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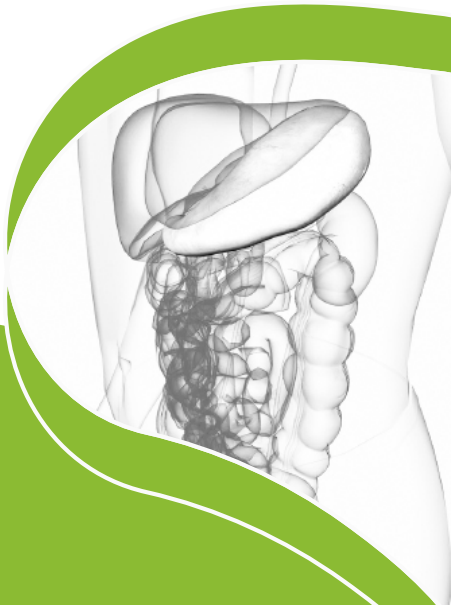

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1. RAPD Objectives and characteristics: The Revista Andaluza de Patología Digestiva is the official publication of the Andalusian Society of Digestive Pathology (SAPD), which since 2007 has been published in electronic format only, under the name RAPD 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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1° Full title of the paper in Spanish and English
2° Surnames and first names of all authors.
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4° Full postal address of the responsible author, to whom correspondence should be addressed, including telephone, fax and email address.
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 (optional also in English) and 3-5 keywords. The abstract will have a maximum length of 250 words and should be structured as follows:

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.*

Through the Manuscript Centre, and for the submission of Reviews and Issues and Updates, the following information will be required:

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1° Full title of the work (in Spanish and English).
2° Surnames and first names of all authors.
3° Centre(s) of origin(s) (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.
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).
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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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).
4°Acknowledgements
5° Figure captions.
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:

- General data:

1° Full title of the paper in Spanish (optional also in English).
2° Surnames and first names of all authors.
3° Centre(s) of origin(s) (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.

- 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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- General data:

1° Full title of the work in Spanish and English. 2° Surnames and first names of all authors.
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.

Through the Manuscript Centre, and for the submission of an Image of the Month, the following information will be required:

-General data:

1° Full title of the work in Spanish and English.. 2° Surnames and first names of all authors.
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.
5° Type of Image of the Month format chosen.

-Main body of the manuscript, containing:

1° Structured abstract in Spanish and English and 3-5 key words. The abstract will have a maximum length of 250 words.
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).
5° Figure captions.

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

material presented so require. It is not advisable to have more than 3 authors per chapter.

Through the Manuscript Centre, you will be asked to provide the following information:

- General data:

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.
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.
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 250 words.
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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1° Full title of the work in Spanish and English.
2° Surnames and first names of all authors. It is advisable to place a hyphen between the first and second surname.
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:

- Medical journal article: journal names should be abbreviated according to the style of the Index. Medicus/Medline (http://www.ncbi.nlm.nih.gov/journals?itool=sidebar).

- 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

- Article from a journal that is published only on the Internet, but is not conventionally arranged: the authors, the full name of the manuscript, the abbreviation of the journal, the year of publication and the DOI will be listed.

Rossi CP, Hanauer SB, Tomasevic R, Hunter JO, Shafran I, Graffner H. Interferon beta-1a for the maintenance of remission in patients with Crohn's disease: results of a phase II dose-finding study.BMC Gastroenterology 2009, 9:22doi:10.1186/1471-230X-9-22.

-Article published in an abstract or in a supplement of a journal: the authors (surname and first initial, separated by commas between authors), the full name of the manuscript, the word abstract in square brackets, the abbreviation of the journal, the year of publication and after a semicolon the volume of the journal, followed by the abbreviation Suppl, or Supl, in brackets and after a colon the complete numbers of the first and last page of the paper.

Klin M, Kaplowitz N. Differential susceptibility of hepatocytesto TNF-induced apoptosis vs necrosis [Abstract]. Hepatology 1998; 28(Suppl):310A.

- Books: the authors of the book (surname and first initial, comma separated by the authors), the title of the book, the city where it was published, the name of the publisher and the year of publication will be listed.

Takada T. Medical Guideline of Acute Cholangitis and Cholecystitis. Tokyo: Igaku Tosho Shuppan Co; 2005.

- Chapter of a book: the authors of the chapter should be listed (surname and first initial, separated by commas between authors), followed by In: the names of the editors of the book and, after a full stop, the name of the book. The city where it was published, the name of the publisher, the year of publication and after a colon the complete numbers of the first and last page of the work.

Siewert JR. Introduction. In: Giuli R, Siewert JR, Couturier D, Scarpignato C, eds. OESO Barrett's Esophagus. 250 Questions. Paris: Hors Collection, 2003; 1–3.

- Information from a document produced at a meeting: this type of reference should be avoided whenever possible. However, if it has to be cited, the title of the subject, the name of the meeting and the city where it was held should be given. The entity that organised the meeting, and the year. The e-mail address through which the document can be accessed.
U.S. positions on selected issues at the third negotiating session of the Framework Convention on Tobacco Control. Washington, D.C.: Committee on Government Reform, 2002. (Accessed March 4, 2002, at:http://www.house.gov/reform/min/inves_tobacco/index_accord. htm.)

Figures, tables and videos: iconography, whether photographs, radiographs, diagrams or graphs, should be referred to under the generic name of "Figure". References to figures, tables and videos should be highlighted in bold. They should be numbered with Arabic numerals, according to their order of appearance in the text. Panels of two or more photographs grouped together will be considered as a single figure and may be referred to as "Figures 1A, 1B, 1C".

- Photographs: photographs should be sent in digital format TIFF (.TIF), JPEG (.JPG) or BMP, in black and white or colour, well contrasted, with an appropriate resolution (preferably 150-300 dots per inch). In the case of JPEG files, the minimum compression should be used to maintain maximum quality, i.e. in a non-reduced size.

X-ray, ultrasound, CT and MRI images, if not directly available in electronic format, should be scanned in grayscale and saved in JPG format.

Endoscopic images and other techniques generating colour images, if not directly available in electronic format, shall be scanned in colour. Special details shall be indicated by arrows, using for these and any other type of symbols the maximum contrast plot with respect to the figure.

Figure files will be identified according to their order of appearance in the text, with the name of the file, its number and surname of the first signatory (e.g.: fig1_Gómez.jpg) or the title of the article. Each image must have an associated figure caption that serves as a description. Figure captions must be submitted in a separate text document with clear reference to the figures to which they refer. Images may be inserted in Word/PowerPoint files to facilitate their identification or association with the figure captions, but they must always be submitted as separate images in the formats mentioned above.

Photographs of patients must not make them unidentifiable. If it is not possible to obtain them, the publication of the photograph must be accompanied by written permission (Model Photograph Permission Form).

- Diagrams, drawings, graphs and tables: diagrams, drawings, graphs and tables must be sent in digital format, as high resolution images or, preferably, in Word/PowerPoint format with editable text. Schemes, drawings, graphs or figures scanned from other publications will not be accepted. For diagrams, drawings, graphs, tables or any other figures, the colour black should be used for lines and text, and a light background, preferably white. If it is necessary to use several colours, easily distinguishable colours with high contrast to the background should be used. Graphics, symbols and letters should be of sufficient size to be clearly identifiable when reduced. Tables should be made with the -Table- tool (not with the use of tabulators and drawing lines or text boxes).

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ORIGINAL

SHORT- AND LONG-TERM EFFECTIVENESS OF RISANKIZUMAB IN CROHN'S DISEASE: RESULTS IN REAL-WORLD CLINICAL PRACTICE IN TWO TERTIARY HOSPITALS IN MÁLAGA.

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Abstract

Introduction: The therapeutic arsenal for Inflammatory Bowel Disease (IBD) has grown in recent years. Interleukin-23 (IL-23) p19 subunit inhibitors represent an emerging therapy for these patients. Risankizumab is an IL-23 inhibitor approved for the treatment of patients with moderate to severe Crohn's disease (CD).

Objectives: To evaluate the effectiveness, survival, and short- and long-term safety of risankizumab in patients with Crohn's disease (CD).

Methods: Retrospective, multicenter, observational study of Crohn's disease patients from the Virgen de la Victoria University Hospital and the Regional University Hospital of Málaga treated with risankizumab. The primary endpoint was the clinical remission rate, calculated using the Harvey Bradshaw (HBI) clinical index.

Results: A total of 51 patients were included. Clinical remission rates at 12, 26, and 52 weeks were 43.1%, 45.1%, and 49%, respectively. The median duration of treatment was 18 months, with a 12-month survival rate of 84% and a 24-month survival rate of 75%.

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Gutiérrez Martínez F, García Fuentes E, Olmedo Martín R, Fernández Castañer A, Rodríguez González F, VanDussen Martos JV et al. Short- and long-term effectiveness of risankizumab in Crohn's disease: Results in real-world clinical practice in two tertiary hospitals in Malaga. RAPD 2026;49(2):43-49. DOI: 10.37352/2026492.1

Only one patient experienced treatment-related side effects requiring discontinuation.

Conclusion: In this cohort of patients from routine clinical practice, risakizumab treatment was effective in inducing and maintaining remission, with a good safety profile.

Keywords: Crohn's disease, Risankizumab, Effectiveness.

Introducción

Interleukin-23 (IL-23) inhibitors represent one of the emerging advanced therapies for the treatment of inflammatory bowel disease (IBD) in patients who have shown an inadequate response, loss of response, or intolerance to conventional or biologic therapy. These drugs bind to the p19 subunit of IL-23, thereby inhibiting IL-23-dependent cellular signaling and the subsequent release of proinflammatory cytokines[1].

The IL-23 inhibitors approved for the treatment of Crohn's disease (CD) are guselkumab, mirikizumab, and risankizumab.

Focusing on risankizumab, the pivotal study supporting its approval for CD consists of two induction trials (ADVANCE and MOTIVATE) and one maintenance trial (FORTIFY). These studies reported clinical remission rates of 45% and 42% after 12 weeks of treatment and 52% after 52 weeks[2,3].

The objective of this study was to evaluate the effectiveness of risankizumab in patients with CD.

Methodology

Design and study population

We conducted a retrospective, multicenter observational study that included patients diagnosed with CD aged 18 years or older who were being followed at the Virgen de la Victoria Hospital (HVV) and the Regional University Hospital (HRU) in Málaga and who initiated treatment with risankizumab between November 2023 and October 2024. Patients with ulcerative colitis or unclassified colitis were excluded. Data were obtained by reviewing the medical records of participating patients using an anonymous database created for this purpose.

The primary objective of the study was to analyze remission rates and clinical response at 12, 26, and 52 weeks after initiating treatment with risankizumab. Clinical response was defined as a decrease of ≥3 points in the Harvey-Bradshaw Index (HBI), and clinical remission was defined as an HBI score of ≤4. Biological remission was assessed by measuring fecal calprotectin (FCP) using an enzyme-linked immunosorbent assay (ELISA).

Biological remission was defined as FCP values <250 µg/dL.

