Do linfonodo à junção dermoepidérmica: uma possível conexão imunológica

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IDENTIFICAÇÃO

Paciente

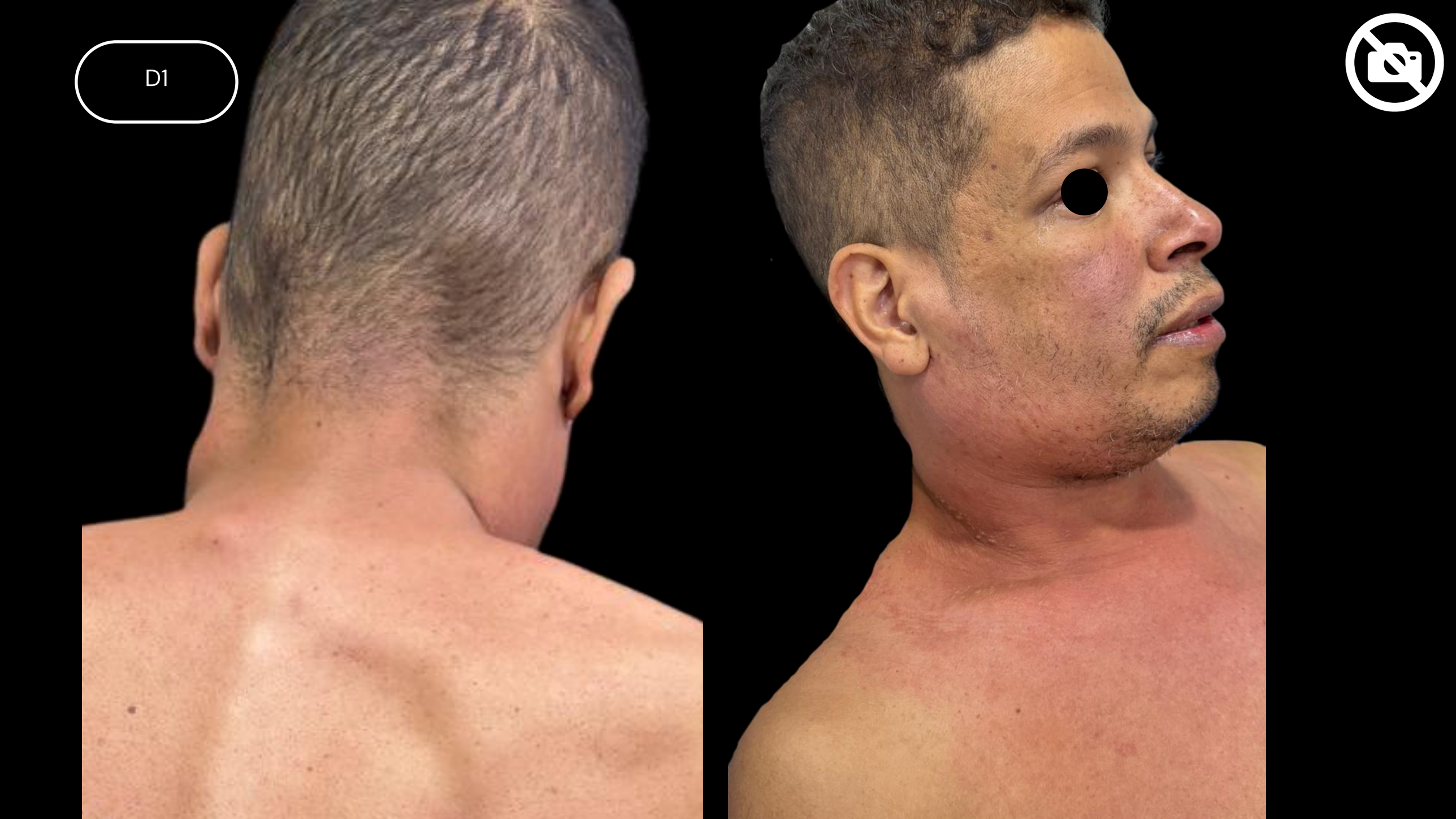
- Homem, 45 anos
- Sem comorbidades

Quadro Clínico

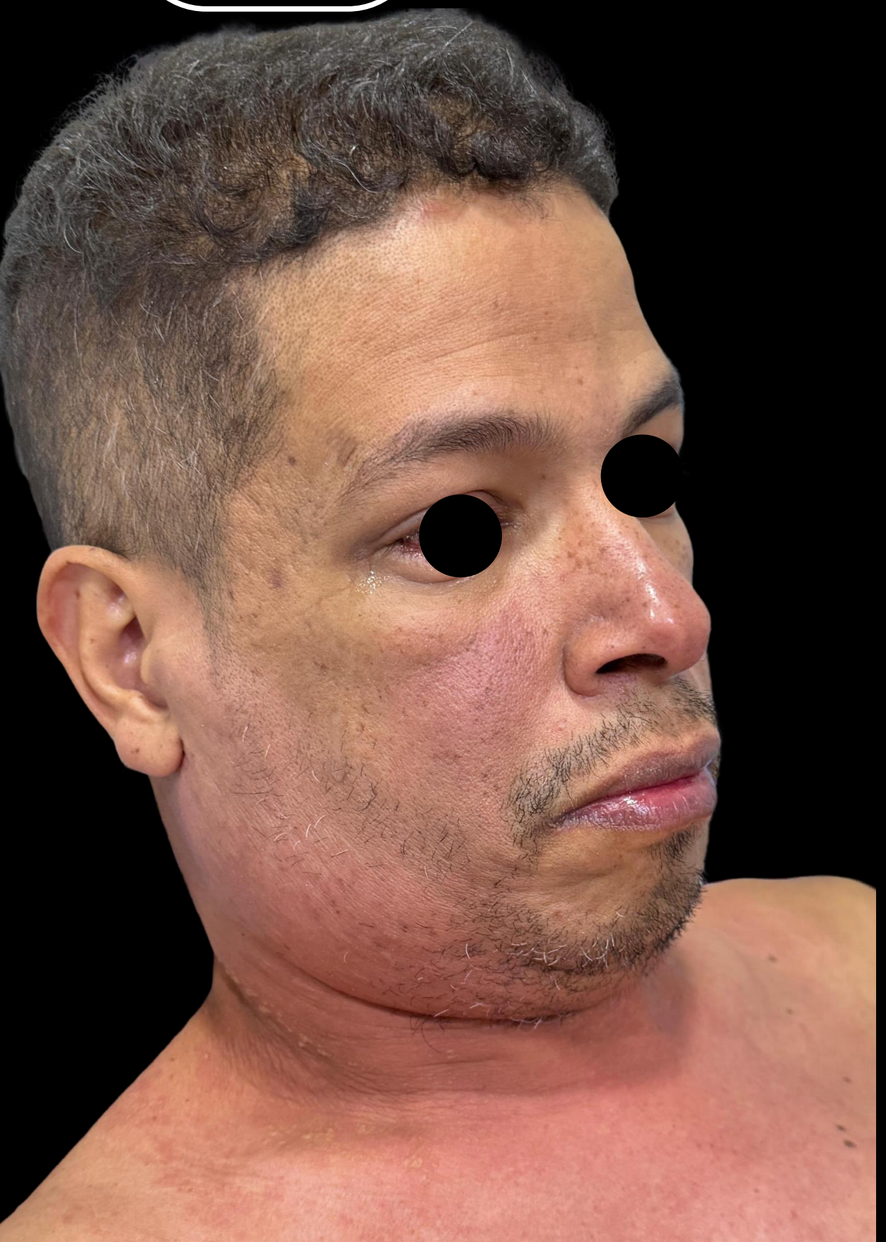
- Linfonodomegalia generalizada em investigação
- Sudorese noturna
- Perda ponderal de 13kg entre janeiro e maio

PARECER PARA DERMATOLOGIA

Paciente refere quadro de fotofobia, hiperemia conjuntival e eritema cutâneo difuso associado a prurido e ardência de início há 4 dias.


