

MARILIA DE JESUS SCTAKE

MICOSE FUNGOIDE NA CRIANÇA

Relato de Caso

Trabalho apresentado à Universidade Federal de Santa Catarina, como requisito para a conclusão do Curso de Graduação em Medicina.

Florianópolis

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Presidente do Colegiado: Prof^o. Dr. Edevard José de Araújo

Professor Orientador: Prof^a. Dra. Maria Marlene de Souza Pires

Florianópolis

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Título.

Dedico este trabalho aos meus pais e família e, em especial, à minha avó Zélia Maria (in memoriam), cujo amor e cuidado permanecem comigo até hoje.

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Aos meus pais que sempre foram suporte e meus maiores incentivadores em cada passo da minha trajetória.

Aos amigos antigos que permaneceram presentes apesar da distância e aos novos que se tornaram motivos de dias mais leves e prazerosos, em especial Maria Luiza e Victor.

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À professora Maria Marlene de Souza Pires pela orientação, dedicação e exemplo de profissional e mestre.

A todos os pacientes e mestres que ao longo desses anos de graduação ensinaram-me a visualizar a realidade e o encanto da medicina através do cuidado, meu mais sincero obrigada.

DECLARAÇÃO DOS CONTRIBUIDORES

Marília de Jesus Sctake desenhou o estudo, realizou a análise de dados, realizou a revisão de literatura, redigiu o manuscrito original e revisou o manuscrito.

Marice El Achkar Mello desenhou o estudo, realizou a coleta e a análise inicial de dados e revisou e corrigiu o manuscrito.

Maria Marlene de Souza Pires desenhou o estudo, coordenou e supervisionou a coleta de dados e revisou e corrigiu o manuscrito.

Amanda Amaro Pereira realizou a análise de dados e revisou e corrigiu o manuscrito.

Todos os autores leram e aprovaram o manuscrito final como submetido e concordaram em ser responsáveis por todos os aspectos do trabalho.

RESUMO

Micose fungoide (MF) é o linfoma cutâneo de células T mais comum, caracterizado pela proliferação de linfócitos T de pequeno a médio tamanho e núcleos cerebriformes. Existem diferentes subtipos clínicos da MF, incluindo MF clássica, bolhosa, hiperpigmentada e hipopigmentada. A MF afeta principalmente adultos com idade média entre 55 e 60 anos, sendo considerada rara em crianças. O presente estudo relatou o caso de uma paciente com um subtipo dessa entidade, ainda pouco descrita na literatura médica pediátrica. A etiologia e patogênese da doença não são totalmente compreendidas, mas há hipóteses de associação com mecanismos imunológicos, genéticos e infecciosos. O diagnóstico da MF é feito por meio da suspeita clínica e biópsia da lesão, podendo ser necessário realizar exames de imagem para avaliar a extensão da doença. O prognóstico depende do estágio da doença, sendo que a MF hipopigmentada apresenta geralmente um prognóstico mais favorável. Não existe um protocolo estabelecido para o tratamento pediátrico e, por isso, a terapêutica é semelhante à dos adultos. Dessa forma, é de suma importância a realização de mais estudos sobre o assunto a fim de permitir protocolos de tratamento e tomadas de decisão com maior segurança por parte dos profissionais.

ABSTRACT

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma, characterized by the proliferation of small to medium-sized T lymphocytes with cerebriform nuclei. There are different clinical subtypes of MF, including classic MF, bullous MF, hyperpigmented MF, and hypopigmented MF. MF primarily affects adults with an average age of 55 to 60 years and is considered rare in children. The present study reports a case of a patient with a subtype of this entity, which is still poorly described in pediatric medical literature. The etiology and pathogenesis of the disease are not fully understood, but there are hypotheses suggesting an association with immune, genetic, and infectious mechanisms. The diagnosis of MF is made through clinical suspicion and biopsy of the lesion, and imaging tests may be necessary to assess the extent of the disease. Prognosis depends on the stage of the disease, with hypopigmented MF generally having a more favorable prognosis. There is no established protocol for pediatric treatment, and therefore, the therapeutic approach is similar to that of adults. Thus, it is of paramount importance to conduct further studies on the subject in order to establish treatment protocols and enable more confident decision-making by healthcare professionals.