Corticosteroid-free clinical remission was defined as an HBI score of ≤4, along with the absence of a need to introduce corticosteroids (systemic or topical) during treatment with risankizumab. For patients who started risankizumab and were previously on active corticosteroid therapy, corticosteroid-free clinical remission was defined as the ability to discontinue corticosteroids within 12 weeks.

Statistical Analysis

Qualitative variables were presented as absolute values and percentages, while quantitative variables were presented as medians and interquartile ranges (IQR).

Statistical comparisons of clinical markers (HBI) and biomarkers (FCP) were performed using the Wilcoxon test. A p-value ≤ 0.05 was considered statistically significant. Qualitative variables were compared using the chi-square test. Drug persistence was calculated using Kaplan–Meier curves. IBM SPSS Statistics was used for the statistical analysis of the data.

Results

Demographic and Clinical Variables

A total of 51 patients were included in the study, 15 from the HVV and 36 from the HRU. Table 1 summarizes the clinical and demographic characteristics, and figure 1 shows the patient flow.

Analysis of Clinical Remission

Table 2 shows the median HBI score at 12, 26, and 52 weeks after the start of treatment. Figure 2 illustrates the rates of remission and clinical response, both with and without concomitant corticosteroid therapy.

The median baseline HBI score for patients was 8 (IQR 6–12), decreasing to 6 (IQR 4–9) at week 12 ($p < 0.001$), to 5 (IQR 0–3) at week 26 ($p < 0.001$), and to 4 (IQR 3–7) at week 52 ($p < 0.001$).

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	Risankizumab
Baseline characteristics	(Patients n=51)
Age (years), median (IQR)	50
Gender, n (%):	
Man	20 (39.2)
Women	31 (60.8)
Smokers, n (%)	9 (17.6)
Duration of disease (years), median (IQR):	13 (7–23)
Extent, n (%)	
Ileal	30 (58.8)
Colonic	3 (5.9)
Ileocolitis	16 (31.4)
High-grade involvement	2 (3.9)
Pattern of involvement, n (%)	
Inflammatory	16 (31.4)
Stenosing	23 (45.1)
Fistulizing	12 (23.5)
Perianal disease, n (%)	13 (25.5)
Previous surgeries, n (%)	27 (52.9)
MEI	
Rheumatology, n (%)	4 (7.8)
Dermatology, n (%)	5 (9.8)
Ophthalmology, n (%)	0 (0)
Hepatobiliary, n (%)	0 (0)
Hematologic, n (%)	0 (0)
Bone, n (%)	1 (2)
Total, n (%)	10 (19.6)
Previous anti-TNF treatment, n (%)	44 (86.3)
Previous treatments, n (%)	
Infliximab	31 (60.8)
Adalimumab	28 (54.9)
Ustekinumab	38 (74.5)
Vedolizumab	11 (21.6)
Upadacitinib	5 (9.8)
Number of previous biologics/small molecules, n (%)	
0	1 (2)
1	11 (21.6)
2	20 (39.2)
3	14 (27.5)
≥4	5 (9.8)
IQR: Interquartile range n: Number EIM: Extraintestinal manifestations Spa: Spondyloarthropathies	

Table 1. ***Demographic and clinical variables.***

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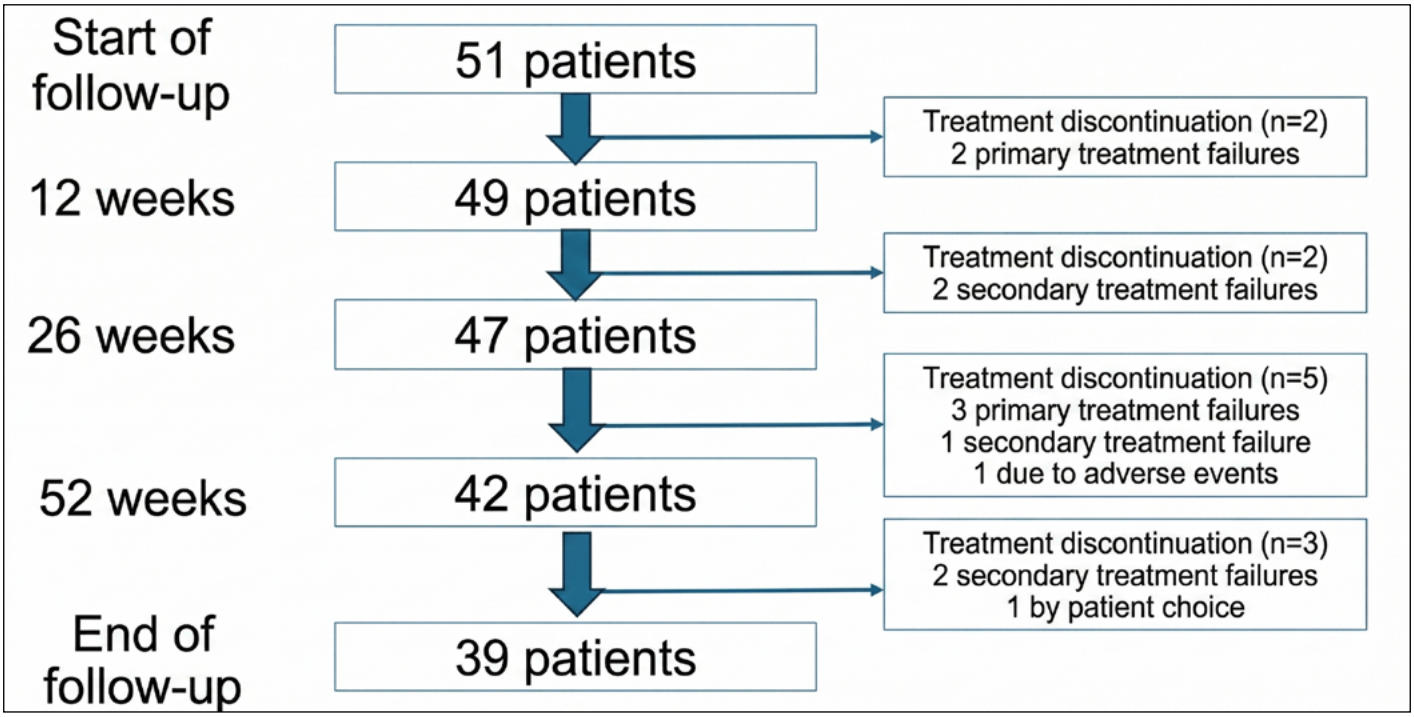

Figure 1. ***Patient flow.***

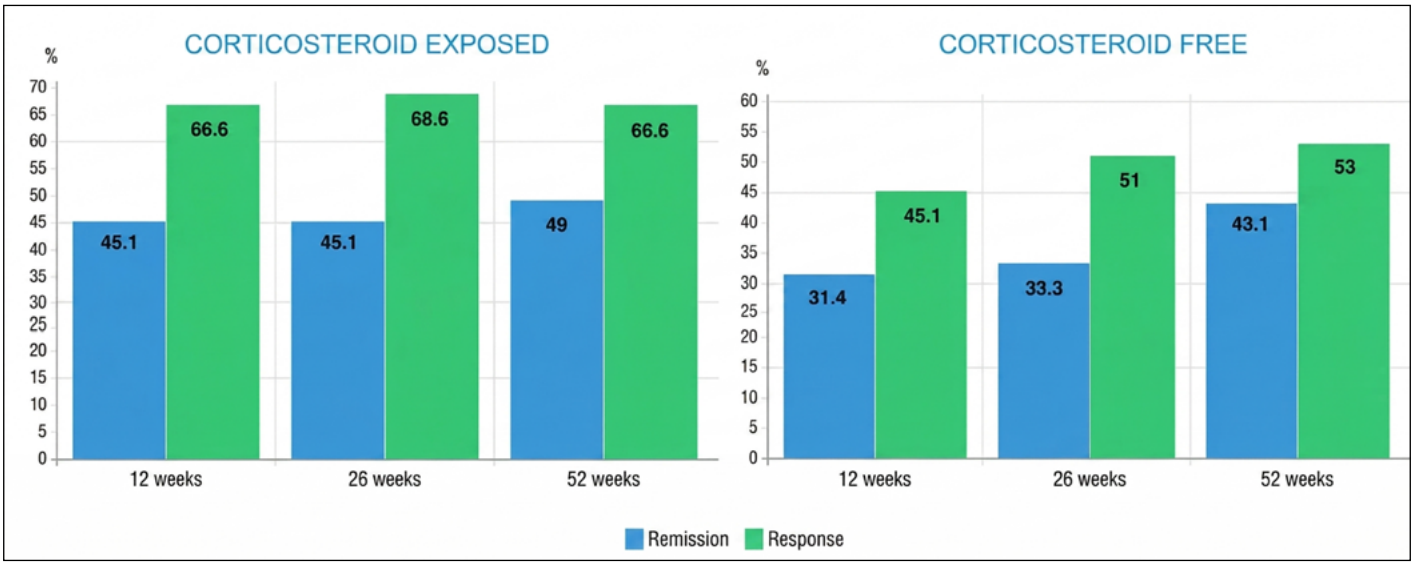

Figure 2. ***Remission and short-, medium-, and long-term clinical response in patients exposed to corticosteroids (A) and in corticosteroid-free patients (B).***

Baseline HBI, median (IQR) [n]	8 (6-12) [n=51]
HBI 12 w, median (IQR) [n]	6 (4-9) [n=51]
HBI 26 w, median (IQR) [n]	5 (3-8) [n=49]
HBI 52 w, median (IQR) [n]	4 (3-7) [n=47]
HBI: Harvey-Bradshaw Index; w: weeks	

Table 2. ***Scores on clinical indices.***

From the 51 patients included at the start of follow-up, at 12 weeks, 66.6% (34/51) achieved a clinical response and 45.1% (23/51) achieved remission. Of the patients who achieved remission, 31.4% (16/51) did so without corticosteroids.

At 26 weeks, 68.6% (35/51) achieved a clinical response. Remission was achieved by 45.1% of patients (23/51), of whom 33.3% (17/51) achieved it without corticosteroids.

66.6% (34/51) responded after 52 weeks of treatment. Of these patients, 49% (25/51) achieved clinical remission,

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and 43.1% (22/51) did so without the need for corticosteroid therapy.

The risankizumab maintenance regimen was intensified in 10 patients who had shown an incomplete response. In all cases, the dosing interval was shortened from 360 mg subcutaneously every 8 weeks to every 6 weeks. The median time to initiation of the intensified regimen was 9.5 months (IQR 6–14). 30% of the patients who received intensified treatment (3 out of 10) experienced a clinical response following this change.

Analysis of Biological Remission

Biological remission, defined as an FCP < 250, was achieved in 11 patients (21.56%) at both 12 and 26 weeks ($p < 0.05$), and in a total of 12 patients (23.52%) at 52 weeks ($p < 0.001$) (Figura 3).

Treatment persistence

The persistence curve for risankizumab is shown in Figure 4.

The median treatment duration was 18 months (IQR 14–20), with treatment persistence at 12 months of 84% and 75% at 24 months. A total of 12 patients (23.5%) discontinued risankizumab during follow-up. The reasons for discontinuation were: primary failure in 5 patients (41.6%), secondary failure in another 5 (41.6%), adverse effects in 1 (8.3%), and 1 case of a patient who voluntarily decided to discontinue treatment (8.3%). The median time to discontinuation was 10 months (IQR 6–13.5).