D1

D1



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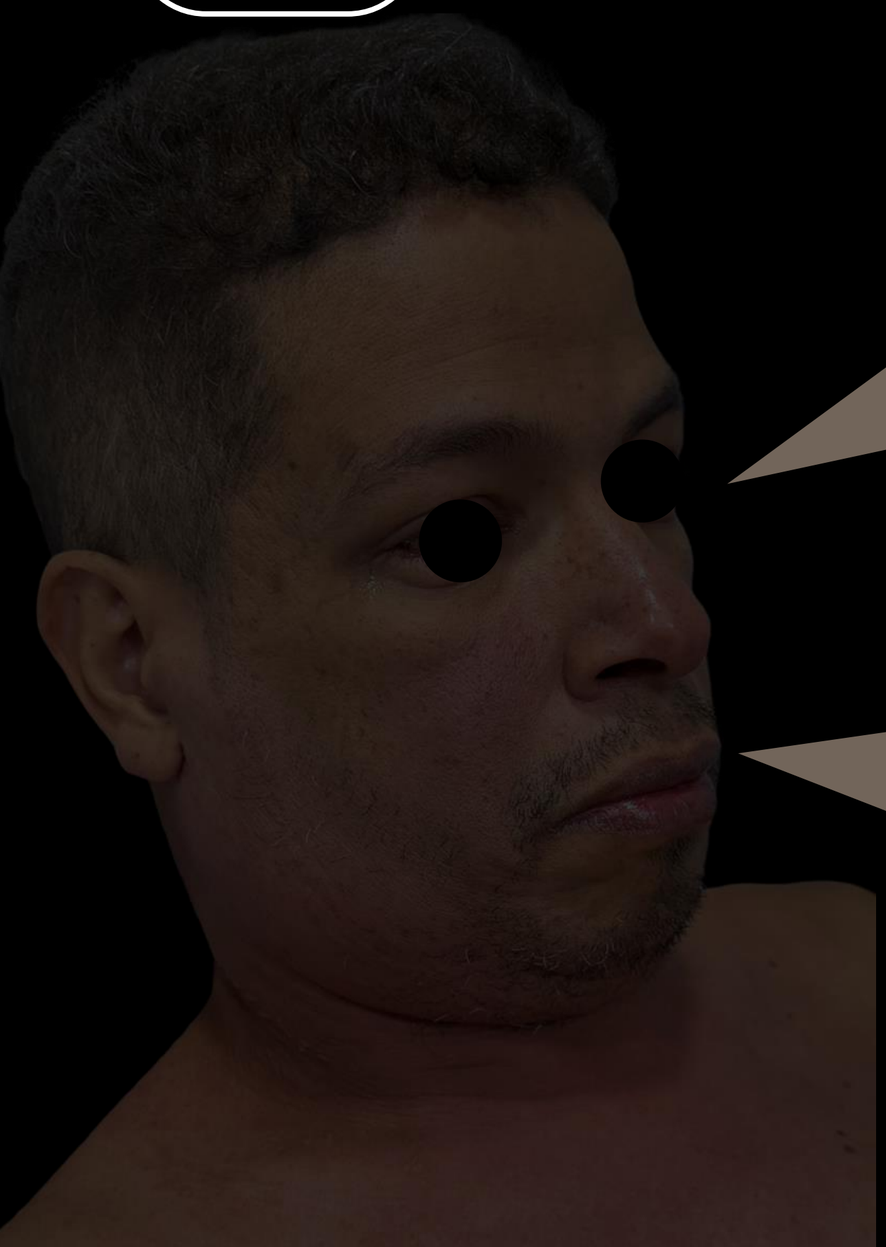

