with no history of abdominal surgery. He presented to the emergency department with abdominal distension, nausea, and a two-day history of cessation of bowel movements. He did not report ingesting any foreign bodies nor did he have a known history of gastrointestinal motility disorders or predisposing factors for bezoar formation. On physical examination, he presented with a distended, soft, and non-tender abdomen, with stable hemodynamic parameters.

Laboratory tests revealed leukocytosis and elevated C-reactive protein levels. An abdominal CT scan with intravenous contrast revealed generalized dilation of the colonic lumen with an abrupt change in diameter at the level of the sigmoid colon, associated with parietal thickening suggestive of mechanical obstruction; a neoplastic process causing stenosis was initially suspected. Retrospectively, two heterogeneous intraluminal images consistent with foreign bodies were identified.

It was decided to admit the patient for initial conservative treatment and to perform a rectosigmoidoscopy, which revealed abundant fecal-like material that prevented the endoscope from advancing, with no significant mucosal lesions. In the absence of recovery of bowel function, a hard, palpable mass persisted in the left iliac fossa. A second abdominal CT scan with intravenous contrast was performed, which showed displacement of one of the intraluminal masses, while the other remained impacted in the sigmoid colon; both were consistent with bezoars.

In light of these findings, an urgent exploratory laparoscopy was performed, revealing two intraluminal bezoars: one impacted in the sigmoid colon with significant thickening and stiffness of the colonic wall, and another located in the descending colon. Both bezoars were removed via colotomy and segmental resection of the sigmoid colon with primary anastomosis. Pathological examination identified both as trichobezoars. The final diagnosis was colonic obstruction secondary to trichobezoar impaction.

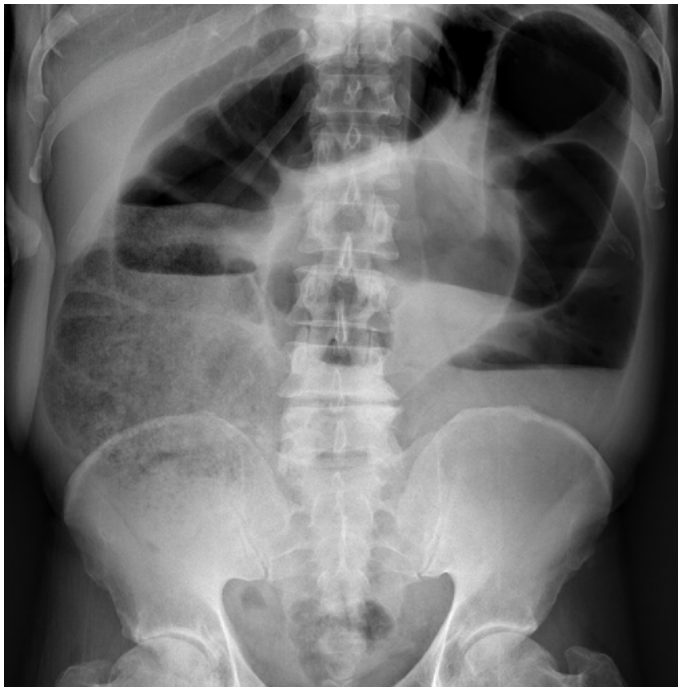


Figure 1. ***Upright plain abdominal X-ray showing generalized dilation of the colonic framework with numerous fluid-air levels, findings consistent with mechanical intestinal obstruction.***



Figure 2. ***Abdominal computed tomography (CT) scan with intravenous contrast, axial view. Dilatation of the proximal colon is observed, along with a heterogeneous intraluminal mass with a mottled pattern and air bubbles within it, located in the descending colon, consistent with a bezoar.***

Discussion

Bezoars are an uncommon cause of mechanical intestinal obstruction, accounting for approximately 0.4–4% of cases; they are usually located in the small intestine, and colonic obstruction is rare[1]. Trichobezoars represent a much less common subtype than phytobezoars and consist of ingested hair; they are classically associated with young patients with trichophagia and psychiatric disorders, making their occurrence in a 66-year-old man exceptional[2,3].