Treatment Safety

17.6% of patients (9/51) reported adverse events during treatment with risankizumab, most of which were mild (headache, rhinitis, dizziness, etc.). Only 5.8% (3/51) experienced a serious adverse event: (a) urinary tract infection, (b) pneumonia, and (c) a neoplastic disease (small intestine adenocarcinoma), the latter being the only patient in the study who permanently discontinued treatment due to an adverse event, although this cannot be directly attributed to the drug.

Discussion

Risankizumab is a drug recently added to the therapeutic arsenal for CD, so references in the literature regarding it are scarce. This study evaluated the efficacy and safety of risankizumab treatment in patients with CD refractory to other therapies in real-world clinical practice at two tertiary care hospitals in the city of Málaga.

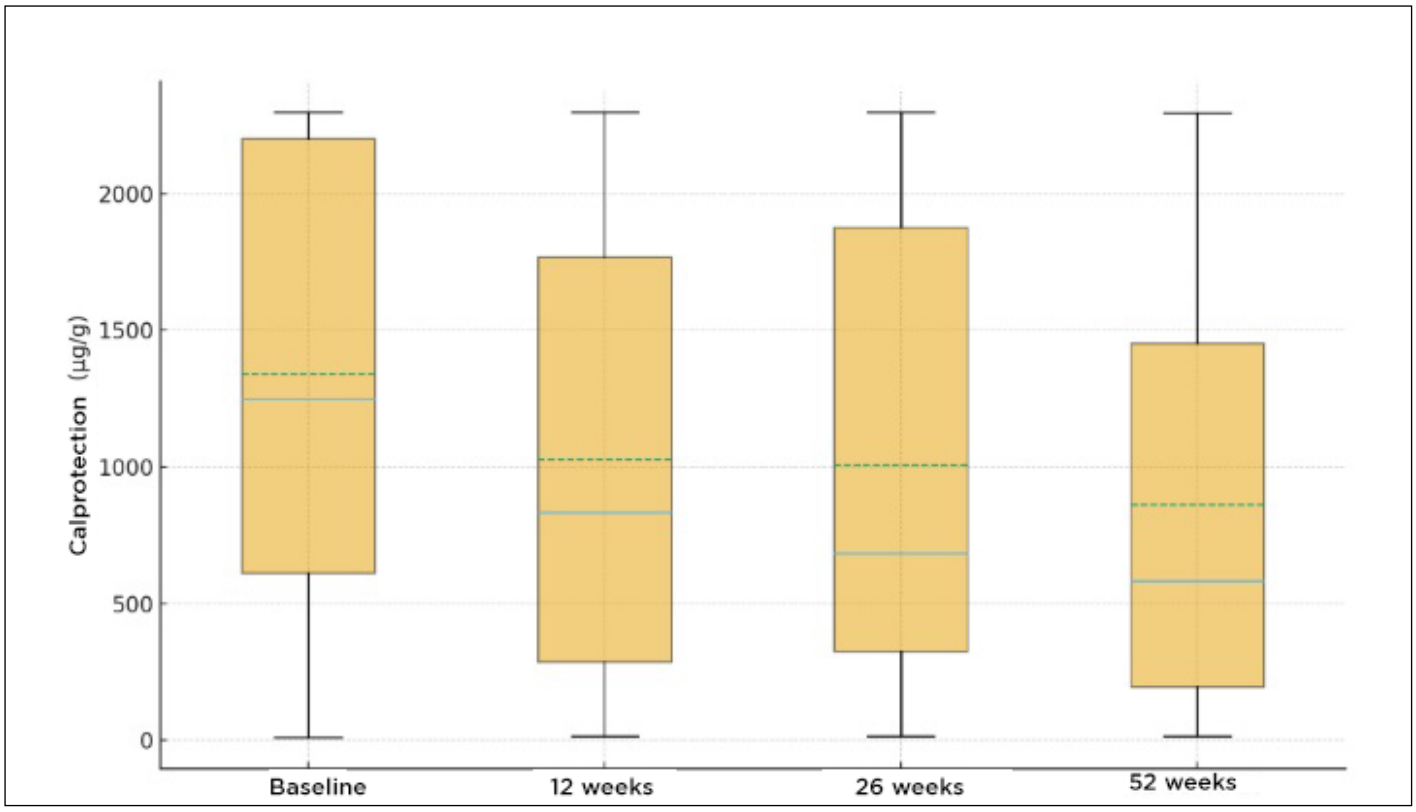

Figure 3. ***Box plots of the FCP at the four evaluation time points.***

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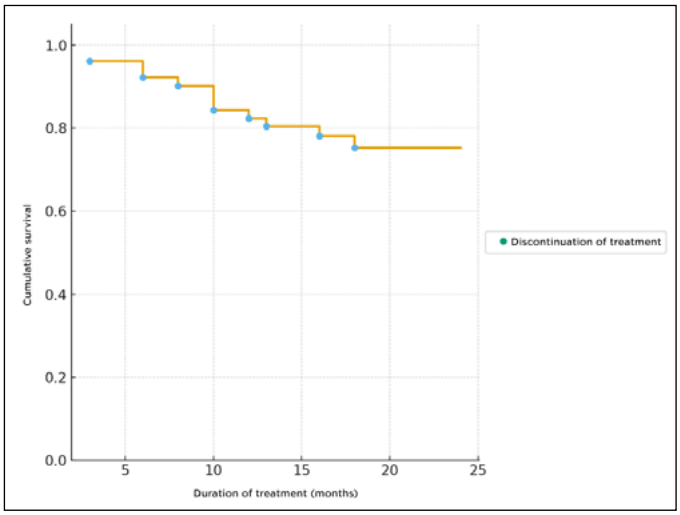

Figure 4. ***Treatment persistence curve.***

The clinical remission rates observed at weeks 12 and 52 were virtually identical to those reported in the pivotal studies (45% and 42% at 12 weeks and 52% at 52 weeks)[2,3], and are also consistent with the major real-world studies published to date, which, like our study, included a highly refractory population[4-8].

Our mid- and long-term results show that risankizumab is effective in maintaining the response over time, with a treatment persistence rate at one year of 84%, data that are consistent with other real-world studies[9-11].

Normalization of FCP was achieved in approximately 1 in 4 patients following induction in our study, findings equivalent to a post-hoc analysis of the pivotal risankizumab study[12].

A favorable safety profile was observed, with a rate of serious adverse events below 6%, a figure similar to that reported in the pivotal studies[2,3] and the main real-world studies[6,7].

The study's limitations stemmed from its retrospective observational nature, small sample size, and the absence of systematic endoscopic evaluation and imaging parameters (ultrasound or enteric MRI) to assess treatment response.

In conclusion, risankizumab is an effective treatment for patients with Crohn's disease who are refractory to other advanced therapies in real-world clinical practice, with a good long-term treatment persistence rate and an acceptable safety profile.

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REVIEW ARTICLE

IgG4-RELATED GASTROINTESTINAL DISEASE

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Abstract

IgG4-related disease (IgG4-RD) is a chronic, immune-mediated, systemic fibroinflammatory disorder characterized by a dense IgG4-positive lymphoplasmacytic infiltrate, storiform fibrosis and, in many organs, obliterative phlebitis[1,2]. Although the pancreas is its hallmark site as type 1 autoimmune pancreatitis, the disease may also involve the biliary tract, liver, gastrointestinal tract, mesentery and several extra-digestive organs[2,4,5]. Clinical heterogeneity and overlap with malignancies, infections and other autoimmune diseases make early recognition challenging[2,8].

Diagnosis relies on the integration of clinical, serological, radiological and histopathological findings. Elevated serum IgG4 may support suspicion, but it lacks specificity and can be normal in a relevant proportion of patients[5,8,26]. Recent advances in immunopathogenesis have highlighted the role of clonal cytotoxic CD4+ T cells and circulating plasmablasts as key drivers of inflammatory activity and fibrosis[2,10,27]. In pancreatic disease, the HISORt criteria remain particularly useful in clinical practice, whereas the 2019 ACR/EULAR classification criteria have helped standardize patient inclusion in research settings[3,13,15].

Glucocorticoids remain the first-line therapy for remission induction, with high response rates[13,23]. Rituximab has become established in refractory or relapsing disease and in selected high-risk patients, although uncertainty remains regarding the optimal maintenance strategy[24,25,30]. In this evolving therapeutic landscape, inebilizumab has emerged as one of the most relevant recent advances after positive phase 3

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results, reinforcing the role of B-cell–targeted therapy in IgG4-RD. This review summarizes current evidence on epidemiology, pathogenesis, diagnosis, gastrointestinal manifestations, treatment and prognosis of IgG4-RD, with special emphasis on its relevance in Digestive Diseases.

Keywords: IgG4, autoimmune pancreatitis, IgG4-related sclerosing cholangitis, Fibrosis, Rituximab.

Introduction

IgG4-related disease (IgG4-RD) was recognized as a distinct entity at the beginning of this century following the description of elevated serum IgG4 levels in patients with sclerosing pancreatitis[1]. It is currently considered a systemic fibroinflammatory disease capable of affecting numerous organs, including the pancreas, biliary tract, liver, salivary glands, kidneys, retroperitoneum, lungs, and gastrointestinal tract[2,3,8]. Its clinical significance lies in its ability to mimic neoplasms or other inflammatory diseases and in the risk of irreversible fibrosis when diagnosis and treatment are delayed[2,8,27].

From a gastrointestinal perspective, type 1 autoimmune pancreatitis is the most common manifestation, but not the only one. IgG4-associated sclerosing cholangitis, liver involvement, gastrointestinal tract infiltration, and sclerosing mesenteritis broaden the clinical spectrum and present significant diagnostic challenges for the gastroenterologist[4-7,12].

The aim of this review is to provide an update on the epidemiological, pathogenic, diagnostic, and therapeutic aspects of IgG4-RD, with an emphasis on gastrointestinal manifestations and the practical elements of greatest clinical utility.

IgG4-related disease

IgG4-RD is a systemic immune-mediated disease characterized by IgG4-positive plasma cell-rich lymphoplasmacytic infiltration, fibrosis, and, depending on the organ, obliterative phlebitis[2,8,11]. Its presentation is heterogeneous and depends on the anatomical location and the number of organs involved. More than half of patients have multiorgan involvement, and prolonged disease progression can lead to irreversible structural damage[8,12,27].

Epidemiology

The disease predominantly affects adults between the ages of 50 and 70, although pediatric and elderly cases have been reported[5,7]. There is a male predominance in the pancreatobiliary and retroperitoneal forms, while head and neck involvement may be relatively more common in women[5,8]. The incidence and prevalence are likely underdiagnosed. Recent population-based studies in the United States estimate an approximate incidence of 0.78–1.39 cases per 100,000 person-years and a rising prevalence, in parallel with increased recognition of the disease[9].

Pathogenesis

The pathogenesis of IgG4-RD is complex and involves a combination of genetic susceptibility, repeated antigenic exposure, and a dysregulated immune response[2,8,10]. Key mechanisms include the activation of follicular T helper cells, which promote isotype switching in B cells toward IgG4 and IgE, and the interaction between B cells, plasmablasts, and effector T cell subpopulations in target tissues[8,10].