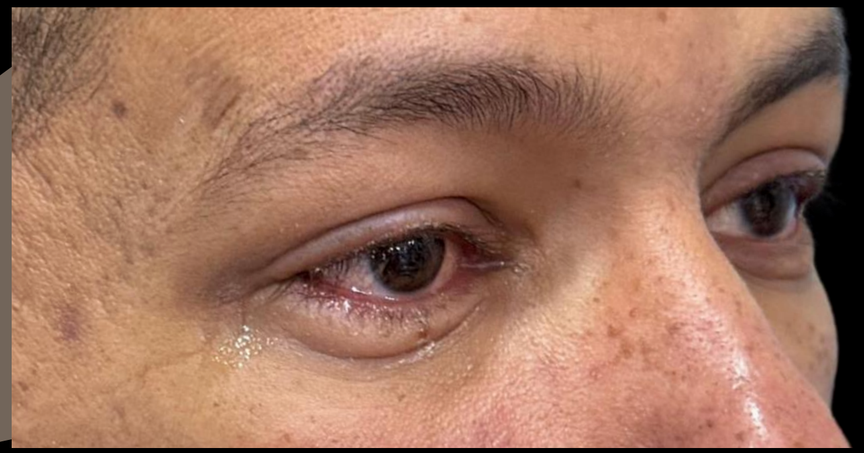

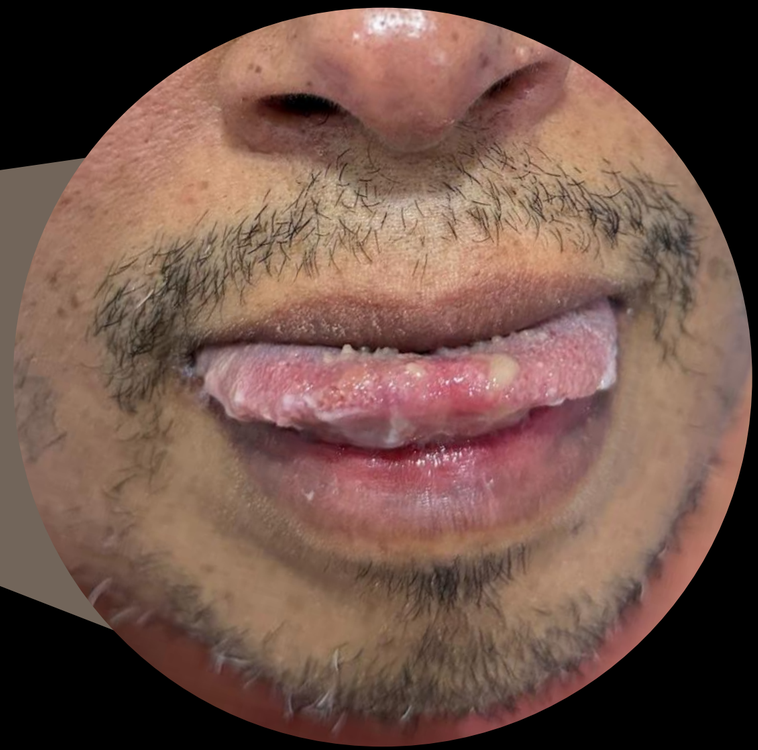