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Figure 3. ***Abdominal computed tomography with intravenous contrast, coronal reconstruction. A sudden change in caliber is identified at the level of the sigmoid colon, associated with parietal thickening and a second impacted heterogeneous intraluminal mass.***



Figure 4. ***Surgical specimen from a sigmoidectomy. The resected segment of the sigmoid colon shows significant wall thickening and stiffness secondary to bezoar impaction.***



Figure 5. ***Two trichobezoars removed during the surgical procedure following a colotomy. Pathological examination confirmed that both were trichobezoars.***



Figure 6. ***Macroscopic view of the trichobezoars removed via colotomy. Comacted hair is visible, forming irregular masses that fragmented during extraction and were responsible for the colonic obstruction.***

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Preoperative diagnosis can be complex, as the clinical presentation is nonspecific and radiological findings may mimic a neoplasm or an inflammatory stenosis. Computed tomography with intravenous contrast is the imaging test of choice, allowing for the identification of heterogeneous intraluminal masses containing air bubbles and the localization of the site of obstruction, although a definitive diagnosis may not be established until surgery or pathological examination[4,5].

Treatment depends on the location and degree of obstruction. In patients with complete obstruction or failure of conservative treatment, surgery is usually necessary to remove the bezoar and treat associated lesions. In cases of trichobezoars, it is also advisable to subsequently assess for trichophagia or underlying psychiatric disorders to prevent recurrences[6].

This case illustrates an unusual form of colonic obstruction caused by trichobezoars, which was initially interpreted as a neoplastic process, and highlights the importance of including this condition in the differential diagnosis of intestinal obstruction, even in patients without a suggestive history.

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CLINICAL CASE

IGA NEPHROPATHY IN PATIENTS WITH CIRRHOSIS: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS. A CASE SERIES.

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Abstract

Renal dysfunction in patients with liver cirrhosis represents a diagnostic challenge due to the coexistence of multiple etiologies and the overlap between functional and structural mechanisms. In this setting, errors in etiological attribution may lead to inappropriate therapeutic decisions. We report two cases of IgA nephropathy in cirrhotic patients illustrating opposite diagnostic pitfalls. The first case involved a patient with liver cirrhosis in whom renal dysfunction was initially attributed to hepatorenal syndrome despite abnormal urinary sediment findings, delaying the diagnosis of IgA nephropathy until kidney biopsy was performed. The second case concerned a patient with IgA nephropathy initially considered primary and treated with immunosuppressive therapy until decompensated liver cirrhosis was subsequently identified, leading to reclassification as secondary IgA nephropathy. These cases highlight how a simplified interpretation of renal dysfunction in cirrhotic patients may result in diagnostic errors with relevant therapeutic implications. Dynamic clinical reassessment, integration of clinical and laboratory findings, and consideration of kidney biopsy in selected cases are essential to establish an accurate etiological diagnosis.

Keywords: IgA nephropathy, cirrhosis, hepatorenal syndrome, renal biopsy.

Introduction

The deterioration of renal function in patients with liver cirrhosis poses a complex diagnostic challenge due to the coexistence of multiple etiologies and the overlap of functional and structural mechanisms. In this context, diagnostic biases can lead to incorrect etiological attribution, with significant therapeutic implications. We present two clinical cases that illustrate contrasting scenarios of IgA nephropathy in patients with cirrhosis and highlight the need for diagnostic reevaluation in the face of clinical discordance or lack of response to treatment.

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Lorente Martínez MÁ, González Peregrina SM, Martín Navas MÁ, Ruiz Escolano E. IgA nephropathy in patients with cirrhosis: diagnostic and therapeutic implications. A case series. RAPD 2026;49(5):178-182. DOI: 10.37352/2026495.5

Clinical Case 1

A 56-year-old man with a history of chronic hepatitis B virus (HBV) infection without antiviral treatment and long-standing harmful alcohol use presented to the emergency department with progressive abdominal distension and deterioration of his general condition.

