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Clinical features and management of VEXAS syndrome in critical care: a scoping review protocol V.2

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Abstract

Objective: This study aims to understand the scope and types of evidence regarding the clinical characteristics and management strategies of VEXAS syndrome in critical care settings.

Introduction: VEXAS syndrome is a newly identified autoinflammatory disease, first described in 2020, which primarily affects men over 50 years of age. While the mortality rate of VEXAS syndrome is high, ranging from 20-50%, its clinical manifestations are diverse. As a newly discovered disease, the diagnosis and management of VEXAS syndrome pose significant challenges. Although patients with VEXAS syndrome may exist in critical care settings, there is a lack of systematic evidence regarding its diagnosis and management. Therefore, this study aims to conduct a scoping review of VEXAS syndrome in critical care to demonstrate the scope of currently available evidence.

Inclusion criteria: The target participants include patients with VEXAS syndrome who require critical care, regardless of age, sex, or disease duration. The concept is to explore the clinical characteristics and management strategies. The context does not restrict patient location, region, race, or gender; all English language literature is considered.

Methods: A literature search uses the keyword "VEXAS syndrome" or “Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic” in MEDLINE, CENTRAL, Embase, and Web of Science databases. In the initial screening step, two independent reviewers assessed all titles and abstracts, excluding irrelevant articles. The second screening follows the same inclusion criteria, thoroughly examining full texts.

Introduction

1 Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic (VEXAS) syndrome is an acquired autoinflammatory disorder that primarily affects men over 50 years of age and was identified in 2020 as a new disease concept associated with mutations in the Ubiquitin-like modifier activating enzyme 1 (UBA1) gene.[1] Clinical manifestations include inflammatory symptoms such as fever and arthritis or hematological abnormalities such as macrocytic anemia and thrombocytopenia.[2] The mortality rate is reported to be 20-50%.[3] VEXAS syndrome has only recently been identified, and its clinical signs resemble those of diseases commonly encountered in intensive care settings, such as sepsis. Moreover, many medical institutions cannot perform genetic testing for the associated mutation. Consequently, there is a concern that patients in intensive care units may receive inappropriate treatment due to unidentified causes or misdiagnosis. A report published in 2023 described an elderly male patient with a one-year history of skin lesions and deep vein thrombosis episodes who experienced an in-hospital cardiac arrest and was admitted to the intensive care unit, ultimately being diagnosed with VEXAS syndrome.[4] The patient was initially diagnosed with heparin-induced thrombocytopenia. It is important to clarify the characteristics of patients with severe VEXAS syndrome and how they are treated, as there are patients with this serious condition who are receiving treatment without a true understanding of the underlying cause.
This study aims to conduct a scoping review of VEXAS syndrome in critical care settings to demonstrate the extent of current knowledge regarding its pathophysiology and management.

Review question

2 The review questions of this study are as follows: (1) What are the clinical characteristics of VEXAS syndrome in critical care settings? and (2) What are the management strategies for VEXAS syndrome in critical care?

Inclusion criteria

3 **Participants**

- Patients with VEXAS syndrome who require or are estimated to require critical care (e.g., those with high severity or requiring treatment in the intensive care unit)
- A broad patient population, regardless of age, sex, or disease duration

Concept

(1) Clinical characteristics
Symptoms and signs exhibited by VEXAS syndrome patients or diseases that mimic VEXAS syndrome requiring critical care
(2) Management strategies
Treatment of VEXAS syndrome in critical care (e.g., definitive treatment, supportive therapy, and life-sustaining treatment)

Context

There are no restrictions on patient location, region, race, or gender. The publication period of the literature is not limited, and only English-language publications are considered. Both published and unpublished studies are searched.

Types of sources

This study considers experimental and quasi-experimental research designs, including randomized controlled trials, non-randomized controlled trials, before-and-after studies, and interrupted time-series analyses. Additionally, analytical observational studies, including prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies, are considered. Descriptive observational study designs, such as case series, individual case reports, and descriptive cross-sectional studies, are also included. Qualitative research focusing on qualitative data and descriptions is also considered. Furthermore, systematic reviews that meet the eligibility criteria based on the research question are considered. Opinion papers and conference proceedings are also included. The review includes studies without any limitations on language, publication date, or publication status.

Methods

4 This protocol was written in accordance with PRISMA-P.[5] The study follows the Joanna Briggs Institute (JBI) methodology for scoping reviews[6] and registered on Protocols.io.

Search strategy

The following databases are systematically searched electronically: MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Embase, and Web of Science.
The full search strategy for the five databases is developed using words contained in the title and abstract of relevant articles and the index terms used to describe the articles (see **Appendix**). The reference lists of the collected literature are screened for additional studies.
Study/Source of evidence selection
After the search, all identified citations are uploaded to Rayyan (Rayyan, Massachusetts, USA), and duplicates are removed. Following a pilot test, two independent reviewers (KS and KO) screen the titles and abstracts against the review's inclusion criteria. Relevant sources are fully retrieved, and their citation details are imported into Rayyan. The main text records and reports the reasons for excluding sources not meeting the inclusion criteria during full-text screening. Any disagreements between reviewers at each stage of the selection process are resolved through discussion or with an additional reviewer (TG). The search results and the study inclusion process are reported in the final scoping review manuscript and presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) flow diagram.[5]

Data extraction

Two independent reviewers (KS and KO) extracted data from the screened papers using a data extraction form, a spreadsheet created by the authors. The extracted data include details on

Participants, Concept, Context, Methods, and key findings relevant to the Review question. The draft data extraction form includes information on the author, year of publication, country of origin, study design, study purpose, population and sample size, study methodology, outcomes and details, clinical information of cases for case reports, and key findings relevant to the scoping review question. The draft data extraction form is modified and revised as necessary while extracting data from the screened papers. Modifications are detailed in the scoping review. Any disagreements with the reviewer are resolved through discussion or with an additional reviewer. If necessary, the authors of the papers are contacted to request missing or additional data.

Data analysis and presentation

The data are presented in graphical or tabular form. The insights and evidence from the reviewed papers are described separately for (1) clinical characteristics and (2) management strategies.

References

5

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Appendix

6

Search strategy

- PubMed search strategy: “VEXAS”[tiab] OR “Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic”[tiab]
- CENTRAL search strategy: “VEXAS”:ti,ab OR Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic”:ti,ab
- Embase search strategy: ti(VEXAS) OR ab(VEXAS) OR ti(Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) OR ab(Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic)
- Web of Science search strategy: TS=("VEXAS" OR "Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic")

Protocol references

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