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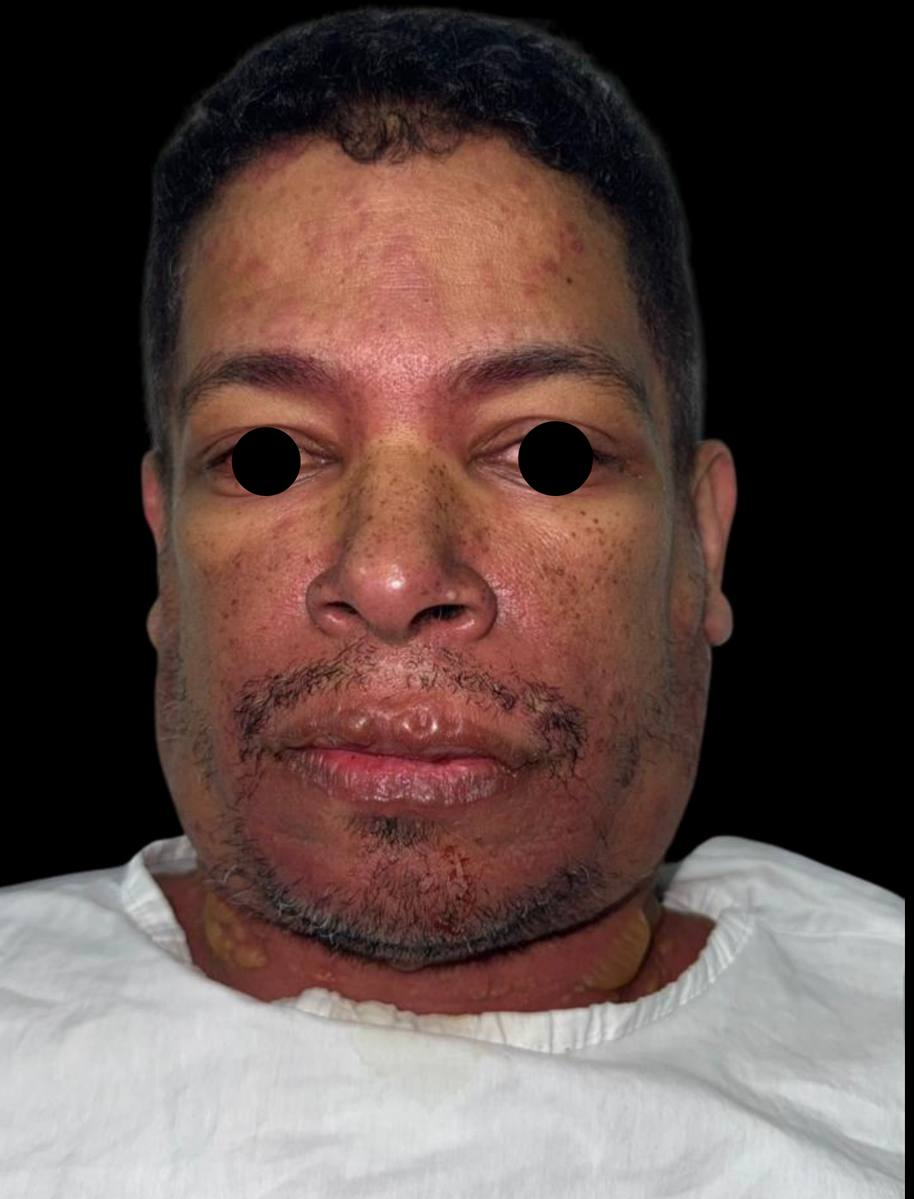