Recent studies have established the central role of clonal cytotoxic CD4+ T cells, particularly those with the SLAMF7+ phenotype, as the primary effectors of tissue damage[10,27]. These cells produce profibrotic cytokines such as TGF-β and IFN-γ, exhibit clonal expansion in peripheral blood and affected tissues, and correlate with disease activity[10,27]. It has also been suggested that part of the therapeutic effect of rituximab may depend on the disruption of the antigenic support that B cells provide to these effector T cell populations[2,10,27].

Likewise, circulating plasmablasts have emerged as a dynamic biomarker of inflammatory activity. Their quantification appears to offer greater sensitivity than serum IgG4 in some contexts, including in patients with normal levels of this immunoglobulin, which reinforces their potential utility for monitoring[10,26,27].

Despite the association between the disease and elevated serum and tissue IgG4 levels, the exact role of IgG4 in the pathogenesis remains unclear. Rather than necessarily acting as a direct mediator of tissue damage, it may serve as a marker of a more complex abnormal immune response[8,10].

Histopathology

Histopathology is a cornerstone of diagnosis. The three classic features are: dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis[8,11]. The expression of each of these features varies depending on the affected organ, and they are not always present simultaneously. The diffuse lymphoplasmacytic infiltrate represents one of the

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most characteristic findings on histological examination (Figure 1), while storiform fibrosis constitutes another of the most representative morphological features of the condition (Figure 2)[8,11]. Obliterative phlebitis, when present, also carries significant diagnostic weight (Figure 3)[8,11]. Immunohistochemistry demonstrates an increase in IgG4+ plasma cells and an elevated IgG4+/IgG+ ratio, typically exceeding 40%, although the cutoff value should be interpreted according to the tissue analyzed[8,11].

Storiform fibrosis represents a whorled arrangement of collagen bundles, particularly useful for diagnosis in deep organs[11]. It should be noted that the patchy distribution of lesions may limit the yield of small biopsies, especially in needle-core samples[11,15].

Serology and biomarkers

Most patients have elevated serum IgG4 levels, although these may be normal in a significant percentage of cases[5,8,26]. Furthermore, elevated serum IgG4 is nonspecific and can be observed in other inflammatory, infectious, or neoplastic diseases[5,8,26]. Therefore, its utility is complementary and never sufficient to confirm the diagnosis on its own.

In addition to serum IgG4, other immunological abnormalities of interest have been described. Peripheral eosinophilia and elevated serum IgE are relatively common findings and reflect a predominantly Th2 immune profile[10,26]. In patients with renal involvement, hypocomplementemia may be observed, with decreased C3 and C4 levels, associated with increased inflammatory activity[26]. However, there is currently no single biomarker with sufficient sensitivity and specificity to establish a diagnosis of IgG4-RD on its own[2,10,26].

Clinical presentation

The clinical presentation of the disease is highly variable and often insidious[2,5,8]. General symptoms include asthenia, weight loss, low-grade fever, pain or enlargement of the affected organ, and, in some cases, systemic symptoms[5,8,12]. This nonspecific profile necessitates a broad differential diagnosis, which includes neoplasms, lymphomas, infections, and other autoimmune or fibroinflammatory diseases[2,8,27].

Imaging tests and classification criteria

Imaging techniques play a fundamental role in both diagnosis and in assessing extent and monitoring[4,5,13,16]. Contrast-enhanced computed tomography (CT) is useful in the initial evaluation, especially of the pancreas, biliary tract, retroperitoneum, and large vessels[4,5,16]. Magnetic resonance imaging (MRI) and magnetic resonance cholangiography (MRCP) provide better tissue and ductal characterization[4,5,16]. Positron emission tomography (PET-CT) can identify subclinical multiorgan involvement and is particularly valuable in systemic disease[2,4]. Endoscopic ultrasound allows for targeted tissue sampling in the pancreas and biliary tract[4,13].

In 2019, the American College of Rheumatology and the European League Against Rheumatism developed classification criteria with the aim of standardizing patient inclusion in

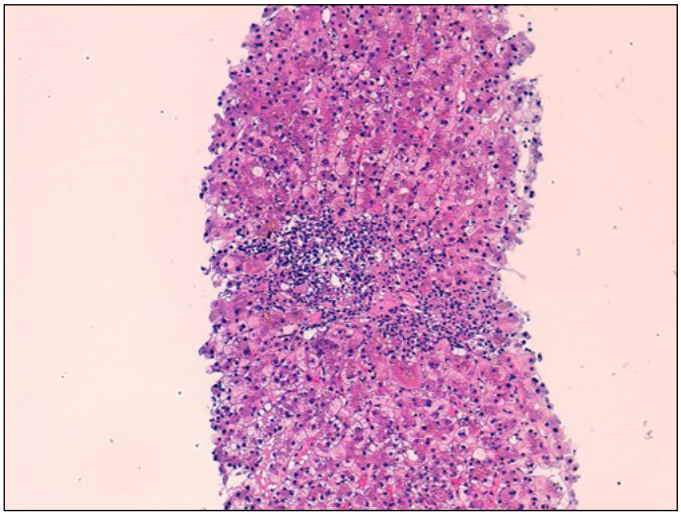

Figure 1. ***Histological image showing a dense, diffuse lymphoplasmacytic infiltrate. Courtesy of Dr. Teresa Pereda, Costa del Sol Hospital (Marbella).***

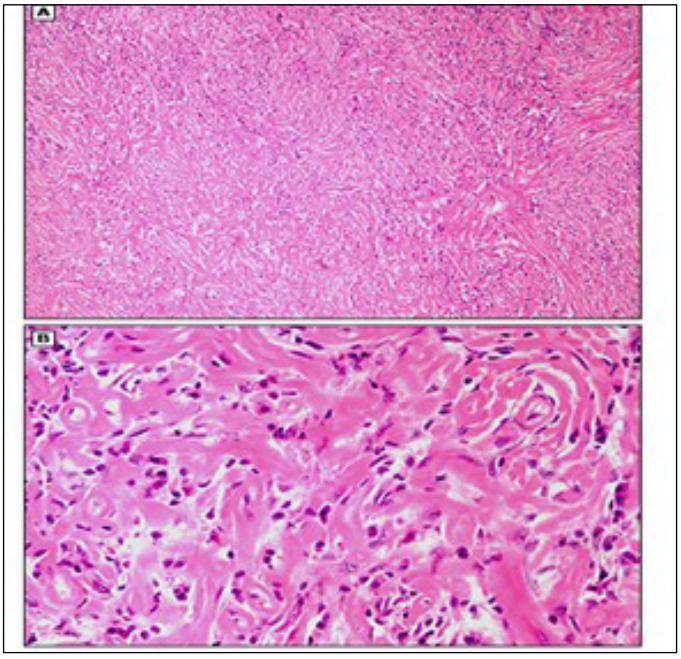

Figure 2. ***Histological image showing swirling fibrotic tissue surrounding a cellular infiltrate within collagen fibrils (A). Image B shows stellate fibrosis surrounded by a lymphoplasmacytic infiltrate.***

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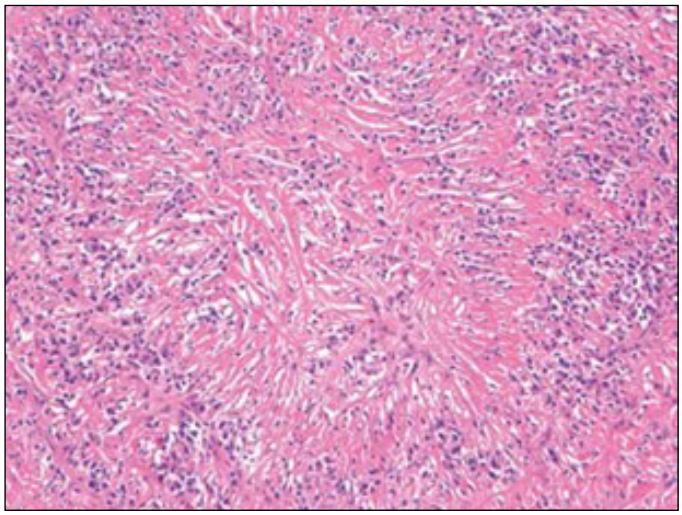

Figure 3. ***Histological image showing partial or complete obliteration of the medium-sized veins, secondary to lymphoplasmacytic infiltration, consistent with obliterative phlebitis.***

clinical studies[3]. These criteria were designed for classification purposes rather than strictly for diagnosis; therefore, their application in clinical practice must be contextualized within a comprehensive evaluation[2,3]. The diagnosis of IgG4-RD continues to be based on a combination of clinical, serological, radiological, and histopathological findings, with the exclusion of mimicking conditions[2,3,8]).

General diagnosis

In the context of pancreatic involvement, the HISORt criteria remain highly clinically useful, especially when histological confirmation is not feasible[13,15]. This approach integrates histology, imaging, serology, involvement of other organs, and response to treatment[13,15]. Response to glucocorticoids, in the absence of data suggestive of malignancy, remains a relevant guiding factor, although it should never be used in isolation if suspicion of cancer persists[2,13,15].

Gastrointestinal manifestations

Autoimmune Pancreatitis

Pancreatic involvement is the most common and best-characterized manifestation of IgG4-related disease[45,12,13]. Type 1 autoimmune pancreatitis corresponds to the IgG4-related variant, whereas type 2 does not fall within this spectrum[13,14]. The type 1 form is characterized by an IgG4+ cell-rich lymphoplasmacytic infiltrate, periductal fibrosis, and progressive sclerosis[13-15].

Clinically, it may present as painless obstructive jaundice, a focal pancreatic mass, diffuse pancreatic enlargement, or, less frequently, episodes of acute pancreatitis[13-15]. In advanced stages, it may progress to endocrine or exocrine pancreatic insufficiency[13,14]. From a radiological perspective, the diffuse form typically shows the classic "sausage-shaped pancreas"(Figure 4), while the focal form may mimic pancreatic adenocarcinoma (Figure 5)[5,14,16]. The capsular halo sign is another classic imaging finding and may support the diagnosis(Figure 6), although it is not pathognomonic[5,14,16].