Physical examination revealed painless hepatomegaly and dullness in the flanks. Initial laboratory tests showed acute renal dysfunction, with a serum creatinine level of 1.82 mg/dL (previous levels were within the normal range). Urinalysis revealed mild proteinuria and microscopic hematuria. Abdominal ultrasound revealed findings consistent with advanced chronic liver disease and moderate ascites, with no structural renal abnormalities. Liver function at admission was classified as Child-Pugh Class C (11 points), with a MELD score of 18 and a MELD-Na score of 21.

HBV infection was confirmed, and antiviral treatment with entecavir was initiated. Infectious precipitating factors were ruled out through diagnostic paracentesis, blood cultures, urine culture, and chest X-ray, as well as recent alcohol consumption. Immunological testing was negative, except for IgA hypergammaglobulinemia (674 mg/dL) and mild hypocomplementemia (C3: 72 mg/dL; C4: 11 mg/dL).

The progressive worsening of renal function (from 1.82 to 3.7 mg/dL), despite volume expansion therapy with albumin, reinforced the initial clinical suspicion of hepatorenal syndrome, and treatment with terlipressin was initiated. Despite reaching maximum doses, no improvement in renal function was observed, prompting a reconsideration of the initial diagnosis and an evaluation of structural causes of renal damage.

It was decided to perform a renal biopsy, the histological findings of which were consistent with IgA nephropathy (Figure 1). Terlipressin treatment was discontinued, and antiviral therapy was continued; partial recovery and stabilization of renal function were observed in the following months. Given the progressive deterioration of liver function (Child-Pugh C [10 points] and MELD and MELD-Na scores of 26 points), the patient was evaluated for a liver transplant, which was performed successfully, resulting in a significant improvement in renal function (Cr 1.77 mg/dL).

Clinical Case 2

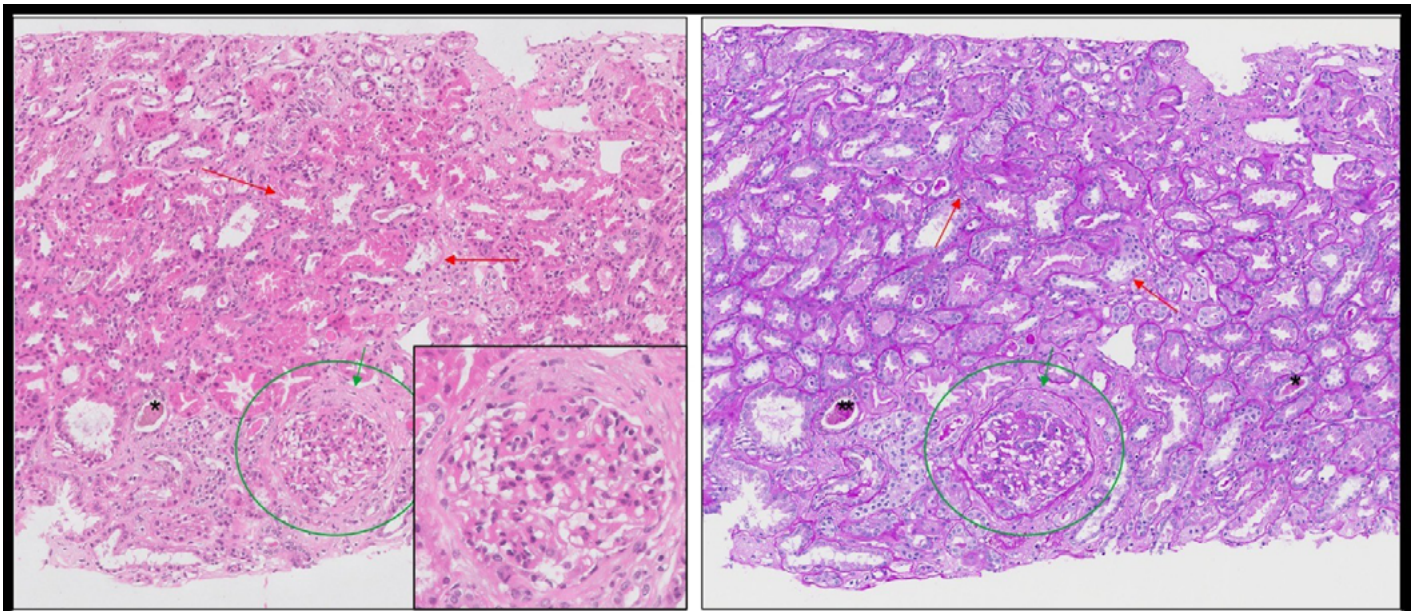
A 49-year-old man with active harmful alcohol use, under evaluation for nephrotic-range proteinuria. The physical examination revealed pitting edema extending to the pretibial region. Tests for autoimmunity (ANA, anti-PLAR2, ANCA, ENA, anti-MBG), complement, light chains, and protein profile were within normal limits. No structural abnormalities of the kidneys or liver were detected on ultrasound. Consequently, a renal biopsy was performed; the histopathological findings were consistent with IgA nephropathy, which—in the absence of initial evidence of liver disease or other triggering conditions—was attributed to a primary etiology.