LISTA DE ABREVIATURAS E SIGLAS

MF	Micose fungoide
MFH	Micose fungoide hipopigmentada
WHO-EORTC	Organização Mundial da Saúde-Organização Europeia para Pesquisa e Tratamento do Câncer

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INTRODUÇÃO

Micose fungoide (MF) é o linfoma cutâneo de célula T mais comum, caracterizado pela proliferação de linfócitos T de pequeno a médio tamanho e núcleos cerebriformes [1]. Pelo consenso WHO-EORTC, o termo MF é usado somente para o tipo clássico “Alibert-Bazin” caracterizado pela evolução de manchas, placas e tumores, ou para subtipos que apresentam um curso clínico semelhante, como a MF bolhosa, hiperpigmentada ou hipopigmentada [1].

A doença foi descrita pela primeira vez em 1806 pelo francês Jean-Louis Alibert como “*pian fungoides*” e renomeada posteriormente com o atual termo após a observação dos tumores cutâneos em forma de cogumelos. Em 1870, Ernest Bazin contribuiu descrevendo a evolução natural da doença e definindo seus estágios, incorporados ao atual estadiamento [1]. Tipicamente a MF afeta mais o sexo masculino que feminino (1.6-2.0:1) e adultos com idade entre 55 e 60 anos [1]. Considerada doença rara em pediatria, apenas 0,5% a 7,0% do total de casos ocorre em crianças [2], com média de início dos sintomas e de diagnóstico aos 8 e 12 anos, respectivamente [2-4]. Com etiologia e patogênese incertas, há hipóteses sugerindo mecanismos imunológicos, genéticos e infecciosos relacionados à estimulação crônica de linfócitos [5].

Usualmente a doença apresenta curso indolente [3], com surgimento na infância e lesões capazes de mimetizar afecções de pele mais comuns que podem retardar o diagnóstico para a vida adulta [2, 6]. A apresentação clínica depende da faixa etária e do subtipo da doença, apresentando como forma mais comum na pediatria a micose fungoide hipopigmentada (MFH) [3]. O diagnóstico é confirmado com biópsia e, assim que estabelecido, a escolha da terapia depende do estágio e estadiamento da doença, que também servem como melhor fator avaliativo para prognóstico [7].

RELATO DE CASO

Paciente feminina, 7 anos de idade, raça branca, com histórico de rinite e dermatite atópica, apresentava quadro de máculas hipocrômicas, não descamativas, assintomáticas, com início cerca de 18 meses antes da consulta. Lesões iniciaram pelo tronco e espalharam-se progressivamente para membros.