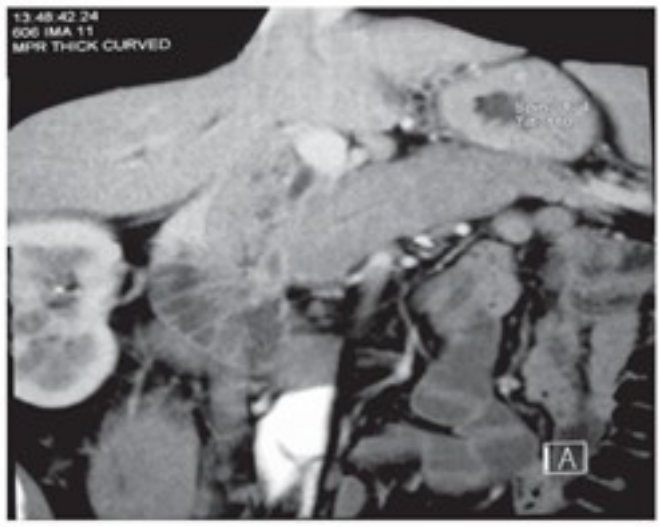

Figure 4. ***A cross-sectional CT scan of the abdomen showing (red arrows) a hypodense peripheral ring surrounding the pancreas, known as the "halo sign."***

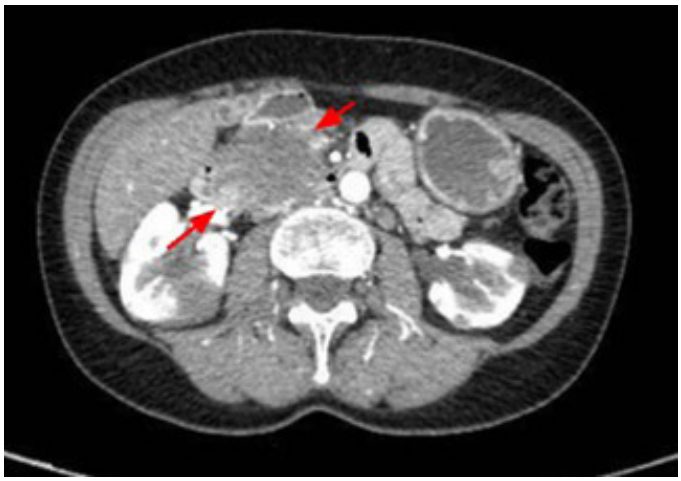

Figure 5. ***Coronal CT scan of the abdomen showing diffuse enlargement of the pancreas without peripancreatic inflammatory changes, consistent with "sausage-shaped pancreas."***

Differential diagnosis with pancreatic cancer is a priority. Integrating clinical, serological, radiological, histological, and extrapancreatic data helps improve diagnostic accuracy and avoid unnecessary surgeries[2,13-16].

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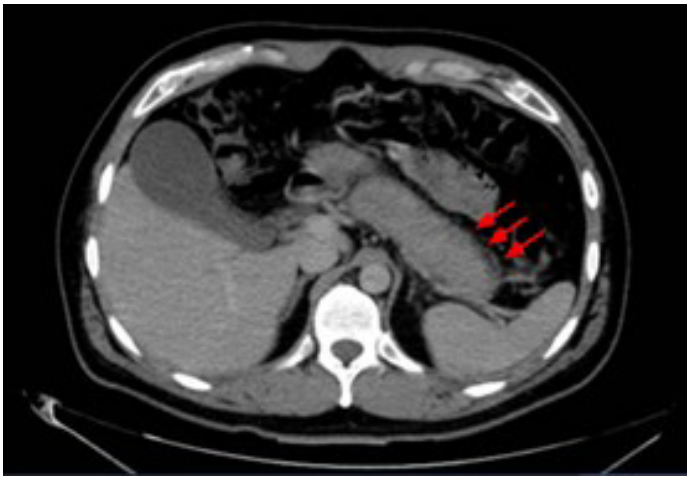

Figure 6. Abdominal CT cross-section showing focal involvement of the pancreatic head (red arrows) in the context of PAI. Malignancy must be ruled out.

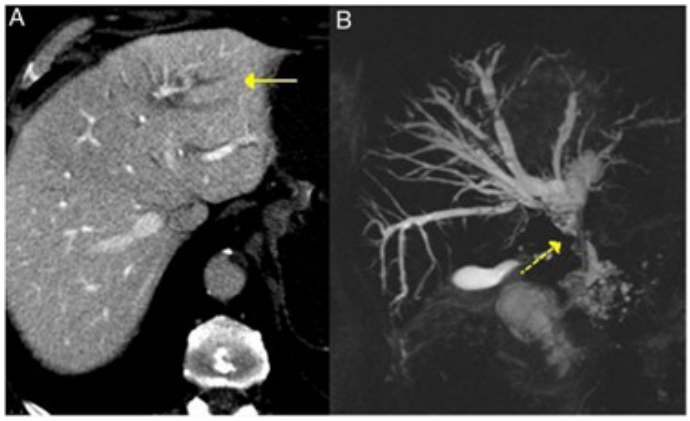

Figure 7. Image A shows a CT slice with dilation of the left intrahepatic bile duct (solid arrow). Image B shows an MR cholangiography slice with dilation of the left and right intrahepatic bile ducts and the extrahepatic bile duct, with stenosis in the middle third of the common bile duct (dashed arrow).

Hepatic and biliary involvement

The most significant biliary manifestation is IgG4-associated sclerosing cholangitis, which frequently occurs in patients with type 1 autoimmune pancreatitis[4,5,17,23]. It typically presents as obstructive jaundice or abnormal liver function tests[5,17]. Imaging studies show long, smoothly contoured strictures, unlike the typical pattern of primary sclerosing cholangitis; CT and MR cholangiography demonstrate biliary dilation and characteristic stenotic segments (Figure 7)[5,17,23]. Response to glucocorticoids is a highly informative clinical finding[17,23].

IgG4-associated autoimmune hepatitis remains a controversial area. Although a subgroup of patients with classic autoimmune hepatitis and abundant portal infiltration of IgG4+ plasma cells has been described, it is not yet fully clarified whether this represents a true hepatic manifestation of IgG4-RD or a subtype of autoimmune hepatitis[18-20].

Hepatic pseudotumors represent a less common form of presentation. Histologically, they may show a fibroinflammatory or lymphoplasmacytic pattern, and it is essential to differentiate them from primary or metastatic neoplasms[4,12].

Involvement of the gastrointestinal tract

Direct involvement of the gastrointestinal tract is rare and remains one of the most controversial aspects of the disease spectrum[4,6,7,12]. In clinical practice, IgG4-related gastrointestinal disease is primarily confined to the pancreas and biliary tract, whereas primary involvement of the rest of the gastrointestinal tract appears much less common and is supported by less robust evidence, based largely on isolated cases or small series. This limitation necessitates cautious interpretation of many published findings and the avoidance of overdiagnosis in inflammatory lesions with an IgG4+ cell-rich infiltrate but without the clinical, radiological, and histological features characteristic of the disease[4,6,7,12].

Cases have been described in the esophagus, stomach, small intestine, colon, and major papilla[4,6,21]. In many of these cases, there is infiltration by IgG4+ plasma cells in the mucosa or submucosa, although not all classic histological criteria for IgG4-RD are always identified, which has fueled the debate over whether this represents true gastrointestinal involvement or an associated phenomenon[6,7,12].

Cases of dysphagia, odynophagia, stenosis, or pseudotumoral masses have been reported in the esophagus[4,6]. In the stomach, the disease may present as ulceration, diffuse parietal thickening, polyps, or pseudotumoral lesions[6,21]. In the small intestine and colon, the available evidence is based primarily on isolated cases or short series[4,6,12]. Involvement of the major papilla, due to its relative frequency in patients with autoimmune pancreatitis, may provide additional diagnostic information[4,12].

Sclerosing mesenteritis

IgG4-associated sclerosing mesenteritis represents a rare but clinically relevant manifestation[4,22]. It may present with abdominal pain, a palpable mass, distension, weight loss, or even intestinal obstruction[4,22]. Imaging studies show mesenteric masses, fibrotic retraction, and lymphadenopathy, and the differential diagnosis includes lymphoma, peritoneal carcinomatosis, mesothelioma, sarcoidosis, and Crohn's disease[4,22]. Histological demonstration of a compatible infiltrate and response to treatment help establish the diagnosis[4,22].

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Treatment

Treatment should be personalised according to the affected organs, clinical severity, risk of irreversible damage, and likelihood of relapse[2,23,27]. The goals are to induce remission, prevent progressive fibrosis, and reduce cumulative exposure to glucocorticoids[2,23,27].

Induction of remission

Glucocorticoids remain the first-line treatment in most patients[2,13,23]. Prednisone is typically used at a dose of 0.5–1 mg/kg/day, maintained for 2–4 weeks and followed by gradual tapering[2,23]. The response is usually rapid from both a clinical and radiological perspective, especially in autoimmune pancreatitis and biliary involvement[13,17,23].

Rituximab, an anti-CD20 monoclonal antibody, has demonstrated high efficacy in both inducing and maintaining remission[2,24,25,27]. Although initially reserved for refractory cases or those with frequent relapses, its use as first-line therapy in selected patients is gaining acceptance, especially in severe multiorgan disease, high risk of relapse, or contraindications to glucocorticoids[2,24,27]. Available studies have shown high rates of sustained remission and a significant reduction in cumulative corticosteroid exposure[24,25,27]. However, significant uncertainties remain regarding the best rituximab maintenance regimen, the optimal duration of treatment, and the ideal selection of patients for scheduled versus on-demand retreatment; therefore, its use should be individualised according to each patient's clinical profile and disease progression[30].

In recent years, the development of B-cell-targeted therapies has broadened the therapeutic landscape. In this context, inebilizumab, an anti-CD19 monoclonal antibody, represents the most significant therapeutic advancement. The phase 3 MITIGATE trial showed that inebilizumab reduced the risk of disease flare-ups and increased the probability of complete remission free of flare-ups at one year, confirming the role of CD19-targeted B-cell depletion as an effective strategy in IgG4-RD[29]. This finding reinforces the idea that disease control may benefit from approaches targeting broader B-cell lineages than those reached by anti-CD20 blockade and points to a possible paradigm shift in patients with relapsing, multiorgan, or glucocorticoid-dependent disease[29].

Glucocorticoid-sparing drugs such as azathioprine, mycophenolate, methotrexate, or leflunomide have also been used, although the evidence supporting their benefit is less robust and results are variable[2,23,27]. Other emerging strategies, such as belimumab, obexelimab, rilzabrutinib, or JAK-STAT pathway inhibitors, remain promising, but for now they have a clearly weaker evidence base than that accumulated for rituximab and inebilizumab[30].

Maintenance

The high relapse rate justifies considering maintenance therapy in selected patients, especially those with early-onset disease, multiorgan involvement, persistent elevated IgG4 levels, extensive pancreatobiliary disease, or a history of relapse[23-25]. The most commonly used strategies include low-dose glucocorticoids, periodic rituximab, and, in certain cases, immunomodulators as glucocorticoid-sparing therapy[23-25,27]. Nevertheless, the optimal maintenance strategy remains undefined and should likely be tailored to the affected organs, initial severity, cumulative toxicity, prior treatment response, and estimated risk of relapse[24,25,30].

Monitoring

Monitoring should be personalised and combine clinical evaluation, laboratory tests, and imaging based on the location of the disease[2,23,26,27]. Serial measurement of serum IgG4 may be useful in some patients, although its value is limited as a sole marker of disease activity[10,26]. Circulating plasmablasts and other emerging biomarkers could improve monitoring in the future[10,26,27]. Given the frequency of subclinical relapses, periodic reevaluation is recommended even in the absence of symptoms. A practical outline of clinical, laboratory, and radiological follow-up is summarized in the monitoring protocol proposed by the authors (Figure 8)[23,25,27].