During follow-up, the patient developed progressive deterioration of renal function (creatinine from 1.05 to 2.23 mg/dL) associated with a sustained increase in proteinuria (from 2 to 8 g/24 h). Given the suspicion of progression of primary IgA nephropathy, immunosuppressive therapy with mycophenolate mofetil and prednisone was initiated.

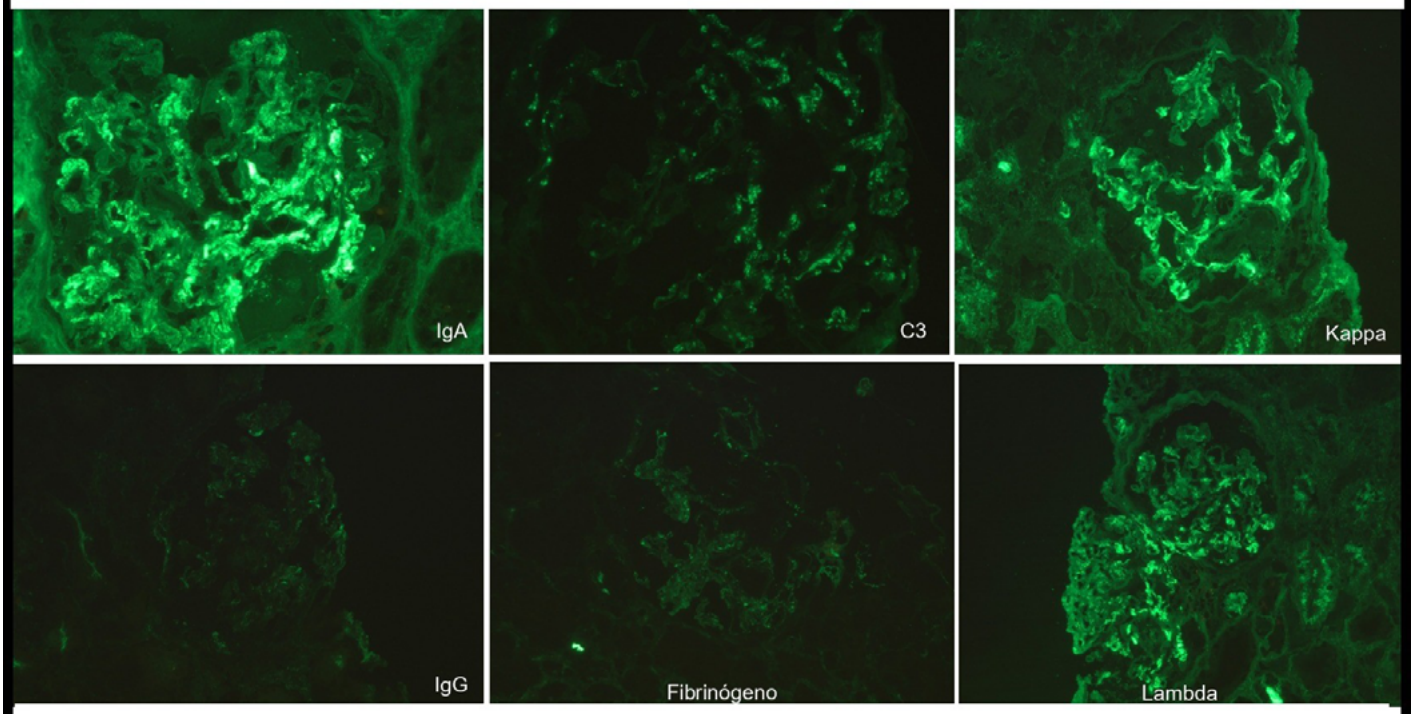
Despite treatment, renal function continued to deteriorate, with worsening edema in the lower extremities and the development of tension ascites. Analysis of the ascitic fluid confirmed a secondary cause related to portal hypertension, and abdominal ultrasound revealed findings consistent with advanced chronic liver disease, which had not been diagnosed previously. At the onset of liver disease, the Child-Pugh stage was B (9 points), with a MELD and MELD-Na score of 15 points.