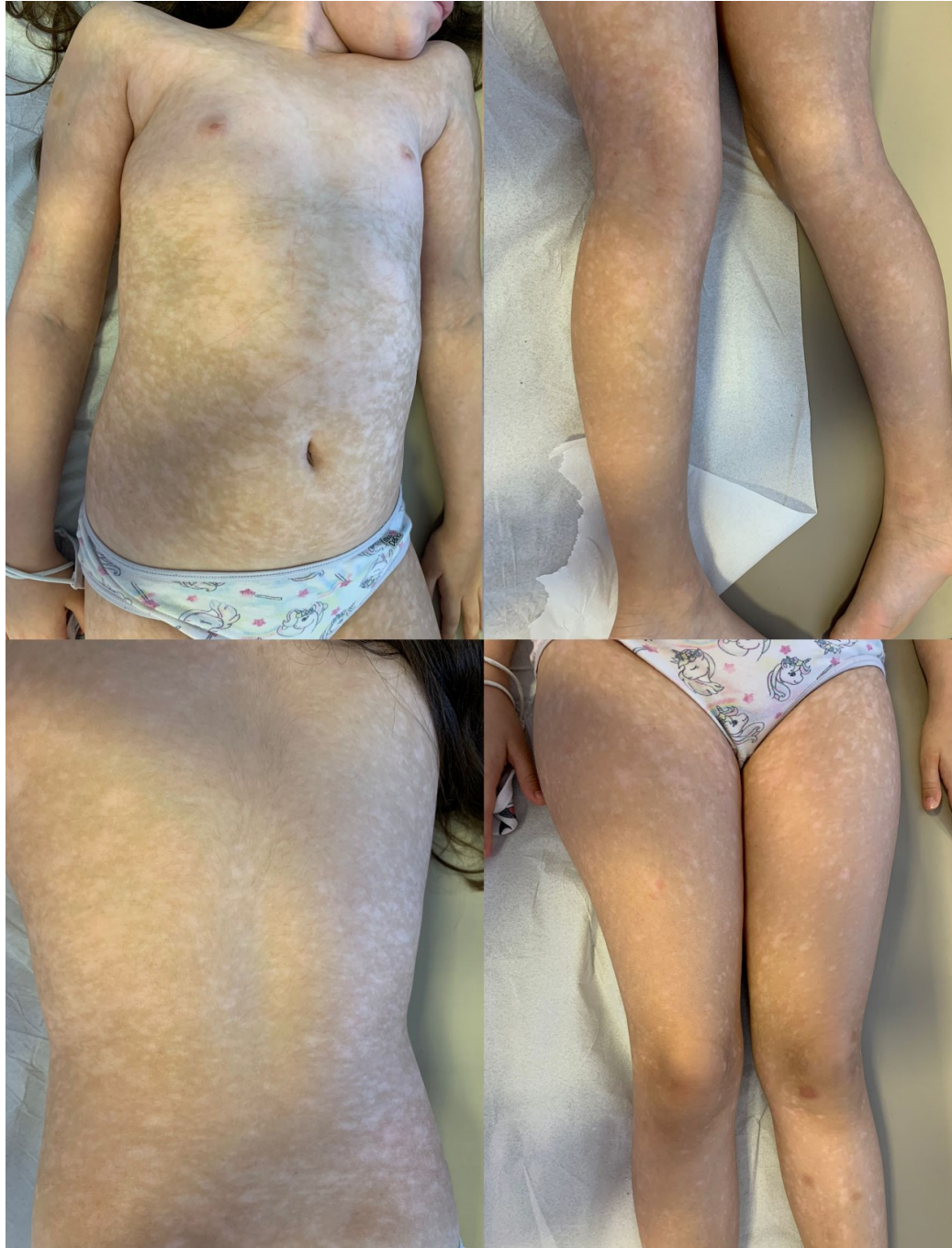
Inicialmente atendida em outro serviço de dermatologia com a hipótese diagnóstica de pitíriase versicolor, tratada com antifúngico tópico sem melhora do quadro clínico. Posteriormente, pensando-se em infecção de pele, foi tratada com antibiótico oral, sem resposta ao tratamento e progressão das lesões. Paciente buscou alergista que indicou o uso de imunomodulador tópico para tratar pitíriase alba, devido ao histórico de dermatite atópica. Após quatro meses de tratamento e piora progressiva do caso, a paciente buscou nosso serviço.

Ao exame físico, identificaram-se máculas hipocrômicas em tronco e membros (Fig. 1) e raras pápulas eritematosas em membro superior. Realizada biópsia de lesão papular eritematosa de membro superior direito, cujos achados histopatológicos apresentaram múltiplos focos de epidermotropismo, linfócitos pequenos e hiper Cromáticos alinhados na junção dermoepidérmica (Fig. 2a e 2b) e linfócitos formando microabscessos de Pautrier (Fig. 2c). Quanto ao estudo imunohistoquímico, estes linfócitos expressaram negatividade dos antígenos CD4 (Fig. 2d), CD7 (Fig. 2e) e CD30 e, positividade dos antígenos CD8 (Fig. 2f), CD3 e CD5.

Com os achados histopatológicos e de imunohistoquímica associados à apresentação clínica foi estabelecido o diagnóstico de MFH CD8+. Após o diagnóstico, a paciente foi encaminhada para estadiamento com a

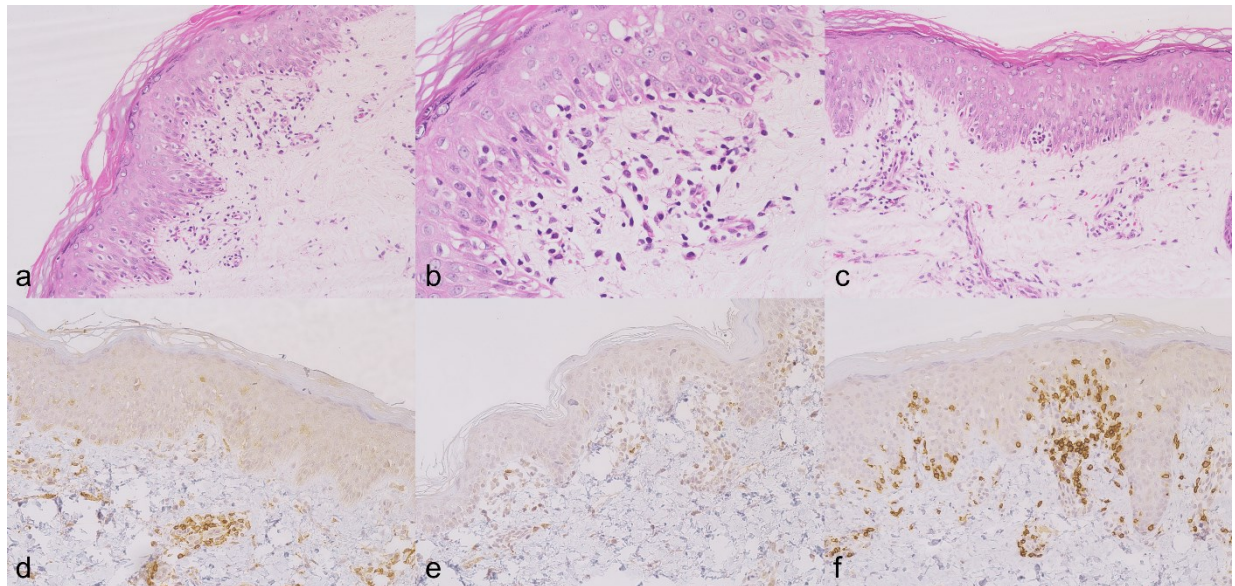
oncologia pediátrica, não evidenciando acometimento de nenhum outro órgão, iniciando na sequência tratamento com fototerapia.