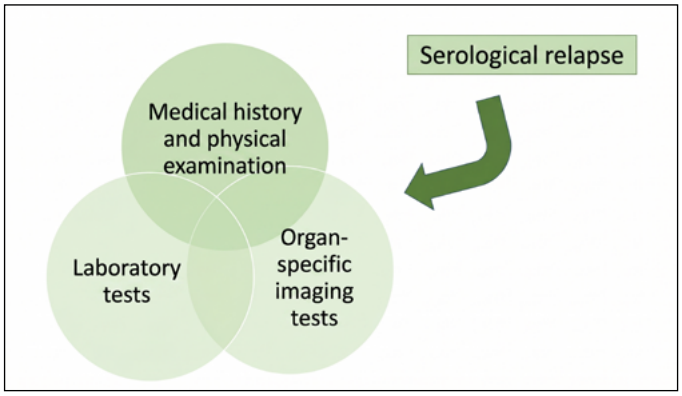

Figure 8. ***Monitoring. Developed by the author.***

A summary table is also provided, which includes the diagnostic and therapeutic management of IgG4-associated gastrointestinal disease (Figure 9).

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	Diagnostic Management	Therapeutic Management
Clinical suspicion	· Gastrointestinal symptoms vary depending on the affected organ: abdominal pain, obstructive jaundice, weight loss, diarrhea, nausea, vomiting, early satiety. · Common associations: autoimmune pancreatitis, IgG4-related sclerosing cholangitis, retroperitoneal disease, sialadenitis, nephritis, etc.	· Do not initiate treatment until the diagnosis is confirmed, unless there is severe organ involvement requiring initial management.
Laboratory diagnosis	· Elevated serum IgG4 (>135 mg/dL is suggestive; >2× the upper limit of normal has higher specificity). · Total IgG, ESR, and CRP may also be elevated.	Not applicable
Imaging diagnosis	· Ultrasound, CT, or MRI depending on the affected organ. · Typical findings: wall thickening, masses or pseudotumors, strictures, ductal dilatation, delayed homogeneous enhancement.	Not applicable
Histopathological diagnosis	· Biopsy of the affected organ is essential for definitive diagnosis. · Characteristic findings:– Dense lymphoplasmacytic infiltrate.– Storiform fibrosis.– Obliterative phlebitis.– IgG4-positive plasma cell infiltrate (>10 cells/HPF) and IgG4+/IgG+ ratio >40%.	Not applicable
Integrated diagnosis	· Established by combining clinical features, elevated serum IgG4, imaging findings, and histological confirmation. · Apply consensus classification criteria when possible (e.g., ACR/EULAR 2019).	**FIRST-LINE TREATMENT: CORTICOSTEROIDS** · Prednisone 0.6 mg/kg/day (max 40 mg/day) for 2–4 weeks. · Then gradual taper (5 mg every 1–2 weeks) to 5 mg/day. · Total duration: 3–6 months depending on clinical, biochemical, radiological, and histological response. **MAINTENANCE / STEROID-SPARING THERAPY** · For relapses or extensive disease.· Options: azathioprine (2 mg/kg/day), mycophenolate mofetil (1–2 g/day), methotrexate (10–15 mg/week). **BIOLOGIC THERAPY (SECOND LINE)** · Rituximab (anti-CD20): 1 g IV on days 1 and 15 (for refractory disease, frequent relapses, or intolerance). · Inebilizumab (anti-CD19): under evaluation. **MANAGEMENT OF COMPLICATIONS** · Endoscopic or surgical interventions in specific cases (e.g., obstruction, strictures, cholangitis). **FOLLOW-UP** · Clinical and laboratory evaluation (serum IgG4, LFTs, amylase/lipase depending on organ) every 3–6 months. · Periodic imaging to assess response and detect relapses. · Relapse: consider reintroduction or escalation of steroids ± immunosuppressant.
Note: Management should be individualized and carried out by a multidisciplinary team (gastroenterology, rheumatology, radiology, pathology).		

Figura 9. ***Summary table on the diagnostic and therapeutic management of IgG4-associated gastrointestinal disease. Developed by the author.***

Prognosis and future outlook

The prognosis is generally favorable when the diagnosis is made early and appropriate treatment is initiated[2,27]. However, established fibrosis can lead to permanent sequelae and cause persistent organ dysfunction. Relapse is one of the main long-term problems, especially in pancreatobiliary involvement[23-25,27].

The association between IgG4-RD and malignancy remains a subject of debate. Although causality has not been proven, recent studies continue to suggest an increased overall

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risk of cancer and of specific tumors in patients with IgG4-RD, with particular attention to pancreatobiliary neoplasms and certain hematologic malignancies, as well as a possible peak in risk during the first few months or the first year following diagnosis of the disease[28,31,32]. This pattern necessitates careful clinical monitoring and reasonable screening for neoplastic processes when the clinical presentation suggests it, although current evidence does not, on its own, justify cancer screening strategies other than those tailored to each patient's age, risk factors, and clinical context[31,32].

A better understanding of the immunopathogenesis is driving the development of more targeted therapies and personalized medicine strategies. In this regard, the identification of dynamic biomarkers of disease activity and advances in treatments targeting B cells, plasmablasts, and immune signaling pathways represent particularly promising lines of research[210,26,27,29,30]. The incorporation of inebilizumab into the therapeutic landscape and the development of other targeted agents reinforce the idea that the management of IgG4-RD could evolve in the coming years toward more stratified models based on relapse risk, pattern of organ involvement, and the patient's immunobiological profile[29,30].

Conclusions

IgG4-related disease is a systemic fibroinflammatory condition of great relevance to gastroenterologists due to its frequent involvement of the pancreas and biliary tract and its ability to mimic neoplastic processes[2,4,5,23]. Its diagnosis requires a rigorous integration of clinical, radiological, serological, and histological findings, avoiding isolated interpretations of serum IgG4 or the therapeutic response[23,8,26].

Glucocorticoids remain the cornerstone of initial treatment, while rituximab has established itself as an effective option for refractory, relapsed, or high-risk disease, although questions remain regarding the optimal maintenance strategy[24,25,30]. The emergence of inebilizumab, supported by positive phase 3 evidence, reinforces the role of B-cell-targeted therapies and points to a new era in the management of the disease[29]. Expanding knowledge of immunological mechanisms and biomarkers, along with the development of new targeted therapies, will likely transform the approach to this condition in the coming years[2,10,26,27,29,30].

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CLINICAL CASE

RICHTER'S SYNDROME AS A MANIFESTATION OF INTESTINAL LYMPHOMA: A RARE FORM OF AGGRESSIVE TRANSFORMATION OF CHRONIC LYMPHOCYTIC LEUKEMIA.

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Abstract

Richter syndrome (RS) is an uncommon but highly aggressive complication in patients with chronic lymphocytic leukemia (CLL), defined by histologic transformation, most frequently into diffuse large B-cell lymphoma (DLBCL). The cumulative risk of RS is estimated at 2–10% over the course of CLL, with an approximate annual incidence of 0.5–1%, and an overall poor prognosis. Gastrointestinal involvement is exceptional and may present with abdominal pain, anemia, or ulcerative endoscopic lesions, mimicking primary gastrointestinal disease and leading to diagnostic delays. Although rare, gastrointestinal involvement may represent a presenting feature of RS and should be considered in patients with abdominal symptoms associated with systemic findings or suggestive PET-CT abnormalities, as early recognition may facilitate targeted biopsy and expedite therapeutic decision-making.

We report the case of a 54-year-old man with treated B-cell CLL who developed systemic and abdominal symptoms. PET-CT revealed hypermetabolic lymphadenopathy and wall thickening of the right colon and cecum. Colonoscopy showed involvement of the ileocecal valve with ulceration and infiltrative changes, and biopsy confirmed transformation to non–germinal center DLBCL with an immunophenotype consistent with RS. The clinical course rapidly deteriorated.

Keywords: Richter's syndrome, intestinal lymphoma, chronic lymphocytic leukemia.

Introduction

RS represents one of the most serious complications of CLL and is characterized by transformation to an aggressive lymphoma, predominantly DLBCL. Its annual incidence is

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around 0.5–1%, and the cumulative risk throughout the course of the disease has been estimated at between 2–10%. The usual presentation includes accelerated adenopathic growth, B symptoms, and marked elevation of LDH, with median survival generally less than one year. Gastrointestinal tract (GIT) involvement is rare and can make diagnosis difficult by mimicking primary digestive neoplasms, inflammatory bowel disease, or infectious processes.[1-3].

Clinical case

A 54-year-old man with a history of Hodgkin's disease treated with chemotherapy in 2003. In 2021, he was diagnosed with B-CLL, initially stage 0. In 2022, in the presence of lymphocyte duplication, 13q and 17p deletions were detected, and treatment with ibrutinib was initiated.

In January 2025, he was admitted for abdominal pain, asthenia, and weight loss, with severe anemia, lymphocytosis, and splenomegaly. Laboratory tests showed hemoglobin of 7.4 g/dL, LDH of 1,120 U/L, beta-2 microglobulin of 6.8 mg/L, and corrected serum calcium of 11.3 mg/dL.

PET-CT revealed hypermetabolic lymphadenopathy, splenomegaly, and nonspecific thickening in the right colon and cecum. Colonoscopy was performed, revealing a thickened and ulcerated ileocecal valve with an infiltrative appearance. Biopsy confirmed infiltration by lymphoid neoplasia.

The histological study was consistent with RS due to transformation from CLL to DLBCL, non-germinal center variant. Immunohistochemistry showed CD20+, CD5+, CD23+, BCL2+, MUM-1+ B cells, with a Ki-67 proliferative index of 35–40%, with no evidence of Epstein–Barr virus infection. The conclusion was aggressive transformation with lymphatic and splenic dissemination, with fulminant progression and fatal outcome.

Discussion

RS is a clinically heterogeneous entity with a poor prognosis. Around 90% of transformations correspond to DLBCL, while the Hodgkin lymphoma variant accounts for approximately 5–10%. Biological aggressiveness is often associated with high-risk genetic alterations, including TP53, NOTCH1, and MYC, which are implicated in therapeutic resistance and lower survival. The presence of 17p deletion in our patient, widely linked to TP53 dysfunction, is an unfavorable prognostic marker and may contribute to rapid clinical progression[1,2].

Gastrointestinal involvement by RS is rare and is usually described as infiltrative or ulcerative lesions in the terminal ileum, ileocecal valve, or colon, with symptoms such as abdominal pain, anemia, weight loss, or even gastrointestinal bleeding. Its clinical significance lies in the fact that it can be confused with primary digestive pathology, delaying diagnosis. In these cases, the combination of systemic symptoms (B symptoms), suggestive laboratory data (elevated LDH, anemia, occasional hypercalcemia), and imaging findings can guide suspicion.

PET-CT is particularly useful for locating areas of high metabolic activity and guiding the collection of biopsies from the most representative tissue. In our case, the correlation between hypermetabolic lymphadenopathy and colonic thickening guided the endoscopic study and confirmed the diagnosis[3].