The lack of response to immunosuppressive therapy, along with the incidental diagnosis of decompensated liver cirrhosis, led to a reevaluation of the cause of the nephropathy and the gradual discontinuation of the immunosuppressive regimen. The initiation of intravenous albumin therapy contributed to the resolution of the first episode of ascites decompensation and an improvement in renal function (1.5 mg/dL). Furthermore, cessation of alcohol consumption was accompanied by an improvement in liver function, contributing to further recovery of renal function. The lack of response to immunosuppressive therapy and the improvement in renal function parallel to the improvement in liver function led to a reconsideration of advanced chronic liver disease as the most likely cause of IgA nephropathy.

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H&E (left) and PAS (right) images of a renal core biopsy showing a glomerulus (green circle) with increased mesangial cellularity, mild segmental endocapillary hypercellularity, and an extracapillary component in the form of a predominantly fibrous crescent (green arrow). Mild interstitial fibrosis and tubular atrophy. A proportion of tubules display cytoplasmic microvesiculation, loss of the brush border (red arrow), and nuclear pyknosis, as well as intratubular red blood cell casts (asterisk). These features are accompanied by a sparse lymphocytic infiltrate.



Most relevant direct immunofluorescence findings, demonstrating granular, predominantly mesangial, diffuse, and global positivity for IgA (++/+++), C3 (++), kappa light chains (++), lambda light chains (++), fibrinogen (+), and IgG (+/-).

Figure 1. ***Anatomopathological examination of the renal biopsy, consistent with IgA nephropathy.***

Currently, the patient maintains stable renal function (creatinine 1.8 mg/dL; proteinuria 4 g/24 h) without an immunosuppressive regimen and while receiving weekly albumin infusions, although he has developed refractory ascites and is awaiting evaluation for a liver transplant (Child-Pugh C [11 points] with current MELD and MELD-Na scores of 22 and 24, respectively).

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Discussion

Chronic liver disease is the most common cause of secondary IgA nephropathy, although it can also occur in association with inflammatory bowel disease, celiac disease, neoplasms, or rheumatologic diseases.[1]. Distinguishing between primary and secondary IgA nephropathy is a clinical diagnosis of exclusion, since the histologic findings are indistinguishable between the two forms.[1,2].

IgA nephropathy secondary to chronic liver disease is an underdiagnosed condition, primarily because renal biopsy is not routinely performed in patients with cirrhosis who present with renal dysfunction; rather, it is reserved for cases of treatment failure, unfavorable clinical course, or suspicion of underlying nephropathy[1]. Consequently, it is very difficult to establish a specific prevalence, as reflected in the wide variability (9–64%) observed across different patient cohorts[1,2].