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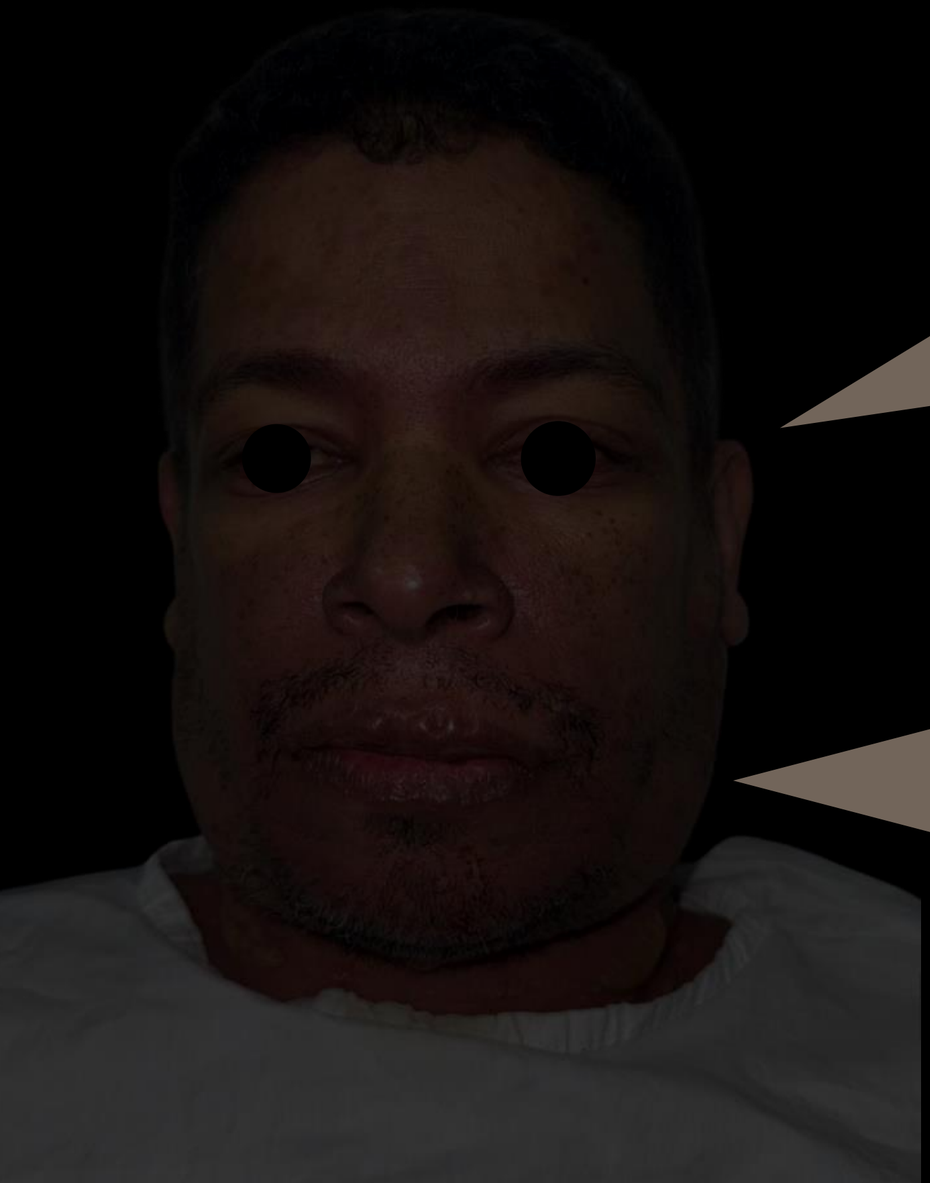