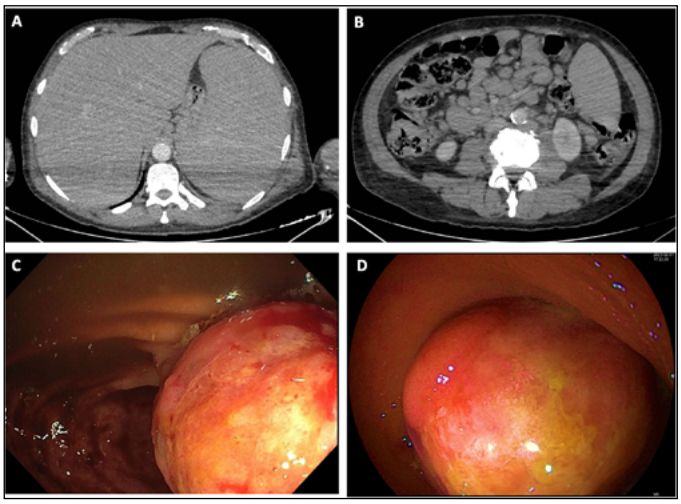

Figure 1. ***A) Abdominal CT image showing hepatosplenomegaly. B) Abdominal CT image showing multiple retroperitoneal adenopathy and nonspecific thickening of the right colon. C and D) Colonoscopy image showing an exophytic neoplastic lesion adjacent to the ileocecal valve with superficial ulceration.***

The treatment of RS is based on R-CHOP or R-EPOCH chemoimmunotherapy regimens, with generally limited responses. In selected patients, combinations with venetoclax, anti-PD1 blockade immunotherapy, and cellular strategies such as CAR-T have been evaluated, especially in refractory or high-risk disease. Even so, overall survival remains poor, reinforcing the importance of early clinical suspicion[4].

In the present case, the fast progression, clinical deterioration, and aggressiveness of the disease resulted in a very limited therapeutic range, making it difficult to initiate intensive treatment. This highlights that gastrointestinal involvement can act as a marker of aggressiveness and dissemination, and underscores the need for rapid diagnosis in the event of atypical digestive manifestations in patients with CLL.

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Conclusion

RS is a rare but highly aggressive complication of CLL. Although gastrointestinal involvement is rare, it should be considered in the presence of abdominal symptoms associated with systemic clinical manifestations or suggestive findings on PET-CT. Endoscopy with targeted biopsy is essential to confirm the diagnosis. Given the poor prognosis, especially in the presence of high-risk alterations such as 17p/TP53 deletion, early recognition may be decisive in planning therapeutic strategies before irreversible clinical deterioration occurs.

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CLINICAL CASE

LUNG CANCER DIAGNOSED BY TRANSESOPHAGEAL ENDOSCOPIC ULTRASOUND

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Abstract

Lung cancer remains one of the leading causes of morbidity and mortality worldwide. Although bronchoscopy and percutaneous approaches are commonly used for diagnosis, certain pulmonary lesions with challenging locations may limit their accessibility. We present the case of a 56-year-old male, an active smoker with moderate chronic obstructive pulmonary disease, in whom follow-up computed tomography revealed significant growth of a paramediastinal pulmonary nodule in the right lower lobe. Positron emission tomography showed marked hypermetabolic activity consistent with primary lung malignancy. Due to the lesion's location and the difficulty of conventional access, transesophageal endoscopic ultrasound was performed, identifying a solid pulmonary mass with pleural and vascular involvement. Fine-needle aspiration confirmed the diagnosis of non–small cell lung carcinoma, adenocarcinoma subtype, with negative PD-L1 and ALK status. This case highlights the value of transesophageal endoscopic ultrasound as a safe and effective diagnostic tool for pulmonary lesions in anatomically challenging locations, enabling histological confirmation and supporting optimal therapeutic planning.

Keywords: lung cancer, endoscopic ultrasound.

Introduction

Lung cancer is one of the most common cancers worldwide and leads to high mortality rates. Several diagnostic techniques are available, such as bronchoscopy and percutaneous procedures. However, there are lesions that are difficult to access using these techniques (mediastinal lesions, those adjacent to major vessels, or those located anterior to the spine), where endoscopic ultrasound plays a significant role.

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Clinical case

A 56-year-old male smoker of 38 packs/years, with moderate emphysematous chronic obstructive pulmonary disease (COPD GOLD 2A) undergoing biannual follow-up by pulmonology.

A follow-up CT scan revealed one 18-mm paramediastinal pulmonary nodule in the right lower lobe (RLL) (previously 3 mm) and two others, one 7 mm in the right upper lobe and one 5 mm in the left lower lobe, with no changes.

The workup was completed with a positron emission tomography (PET) scan, which revealed a hypermetabolic RLL paramediastinal nodule with a maximum standard uptake value (SUV) of 11.9, consistent with a primary pulmonary neoplastic process; the other two nodules showed no significant metabolism.

Given the location of the lesion and the difficulty of conventional access, endoscopic ultrasound was performed, identifying a solid, hypoechoic, spiculated, non-vascularized pulmonary lesion measuring 36 × 34 mm, located 37 cm from the upper dental arch, which bulges into and infiltrates the pleura and the right pulmonary vein. No esophageal infiltration was observed. Fine-needle aspiration using a 22G needle was consistent with non-small cell lung carcinoma, specifically adenocarcinoma. PD-L1 and ALK negative.

Discussion

Endoscopic ultrasound allows for the examination of mediastinal structures where conventional techniques may be limited and enables the collection of tissue samples to confirm the histopathological diagnosis.

Transesophageal endoscopic ultrasound is a crucial technique in the diagnostic arsenal for lung cancer, as it allows safe and effective access to hard-to-reach areas. This not only improves diagnostic accuracy but also optimizes treatment planning and prognosis assessment in patients with this condition.

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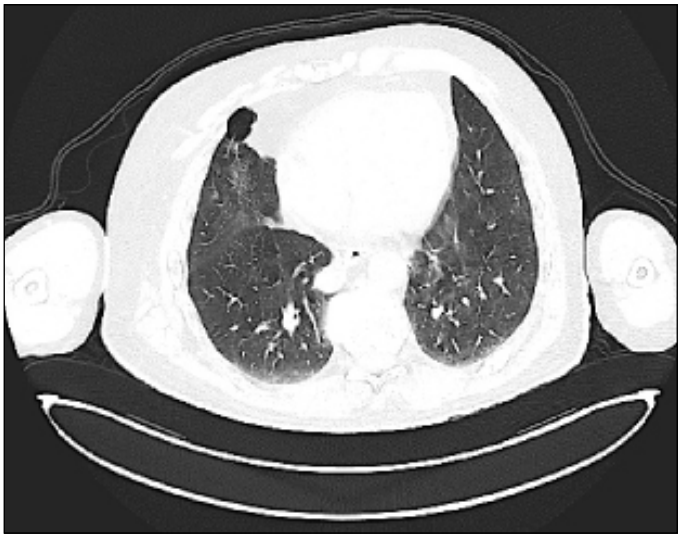

Figure 1. ***Chest CT scan: 18-mm paramediastinal pulmonary nodule in the right lower lobe (RLL).***

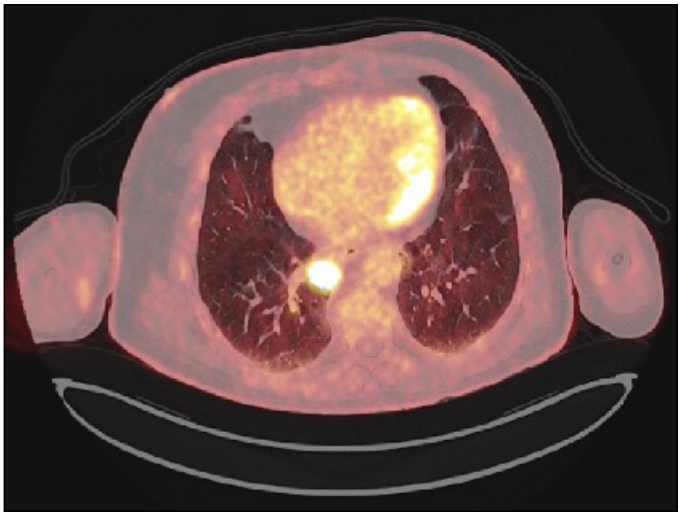

Figure 2. ***Positron emission tomography: hypermetabolic RLL paramediastinal nodule with a maximum standard uptake value (SUV) of 11.9, consistent with a primary pulmonary neoplastic process.***

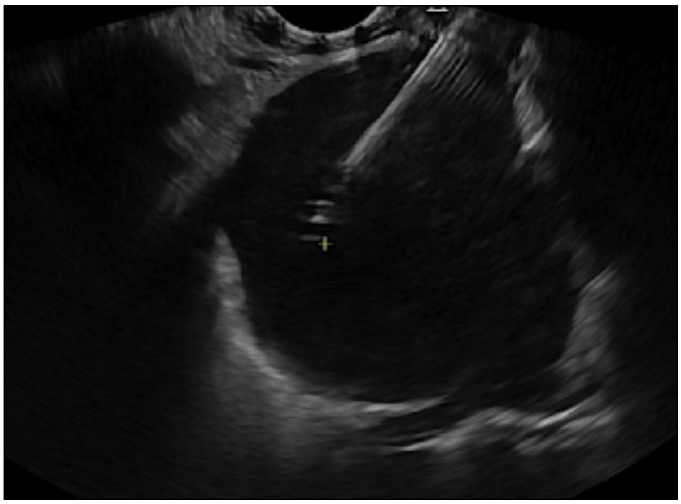

Figura 3. ***Transesophageal endoscopy ultrasound-guided fine-needle aspiration/biopsy.***

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CLINICAL CASE

ALTERNATIVE USE OF THE SALEM PROBE, THINKING OUTSIDE THE BOX.

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Abstract

Colonic decompression is an effective therapeutic option for the management of acute colonic dilation associated with various conditions, including Ogilvie's syndrome, colonic volvulus, and malignant or benign colonic obstruction. Fluoroscopy-guided transanal decompression tube placement has proven to be a safe and cost-effective procedure, capable of avoiding emergency surgery and serving as a bridge to definitive treatment.

We present two clinical cases in which colonic decompression was performed using a Salem tube, previously perforated at its distal end and advanced over a guidewire, as an alternative when specialized devices were not available at our center. In both cases, adequate colonic decompression and favorable clinical outcomes were achieved.

The use of a Salem tube over a guidewire represents an effective and accessible alternative for colonic decompression in selected situations, particularly in resource-limited settings.

Keywords: colonic decompression tube, intestinal obstruction, intestinal pseudo-obstruction.

Introduction

Colonic decompression is a therapeutic strategy indicated in various conditions that cause acute colonic dilation, such as Ogilvie's syndrome, colonic volvulus, and malignant obstruction. The goal of endoscopic decompression is simply to reduce the diameter of the colon and thereby the tension on its wall, thus allowing blood flow and enabling the neural and muscular systems to resume peristaltic movement[1]. This can be performed via simple colonoscopy or with the subsequent

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placement of a transanal decompression tube, with the latter having higher rates of clinical success[1,2].

Typically, this decompression is performed via suction during colonoscopy and by placing a multi-perforated tube with the aid of a guide catheter and wire guide marketed for this purpose; however, these are not always available in all hospitals.

We present an alternative using a Salem tube perforated at its distal end, placed over a guide (Figure 1) in two different clinical scenarios.