The findings of the pathogenic study of IgA nephropathy secondary to chronic liver disease remain insufficient, but several mechanisms appear to be involved: impaired hepatic clearance of immune complexes, increased intestinal translocation of IgA, and elevated plasma IgA concentrations. All these factors promote mesangial deposition of IgA complexes and consequent glomerular damage[3]. Furthermore, as illustrated in Clinical Case 1, the coexistence of chronic HBV infection adds a possible additional pathogenic mechanism. There is evidence that viral antigens (HBsAg, HBcAg) can be deposited in the glomerular mesangium and contribute to the formation of immune complexes that cause IgA nephropathy in chronic carriers of the virus[4,5].

The cases presented illustrate two different clinical scenarios in which an error in etiological classification occurs, with significant therapeutic consequences. The first case demonstrates how the initial assumption of hepatorenal syndrome—despite the presence of abnormalities in the urine sediment—can mask structural kidney disease. Although secondary IgA nephropathy is a recognized cause of renal function impairment in patients with cirrhosis, its diagnosis is complicated by the coexistence of other common conditions, such as hepatorenal syndrome, prerenal renal failure, or drug-induced nephrotoxicity.[6]. In this context, determining the etiology of renal impairment is typically based on clinical criteria, which may be insufficient to distinguish between functional and structural causes. Therefore, the presence of discordant clinical findings, abnormalities in the urine sediment, or a lack of response to medical treatment should prompt a diagnostic reevaluation, with the renal biopsy playing a key role[6].

In the second case, the presence of an initially undiagnosed underlying liver disease acted as a confounding factor in the assessment of renal function and led to a treatment choice with limited effectiveness. Although immunosuppressive therapy has been shown to be effective in certain settings of primary IgA nephropathy[7], current evidence does not support its use in forms secondary to liver cirrhosis. Even the latest update to the KDIGO guidelines[8] moves away from the widespread use of systemic glucocorticoids in primary forms and prioritizes therapies aimed at reducing immune complex formation, blocking the renin-angiotensin-aldosterone system, or inhibiting the sodium-glucose cotransporter type 2. It is important to note that the management of the primary form cannot be fully extrapolated to secondary forms. In fact, there is currently no specific treatment for secondary IgA nephropathy, and its prognosis depends largely on the course of the underlying disease.[3]. In selected cases of IgA nephropathy secondary to chronic liver disease, liver transplantation has been associated with a significant improvement in renal function[9], reinforcing the importance of accurate etiological diagnosis in these patients.

Conclusion

Both cases highlight the need for dynamic assessment of renal impairment in patients with cirrhosis and reinforce the need to maintain a high index of suspicion to prevent underdiagnosis of secondary IgA nephropathy[10], based on the integration of clinical, laboratory, and follow-up findings.

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MESENTERIC LYMPHANGIOMA: CLINICAL PRESENTATION, DIAGNOSIS AND MANAGEMENT. A CASE REPORT.

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Abstract

Mesenteric intestinal lymphangioma is a rare benign lymphatic malformation, typically asymptomatic and often detected incidentally on imaging studies. However, when radiological uncertainty exists, the differential diagnosis should primarily include peritoneal carcinomatosis. We present the case of a 47-year-old woman in whom a mesenteric cystic lesion consistent with this entity was identified. In the absence of symptoms or signs of complication or malignancy, clinical and radiological follow-up was chosen.

Keywords: mesenteric intestinal lymphangioma, incidental finding, peritoneal carcinomatosis.

Introduction

Mesenteric intestinal lymphangioma is a rare malformation of the abdominal lymphatic vessels of unknown etiology, although it may be due to an anomaly during embryonic development. Although benign in nature, it can lead to complications such as intestinal obstruction, gastrointestinal bleeding, chyloperitoneum, mesenteric torsion, or intussusception.

It most commonly presents as an incidental finding on imaging studies and becomes symptomatic when its size causes compression of neighboring structures or in the context of a complication.

