CME-QUIZ | ENGLISH

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Link to the questions:

Cutaneous sarcoidosis in the precision medicine era

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Link to original article in *SKINdeep*:

Abstract

Sarcoidosis is an inflammatory disorder of unknown origin that belongs to the group of granulomatous diseases. It is characterized by the development of typical non-caseating granulomas in affected organs, which may progress to fibrosis and organ dysfunction. The lungs are most frequently involved, followed by the lymph nodes and skin.

Cutaneous sarcoidosis presents with highly variable clinical forms and disease courses. Skin involvement may precede systemic manifestation, occur simultaneously, or develop later in the disease. The treatment of cutaneous sarcoidosis often poses a challenge for physicians, as therapeutic responses vary widely depending on patient heterogeneity and lesion morphology.

Currently, systemic or topical glucocorticoids remain the gold standard of therapy, yet their efficacy is inconsistent, and long-term use is limited by side effects. In contrast to other chronic inflammatory conditions, targeted therapies for sarcoidosis are still scarce. However, recent advances in sarcoidosis research are paving the way for novel treatment options, including mTOR inhibition or targeting of the JAK/STAT pathway. A deeper understanding of disease mechanisms is expected to facilitate the development of more specific and effective therapies for cutaneous sarcoidosis in the future.

15 CME QUESTIONS ABOUT THE ARTICLE "CUTANEOUS SARCOIDOSIS IN THE AGE OF PRECISION MEDICINE"

Question 1: Prevalence of Organ Involvement

Which organ is most commonly affected by sarcoidosis?

A Skin
B Lungs
C Kidneys
D Heart
E CNS

Question 2: Histopathology

Which histopathological finding is typical of cutaneous sarcoidosis?

A Caseating granulomas with pronounced neutrophilic inflammation
B Acanthosis with subcorneal pustules
C Leukocytoclastic vasculitis
D Spongiosis with eosinophilic infiltrates
E Non-caseating, so-called "naked" granulomas

Question 3: Clinical Manifestation

Which statement about lupus pernio is true?

A Lupus pernio is usually self-limiting and heals spontaneously.
B Lupus pernio primarily affects the lower extremities.
C Lupus pernio is a disfiguring subtype of plaque sarcoidosis in the central face.
D Lupus pernio is histologically characterized by caseous necrosis.
E Lupus pernio occurs exclusively in children.

Question 4: Therapy

Which therapy is considered the first-line local treatment for cutaneous sarcoidosis?

A Topical high-potency glucocorticoids
B Systemic methotrexate
C Intravenous infliximab
D Oral doxycycline
E Systemic sirolimus

Question 5: New Targeted Therapeutic Approaches

Which two signaling pathways are considered particularly promising new therapeutic targets for cutaneous sarcoidosis?

A Hedgehog and Wnt signaling pathways
B MAPK and EGFR signaling pathways
C JAK/STAT and mTOR signaling pathways
D BRAF and MEK signaling pathways
E NFAT and calcineurin signaling pathways

Question 6: Th17.1 Cells and Fibroblasts

Which of the following statements about Th17.1 cells and fibroblasts in sarcoidosis are correct?

Multiple answers are possible.

A Th17.1 cells produce, among other factors, *IFN-γ, GM-CSF, TNF-α, and IL-17.*
B Th17.1 cells secrete lymphotoxin-β, which can contribute to the formation of tertiary lymphoid structures.
C Fibroblasts produce extracellular matrix components such as collagen and fibronectin.
D Fibroblasts play exclusively a passive supportive role without any immunomodulatory activity.
E Fibroblasts do not secrete CCL19.

Question 7: Pathomechanism

Which molecular signaling pathway is described as a key driver of granuloma formation in sarcoidosis?

A VEGF signaling pathway
B Sonic Hedgehog signaling pathway
C mTORC1 signaling pathway
D Notch signaling pathway
E TGF-α signaling pathway

Question 8: Sarcoidosis Syndromes

Which triad is typical of Löfgren's syndrome?

A Uveitis, facial nerve palsy, parotid swelling
B Erythema nodosum, bilateral hilar lymphadenopathy, polyarthralgia
C Arthritis, uveitis, dermatitis
D Lupus pernio, fever, hypercalcemia
E Alopecia, nail dystrophy, dactylitis

Question 9: New Therapeutic Approaches and Prognosis

Which statements regarding new therapeutic approaches and prognosis in sarcoidosis are correct?

Multiple answers are possible.

- A Sirolimus is a selective mTORC1 inhibitor.
- B Progressive forms involving the lungs, heart, or nervous system are associated with an increased risk of mortality.
- C JAK/STAT and mTOR inhibitors have not shown any therapeutic potential to date.
- D Involvement of the eyes, kidneys, or liver affects only mortality, not morbidity.
- E In a small study, tofacitinib demonstrated efficacy in steroid-resistant cutaneous sarcoidosis.

Question 10: Treatment

Which statement regarding the systemic treatment of cutaneous sarcoidosis is correct?

- A Hydroxychloroquine does not require ophthalmologic follow-up.
- B Methotrexate is an established option for treatment-resistant forms, such as lupus pernio.
- C TNF-α inhibitors are generally contraindicated in cutaneous sarcoidosis.
- D Glucocorticoids are no longer recommended due to lack of efficacy.
- E Doxycycline must not be used due to lack of evidence.

Question 11: Which statement regarding the epidemiology of cutaneous sarcoidosis is correct?

- A People of African descent have a lower incidence of cutaneous sarcoidosis.
- B The average age of onset in women is generally between 20 and 30 years.
- C African Americans in North America have a higher incidence than Caucasians.
- D Children are affected more frequently than adults.
- E In Europe, the disease occurs exclusively as Löfgren's syndrome.

Question 12: Which statement regarding the role of structural cells in sarcoidosis is correct?

- A Fibroblasts are merely passive matrix producers with no immunological function.
- B Fibroblasts contribute to the spatial organization of immune cells within the granuloma.
- C Fibroblasts generally prevent any fibrosis in sarcoidosis.
- D Sarcoid granulomas contain no structural cells.
- E CCL19 is produced exclusively by macrophages, not by fibroblasts.

Question 13: Etiology and Risk Factors

Which factors are associated with an increased risk of sarcoidosis?

Multiple answers are possible.

- A Exposure to mold
- B UV exposure
- C Hypervitaminosis D
- D Propionibacterium acnes
- E Exposure to pesticides

Question 14: Systemic Involvement

Which statements regarding systemic involvement in cutaneous sarcoidosis are correct?

Multiple answers are possible.

- A In cutaneous sarcoidosis, the probability of pulmonary or thoracic involvement ranges from approximately *50% to 95%*, depending on the cohort.
- B Skin lesions can be the earliest clinical manifestation of sarcoidosis.
- C Once a diagnosis of cutaneous sarcoidosis has been made, further evaluation of other organs is not necessary.
- D In addition to the lungs and lymph nodes, the eyes, joints, liver, nervous system, kidneys, and heart may also be affected.
- E Extrapulmonary involvement is limited to the skin and eyes.

Question 15: Pathomechanisms – Macrophages and mTOR

Which of the following statements regarding the pathomechanisms of sarcoidosis are correct?

Multiple answers are possible.

- A Granuloma formation is independent of the recruitment of peripheral immune cells.
- B mTOR activity is not detectable in granulomas in human sarcoidosis.
- C Proinflammatory macrophages are considered key cells in granuloma formation.
- D mTORC1 is a potent repressor of autophagy and promotes granuloma formation.
- E Under the influence of IL-13, macrophages can adopt an M2-like phenotype.

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