Fig. 1



Máculas hipocrômicas em tronco e membros (Arquivo pessoal Marice Emanuela El Achkar Mello, MD)

Fig. 2



a Epidermotropismo de linfócitos pequenos e hiper Cromáticos, alinhados na junção dermoepidérmica (coloração de hematoxilina-eosina, ampliada 200x). **b** Linfócitos pequenos e hiper Cromáticos, na junção dermoepidérmica (coloração de hematoxilina-eosina, ampliada 400x). **c** Microabscesso de Pautrier (coloração de hematoxilina-eosina, aumento de 200x). **d** Marcadores imuno-histoquímicos com células epidermotrópicas CD4- (ampliada 200x). **e** Marcadores imuno-histoquímicos com células epidermotrópicas CD7- (ampliada 200x). **f** Marcadores imuno-histoquímicos com células epidermotrópicas CD8+ (ampliada 200x). (Arquivo pessoal Amanda Amaro Pereira, MD)

DISCUSSÃO

A MF segue com causas etiológicas incertas e suas principais hipóteses têm foco na relação entre resposta imunológica e ativação de células T, levando à estimulação antigênica crônica, liberação de citocinas inflamatórias, acúmulo de mutações e replicação genômica de linfócitos malignos [8].

Considerada doença rara na pediatria, cerca de 5% dos casos de MF encontram-se nessa população [4]. A média de idade do início dos sintomas é de 8 a 9 anos, enquanto o diagnóstico é feito entre 9 e 13 anos de idade [2, 4]. Apesar disso já foram descritos casos em todas as faixas etárias pediátricas, assim como a paciente deste caso cujos primeiros sintomas iniciaram aos 5,5 anos e o diagnóstico realizou-se aos 7 anos de idade.

As manifestações clínicas dependem da idade do paciente e do subtipo da doença, sendo comum na pediatria o acometimento pelas variantes da doença, com subtipo mais frequente apresentando-se como MFH, em até 59% dos casos. A MFH afeta principalmente indivíduos de pele preta e asiáticos [6, 9] e, caracteriza-se por máculas hipopigmentadas a acrómicas em qualquer área do corpo, com predileção por áreas protegidas do sol [6, 10]. Em pacientes caucasianos é comum o acometimento com lesões hipopigmentadas e eritematosas [10], fato observado na paciente aqui relatada, de raça branca e lesões com características de padrão misto.

O diagnóstico confirma-se com biópsia cuja histopatologia da MF clássica apresenta células mononucleares atípicas de tamanho pequeno a médio com núcleos cerebriformes infiltrando a derme superior e junção dermoepidérmica, tipicamente com fenótipo de linfócitos T auxiliares (CD3+, CD4+, CD8-). Pode-se observar epidermotropismo e formação de agregados intraepidérmicos de linfócitos chamados microabscessos de Pautrier. Quanto à MFH, geralmente apresenta importante epidermotropismo e mínimo envolvimento dérmico com fenótipo de linfócitos T citotóxicos (CD3+, CD8+, CD4-) [3, 6]. Estudos de imagem estão indicados em casos de progressão da doença com acometimento sistêmico em outros órgãos [6].