Clinical case

A 47-year-old woman with no relevant medical history was referred by her primary care physician following incidental findings on a transvaginal ultrasound performed during a gynecological examination: an intra-abdominal mass located in the mesenteric fat at the level of the left renal fossa, requiring further evaluation. The patient is asymptomatic, except for occasional mild abdominal discomfort of long standing, which she treats with antispasmodics. Laboratory tests, including tumor markers, gastroscopy, and colonoscopy, were normal. Abdominal MRI reveals a low-density cystic lesion measuring

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4 × 4 × 3.3 cm that appears to arise from the mesenteric margin and the wall of a small bowel loop on LIF, with a multilocular morphology, no clearly defined wall, and no observable septa, internal solid components showing contrast enhancement, or areas of calcification. All of these findings are consistent with mesenteric intestinal lymphangioma.

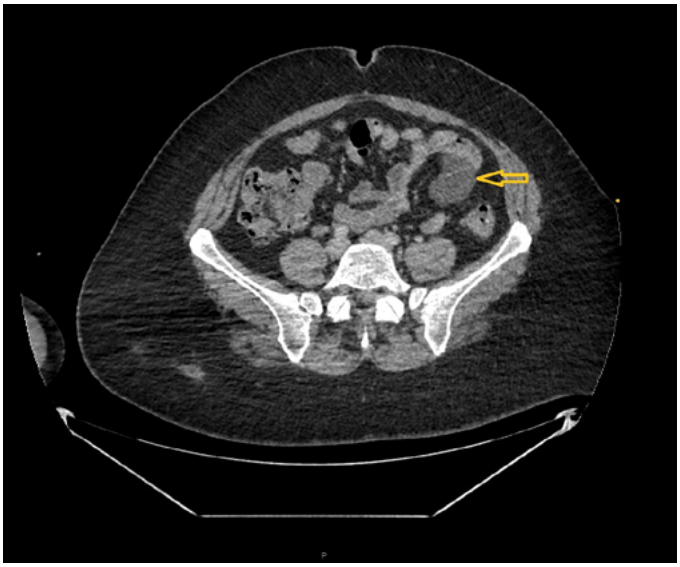


Figure 1. ***Abdominal CT scan Cystic lesion with homogeneous content and a broad base at the mesenteric margin.***

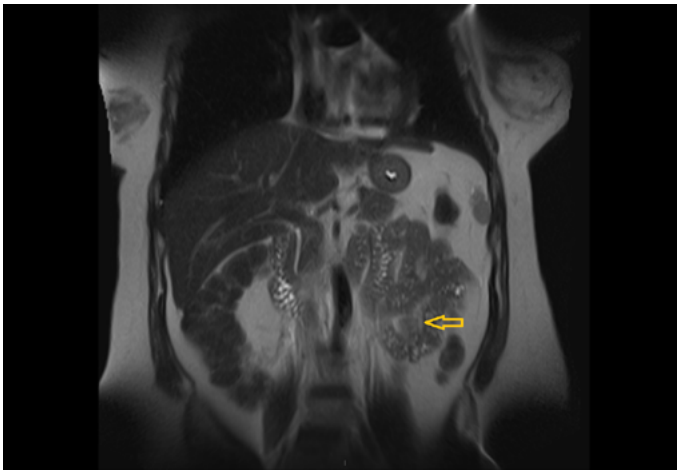


Figure 2. ***Cystic lesion measuring 41 x 32 mm with no clinically significant enhancement or diffusion restriction.***

Discussion

For better characterization, it is recommended to order an abdominal CT scan or MRI, as well as to assess the relationship with intestinal loops and blood vessels[1]. Radiologically, it is characterized as a cystic, multilocular lesion with anechoic content and no organ or vascular invasion; in some cases, it may present with thin septa[1]. However, when lesions are diffuse, they may resemble peritoneal carcinomatosis, requiring a differential diagnosis[2].

For small lesions without a compressive effect or suspected complications, clinical follow-up and annual imaging are recommended. At this point, it is essential to educate the patient about potential warning signs. Surgical resection should be indicated in the event of symptoms or complications; intestinal resection may be required if there is mesenteric infiltration or vascular involvement[3]. Alternatives to surgery may include percutaneous sclerotherapy[4] or sirolimus (an mTOR inhibitor) as an experimental option if there is a high surgical risk.

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