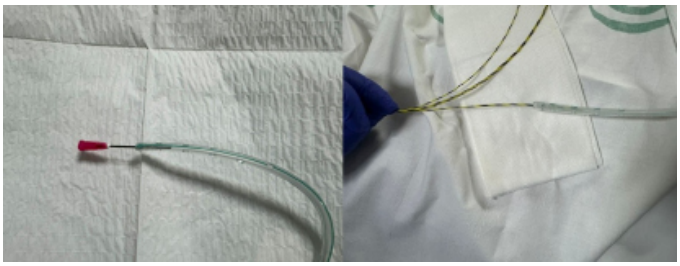

Figure 1. ***Puncturing the distal end of a Salem tube with a needle to place it over a guidewire.***

Clinical case 1

A 62-year-old man with extensive ulcerative colitis being treated with azathioprine, mesalazine, and golimumab was admitted for intestinal subocclusion. An abdominal computed tomography (CT) scan was performed, revealing a complete stricture at the rectosigmoid junction of unknown etiology (inflammatory versus neoplastic).

A colonoscopy was performed, revealing stenosis 30 cm from the anal margin with ulcerated and friable mucosa, without a clear neoplastic appearance. Biopsies were taken, and colonic decompression was performed by passing a guidewire through the stenosis under radiological guidance. We injected contrast via the catheter to confirm the luminogram, and after removing the endoscope, we placed a 16-French Salem-type multi-perforated tube over the guidewire (Figure 2), achieving gas release and decompression of the colon (Figure 3). The tube was maintained with saline irrigation on a rotating schedule until histological confirmation of a neoplastic origin, after which a colostomy was finally performed.

Clinical case 2

A 75-year-old man admitted to the Neurology Unit for subacute cognitive impairment and ataxia of unknown etiology. During hospitalization, he presented with abdominal distension

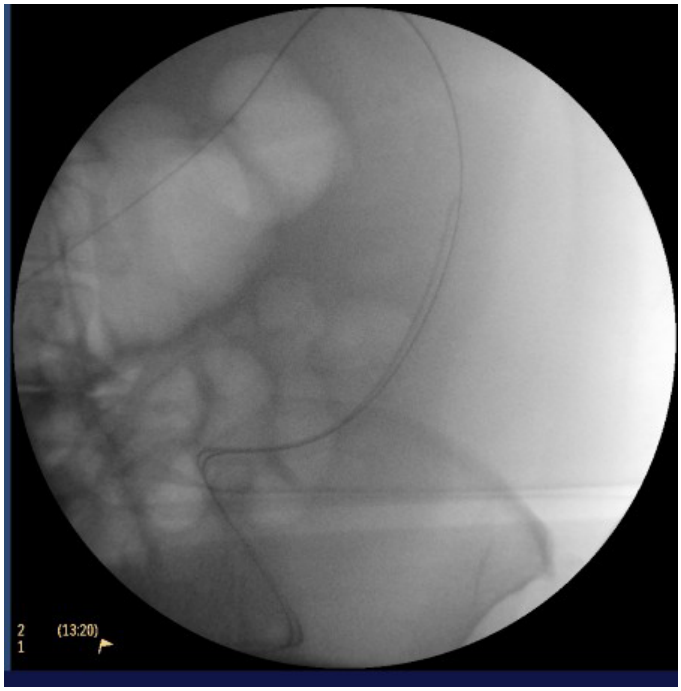

Figure 2. ***Placement of the Salem tube under fluoroscopic guidance.***

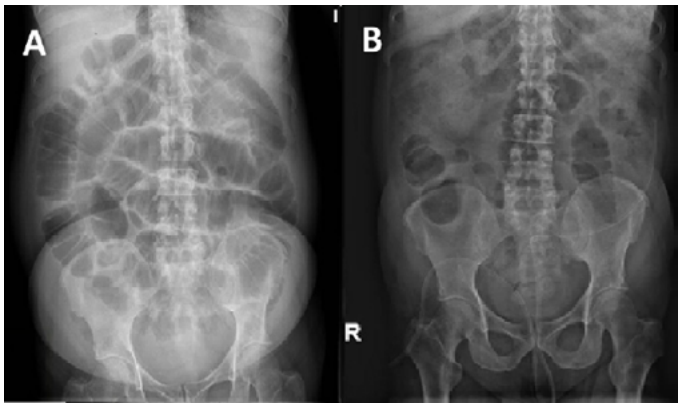

Figure 3. ***Plain abdominal X-ray showing intestinal dilation (A) and improvement following placement of the Salem tube (B).***

and constipation associated with fecal vomiting. Abdominal X-ray and CT scans revealed marked colonic dilation without a mechanical cause, suggestive of Ogilvie's syndrome. After conservative management failed to improve the situation, a decompressive colonoscopy was performed, revealing dilation of the colonic lumen without lesions in any segment. After aspirating gas and fluid, a guidewire was left in place blindly, over which, after removing the endoscope, we advanced a 16-French Salem-type tube under radiological guidance, with its tip positioned in the transverse colon. Initially, we achieved the evacuation of intestinal contents, and after maintaining the tube for a few days with intermittent saline irrigation, the patient's condition improved (Figure 4).

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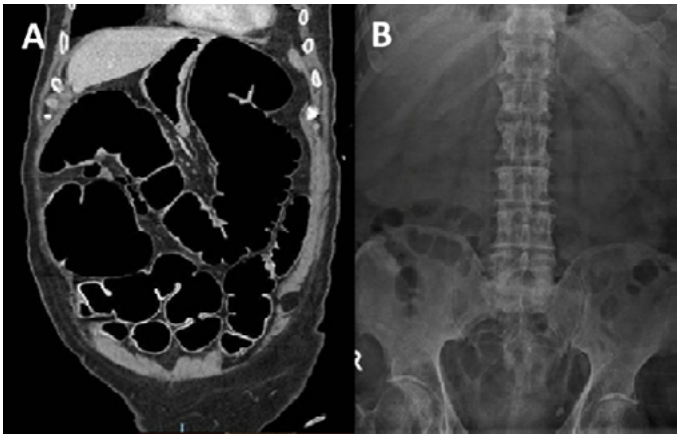

Figure 4. ***Abdominal CT scan with intravenous contrast showing diffusely dilated colonic loops (A). Follow-up abdominal X-ray showing improvement 48 hours after tube placement and its accidental dislodgement (B).***

Discussion

The treatment of colonic decompression via the placement of a fluoroscopically guided transanal decompression tube has been demonstrated to be a safe and effective procedure, regardless of the location or etiology of the obstruction. Furthermore, it helps reduce the recurrence of certain pathologies, such as sigmoid volvulus. It is a simple and cost-effective technique that helps avoid urgent surgical interventions and is useful as a measure prior to elective surgery or the placement of a colonic stent[2-5].

The use of a Salem tube with a pre-perforated distal tip placed over a guidewire constitutes an effective alternative for colonic decompression in settings where specific kits are not available, yielding favorable clinical outcomes.

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LETTER TO THE EDITOR

ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND LYNCH SYNDROME: A COINCIDENTAL ASSOCIATION.

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Abstract

Lynch syndrome is the most common cause of hereditary colorectal cancer and is primarily associated with colorectal and endometrial tumours. Its association with oesophageal squamous cell carcinoma is exceptional and scarcely documented; here, we describe a case with this distinctive feature.

Keywords: esophageal squamous cell carcinoma, Lynch's syndrome.

Introduction

Lynch syndrome is an autosomal dominant disorder caused by mutations in DNA repair genes, which predisposes individuals to an increased risk of neoplasms, primarily colorectal and endometrial cancers. Its association with squamous cell carcinoma of the esophagus is rare and not yet well established; we present a clinical case that highlights this possible correlation.

Clinical case

A 68-year-old patient with no history of substance abuse, a history of endometrial carcinoma treated at age 55 and currently disease-free, was evaluated for de novo constitutional syndrome. A computed tomography (CT) scan was performed, revealing a pancreatic neoplasm that was unresectable due to vascular involvement (Figure 1). Subsequently, an endoscopic ultrasound with fine-needle aspiration (FNA) biopsy was performed, and histological analysis was consistent with squamous cell carcinoma. Given the rare nature of this neoplasm, the case was presented to a multidisciplinary committee, where a possible pancreatic metastasis from an occult squamous cell carcinoma was proposed. A positron emission tomography-computed tomography (PET-CT) scan was requested, which revealed a hypermetabolic lesion in the distal esophagus; biopsy confirmed primary esophageal squamous cell carcinoma with microsatellite instability. Genetic testing was requested, revealing a pathogenic mutation in the PMS2 gene, which confirmed the diagnosis of Lynch syndrome.

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Esophageal squamous cell carcinoma and Lynch Syndrome: a coincidental association.
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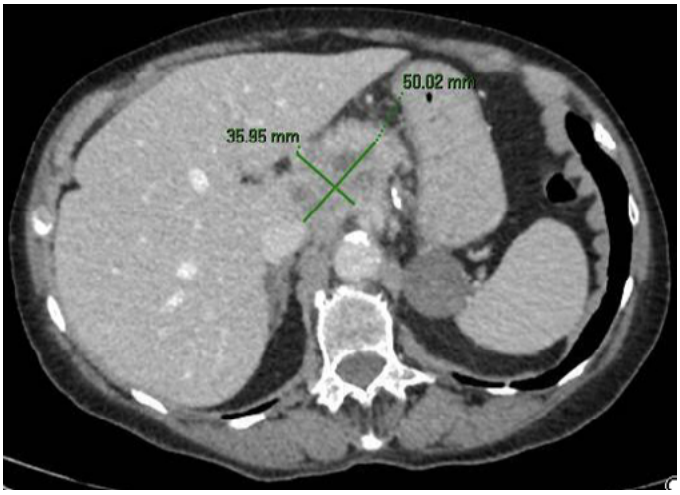

Figure 1. ***A heterogeneous lesion originating from the pancreas, without associated dilation of the bile duct or the duct of Wirsung, which completely encases the proximal third of the branches of the celiac trunk and the origin of the superior mesenteric artery, and comes into contact with the portal vein over an angle of >180°.***

Discussion

Lynch syndrome is the most common cause of hereditary colorectal cancer and is associated with an increased risk of developing other cancers, such as those of the endometrium, stomach, pancreas, urinary tract, and ovary[1]. However, the association between Lynch syndrome and squamous cell carcinoma of the esophagus is rare and has not yet been fully documented[2,3].

Squamous cell carcinoma of the esophagus is primarily associated with environmental factors such as tobacco and alcohol use, or chronic esophagitis. Nevertheless, some studies suggest a possible link to alterations in DNA repair mechanisms. In this context, the presence of mutations in PMS2, as in the case presented, could indicate an additional underlying mechanism that promotes esophageal carcinogenesis[2,3].

Although the association between Lynch syndrome and esophageal squamous cell carcinoma remains uncertain, this case underscores the importance of considering less common neoplasms in the context of hereditary cancer predisposition syndromes. Likewise, the early identification of criteria suggestive of hereditary cancer and the performance of genetic testing facilitate better risk stratification and appropriate follow-up, which positively impacts the management of the patient and their family members[1].

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