A MFH faz diagnóstico diferencial com afecções como vitiligo, pitíriase alba, pitíriase versicolor, tinea corporis, hipopigmentação pós-inflamatória e pitíriase liquenoide [3, 9] e, devido à semelhança clínica, pode haver retardo no diagnóstico correto. A paciente relatada apresentou atraso de 18 meses entre o início dos sintomas e a confirmação diagnóstica, sendo tratada para outras afecções nesse período. O prognóstico depende do estadiamento, extensão das lesões e presença de doença extracutânea [3, 11]. Comumente, a MFH tem prognóstico melhor que a MF clássica, pois seu diagnóstico é precoce e em estágios iniciais. Os dados atuais sugerem que a variedade de imunofenótipos existentes não influencia o prognóstico [12].

Não existe protocolo de tratamento para a MF na população pediátrica, por isso, a abordagem assemelha-se a do público adulto. Utiliza-se principalmente corticosteróides tópicos e fototerapia, porém, quimioterapia tópica, excisão e radioterapia local das lesões também foram descritas na literatura [3, 13, 14]. Haja vista que a maioria dos casos pediátricos se apresenta em estádios iniciais, esses pacientes beneficiam-se das terapias direcionadas apenas à pele e às lesões, sem necessidade de terapia sistêmica [4, 14]. Até o momento, estudos demonstraram ser a combinação de corticosteróides tópicos e fototerapia a primeira linha de tratamento na pediatria [4, 6].

CONCLUSÃO

A MF é rara em crianças e seu desafiador diagnóstico precisa ser realizado com brevidade. Os poucos estudos relacionados a esta afecção na pediatria, resultam em dados limitados sobre tratamento, desfecho e prognóstico. Justifica-se assim a importância em realizar-se mais estudos sobre o assunto para estabelecer protocolos de tratamento e permitir decisões seguras para os profissionais.

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ANEXO: NORMAS DE PUBLICAÇÃO DA REVISTA

TYPES OF MANUSCRIPTS

All manuscripts (except "Correspondence") must include an abstract and a structured text body (e. g. introduction, methods, results, discussion and references). For details regarding special requirements please see "notes" below.

- **Research**
All scientific contributions describing novel findings in the entire field of dermatology and cutaneous research with a maximum length of 3,500 words. No limit on references and figures/tables. Abstract must be 350 words, unstructured.
- **Review**
State-of-the art narrative or systematic review articles written by experts in the field either upon request or by unsolicited submission with a maximum length of 3,500 words. No limit on references and figures/tables. Abstract must be 350 words, unstructured.
- **Study Protocol**
A platform for publishing innovative clinical trial data regardless of their outcome as publication of negative results is of similar importance as of positive ones with a maximum length of 3,000 words. No limit on references and figures/tables. Abstract must be 350 words, unstructured.
- **Correspondence**
Research Letters to the Editor with a maximum length of 500 words, 5 references, and a total of 2 figures/tables.
- **Brief Report**
Small, preliminary studies; survey studies with low response rate, with a maximum length of 1,200 words, 15 references and no more than total of 2 figures/tables. Abstract must be 350 words, unstructured.
- **Guideline**
Clinical practice guidelines; applications of guidelines into practice, development of guidelines; issues surrounding guidelines, with a maximum length of 5,000 words. No limit on references and figures/tables. Abstract must be 350 words, unstructured.
- **Consensus Article**
Proceedings of consensus meetings or conferences, work offering recommendations or setting policy, with a maximum length of 5,000 words. No limit on references and tables/figures. Abstract must be 350 words, unstructured.
- **Protocol**
Study protocols of proposed or ongoing trials. No maximum length and no restrictions on references and tables/figures. Abstract must be 350 words, unstructured.

Important Notes:

- Manuscripts describing mutations

Reports describing mutation(s) will not be considered for review in Archives of Dermatological Research unless at least one of the following conditions is met:

1. No more than three mutation reports implicating the same gene in the same disease have already been published.
2. The findings provide new insights into genotype-phenotype correlation.
3. The findings provide new insights into population genetics, such as founder effect, genetic drift, or bottlenecks.

- **Manuscripts describing effects of natural compounds**

Reports describing the effect(s) of plant extracts or natural compounds will not be considered for review in Archives of Dermatological Research unless the following conditions are met:

1. Chemical definition of the investigated compound(s). The chemical structure(s) must be shown as a figure.
2. The compound(s) investigated must be accessible for other researchers in order to repeat the described experiments. The source must be named and full address supplied.
3. No more than three publications describing similar effects of the investigated compound(s) in the same or similar in vitro or in vivo models.

1.2 MANUSCRIPT SUBMISSION

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

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Please follow the hyperlink “Submit manuscript” and upload all of your manuscript files following the instructions given on the screen.

