Emergency and Critical Care Medicine

OPEN

MELAS syndrome and risk of infection

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Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome is a complex mitochondrial disorder.[1] It exhibits a diverse range of clinical symptoms affecting multiple organ systems.[1] We are exploring the intriguing link between MELAS and an elevated risk of infections. The systemic consequences of mitochondrial dysfunction, disrupting vital energy production processes, extend beyond neurological representation.[1] We emphasize 2 key elements that lead to a higher risk of infection: overall immune system dysfunction and reduced antibody production. Mitochondrial dysfunction compromises immune cell function, making it difficult to build a strong defense against pathogens.[2] Additionally, altered B-cell function raises questions about compromised antibody recognition of pathogens.[3] Moreover, gastrointestinal symptoms in MELAS may disrupt the balance of gut microbiota, further impairing the body's defense mechanisms.[4]

As novel infectious illnesses are being identified, it is essential to explore the world of co-occurring conditions. While learning about the pathophysiology of MELAS syndrome, specific cases of infections occurring simultaneously were worth investigating. Since the coronavirus disease 2019 pandemic, it is necessary to draw attention to the possibility of MELAS increasing infection risk in individuals. Because MELAS is a maternally inherited mitochondrial disorder with an estimated occurrence of 1 in 4000,[5] it was challenging to rule out a connection between a rare genetic issue and sensitivity to infection.

MELAS syndrome is a complex mitochondrial disorder.[1] This disorder can present itself with a wide range of clinical symptoms. These symptoms include stroke-like episodes, dementia, epilepsy, lactic acidemia, myopathy, recurrent headaches, hearing impairment, diabetes, and short stature among various other signs.[1] It is easier to comprehend the range of MELAS symptoms when we take into account how malfunctioning mitochondria affect vital cell functions.

To highlight the role of immunology to MELAS, it is necessary to further investigate certain speculations. The first aspect that we would like to focus on is overall immune system dysfunction. Mitochondria are not only energy producers; they also play a pivotal role in immune cell function, affecting both innate and adaptive immunity.[6] This can prevent immune cells from functioning optimally, particularly while producing an adequate inflammatory response. Regarding the aforementioned theory, we may consider neutrophils and their adenosine triphosphate–dependent mechanisms for detecting stimuli, transduction, chemotaxis, ingestion, degranulation, and killing microorganisms.[7] Consequently, the immune system may struggle to mount a strong defense against pathogens.

Another area to explore is the issue of reduced antibody production. This may be a specific consequence of mitochondrial metabolism inducing differential B-cell function including the development of plasma cells.[6] There is also evidence to suggest mitochondrial role in T-cell activation.[6] Needless to say, antibodies are essential components of the immune system's arsenal against infections. A weakened immune response due to reduced antibody production can elevate the risk of not only common infections but also opportunistic pathogens.[7] This presents a complex challenge for those affected by MELAS.

Further, some individuals with MELAS are known to experience gastrointestinal symptoms, adding to the far-reaching impact of mitochondrial dysfunction.[4] We predict that these gastrointestinal issues may disrupt the balance of the gut microbiota, where beneficial and harmful bacteria coexist. An imbalanced gut microbiota can impair the body's defense mechanisms against infections, leading to increased vulnerability of patients to pathogens.[8]

Even though there is no cure for MELAS, management of the disease often involves a combination of medications to address its symptoms.[1] Unfortunately, some of the therapeutic interventions used to prevent infections, such as immunosuppressive drugs or prolonged antibiotic courses, may further escalate the risk of infections.[9] This leads to an unending cycle of infection development and control. Interestingly, infections themselves can become triggers for MELAS symptoms as well.[10] The physiological stress associated with infections can place an added burden on already compromised mitochondria.[10]

In light of our extensive experience in the last few years controlling infectious diseases, we humbly request greater focus on the field of genetic illnesses and the immunologic effects they can have. Patient treatment becomes increasingly complex due to the intricate interactions between infections and MELAS symptoms and therapeutic approaches. Prioritizing research in this area may open the door to targeted pharmacological management of systemic complications that seem to arise with MELAS syndrome.

Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

All 3 authors participated in the writing of the paper.

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Emergency and Critical Care Medicine (2025) 5:3

Received: 10 March 2024; Accepted: 2 April 2024

Published online: 23 October 2024

http://dx.doi.org/10.1097/EC9.0000000000000130

Funding

None.

Ethical approval of studies and informed consent

Not applicable.

Acknowledgments

None.

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How to cite this article: Saleem M, Sohail M, Akhtar A. Melas syndrome and risk of infection. *Emerg Crit Care Med*. 2025;5(3):121–122. doi: 10.1097/EC9.0000000000000130