Source Files

Please ensure you provide all relevant editable source files at every submission and revision. Failing to submit a complete set of editable source files will result in your article not being considered for review. For your manuscript text please always submit in common word processing formats such as .docx or LaTeX.

Important note:

- **The approval document has to be submitted with the manuscript for all studies requiring review by the responsible local or national ethical committee.**

Proposal of Expert Reviewer

To shorten the time of the editorial process and to increase the quality of manuscripts published in AODR at least 5 reviewers must be proposed. Three of the proposed experts must be from outside of the country of the corresponding author. Members of the Board of Associate Editors cannot be proposed as reviewer.

It is advisable to suggest experts who are active in the respective field and have recently published articles related to topic of the submission. Suggestion of people who are well known in global dermatology but are no longer active as scientist and/or clinician is not advisable. Successful manuscript processing requires at least 2 qualified expert evaluations.

General Remark

Please provide text and figures of your manuscript as separate electronic files (one file for each figure). The text file should include references, figure legends and tables; it should not include figures. Tables and figure legends are placed within the text file at the end of the main text. Depending on the type of paper the text file should contain the following sections:

Scientific style

Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

TITLE PAGE

Title Page

Please make sure your title page contains the following information.

Title

The title should be concise and informative.

Author information

- The name(s) of the author(s)
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Large Language Models (LLMs), such as ChatGPT, do not currently satisfy our authorship criteria. Notably an attribution of authorship carries with it accountability for the work, which cannot be effectively applied to LLMs. Use of an LLM should be properly documented in the Methods section (and if a Methods section is not available, in a suitable alternative part) of the manuscript.

Abstract

Please provide an abstract of 150 to 250 words. The abstract should not contain any undefined abbreviations or unspecified references.

For life science journals only (when applicable)

- Trial registration number and date of registration for prospectively registered trials
- Trial registration number and date of registration, followed by “retrospectively registered”, for retrospectively registered trials

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Statements and Declarations

The following statements should be included under the heading "Statements and Declarations" for inclusion in the published paper. Please note that submissions that do not include relevant declarations will be returned as incomplete.

- **Competing Interests:** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication. Please refer to “Competing Interests and Funding” below for more information on how to complete this section.

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

TEXT

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. We recommend using [Springer Nature’s LaTeX template](#).

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

REFERENCES

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

Reference list

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Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. *N Engl J Med* 341:325–329

- Article by DOI

Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. *J Mol Med*. <https://doi.org/10.1007/s001090000086>

- **Book**
South J, Blass B (2001) The future of modern genomics. Blackwell, London
- **Book chapter**
Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257
- **Online document**
Doe J (1999) Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. Available via DIALOG. <http://www.rsc.org/dose/title> of subordinate document.
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Regardless of whether material is collected from living or dead patients, they (family or guardian if the deceased has not made a pre-mortem decision) must have given prior written consent. The aspect of confidentiality as well as any wishes from the deceased should be respected.

Data protection, confidentiality and privacy

When biological material is donated for or data is generated as part of a research project authors should ensure, as part of the informed consent procedure, that the participants are made aware what kind of (personal) data will be processed, how it will be used and for what purpose. In case of data acquired via a biobank/biorepository, it is possible they apply a broad consent which allows research participants to consent to a broad range of uses of their data and samples which is regarded by research ethics committees as specific enough to be considered “informed”. However, authors should always check the specific biobank/biorepository policies or any other type of data provider policies (in case of non-bio research) to be sure that this is the case.

Consent to Participate

For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles

describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

Consent to Publish

Individuals may consent to participate in a study, but object to having their data published in a journal article. Authors should make sure to also seek consent from individuals to publish their data prior to submitting their paper to a journal. This is in particular applicable to case studies. A consent to publish form can be found

Summary of requirements

The above should be summarized in a statement and placed in a ‘Declarations’ section before the reference list under a heading of ‘Consent to participate’ and/or ‘Consent to publish’. Other declarations include Funding, Competing interests, Ethics approval, Consent, Data and/or Code availability and Authors’ contribution statements.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Sample statements for "**Consent to participate**":

Informed consent was obtained from all individual participants included in the study.

Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

Sample statements for "**Consent to publish**":

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

Sample statements if identifying information about participants is available in the article:

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Authors are responsible for correctness of the statements provided in the manuscript. See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

Images will be removed from publication if authors have not obtained informed consent or the paper may be removed and replaced with a notice explaining the reason for removal.