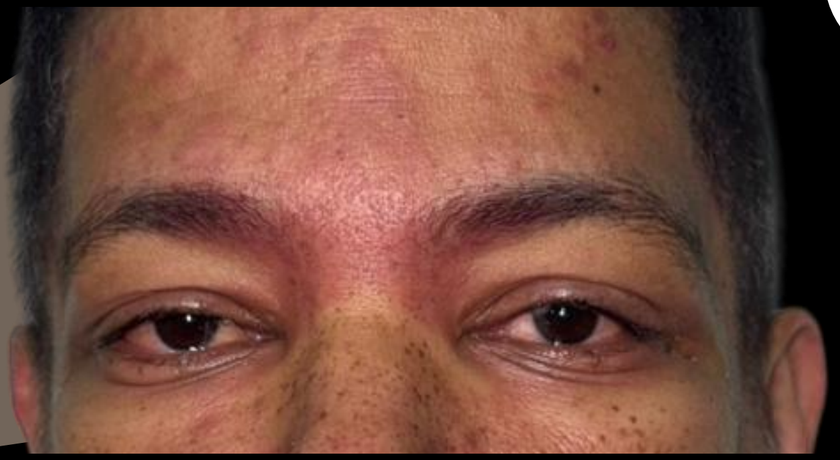
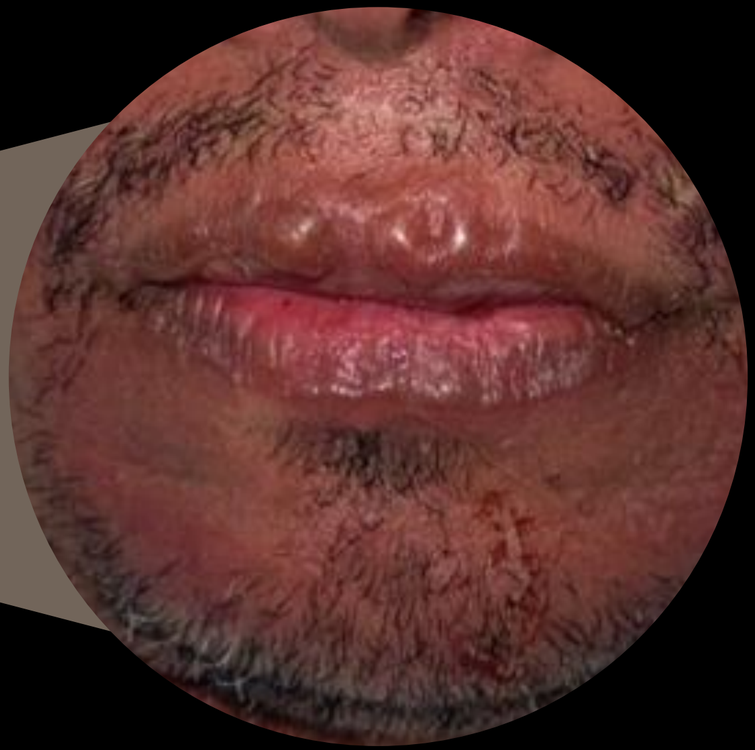
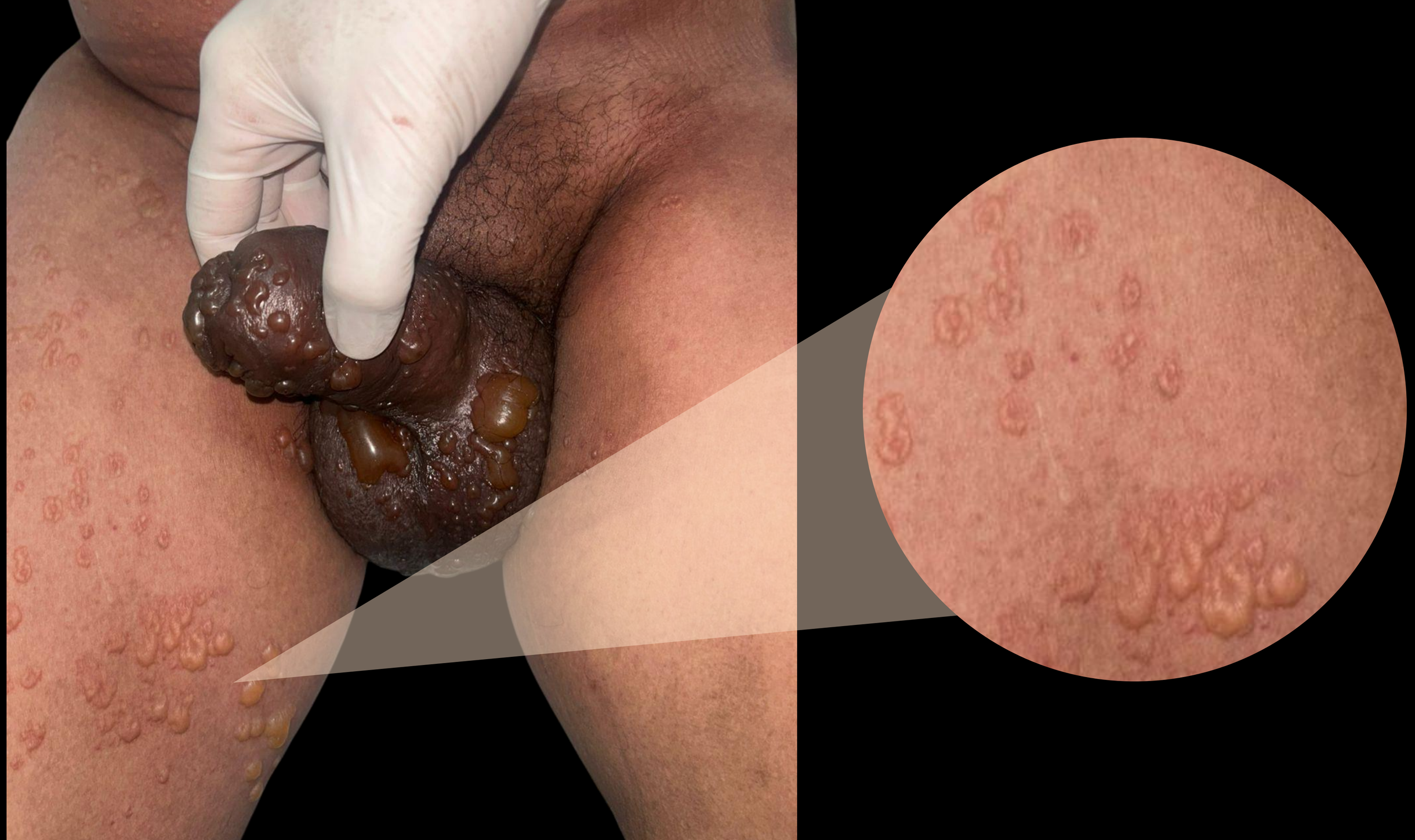
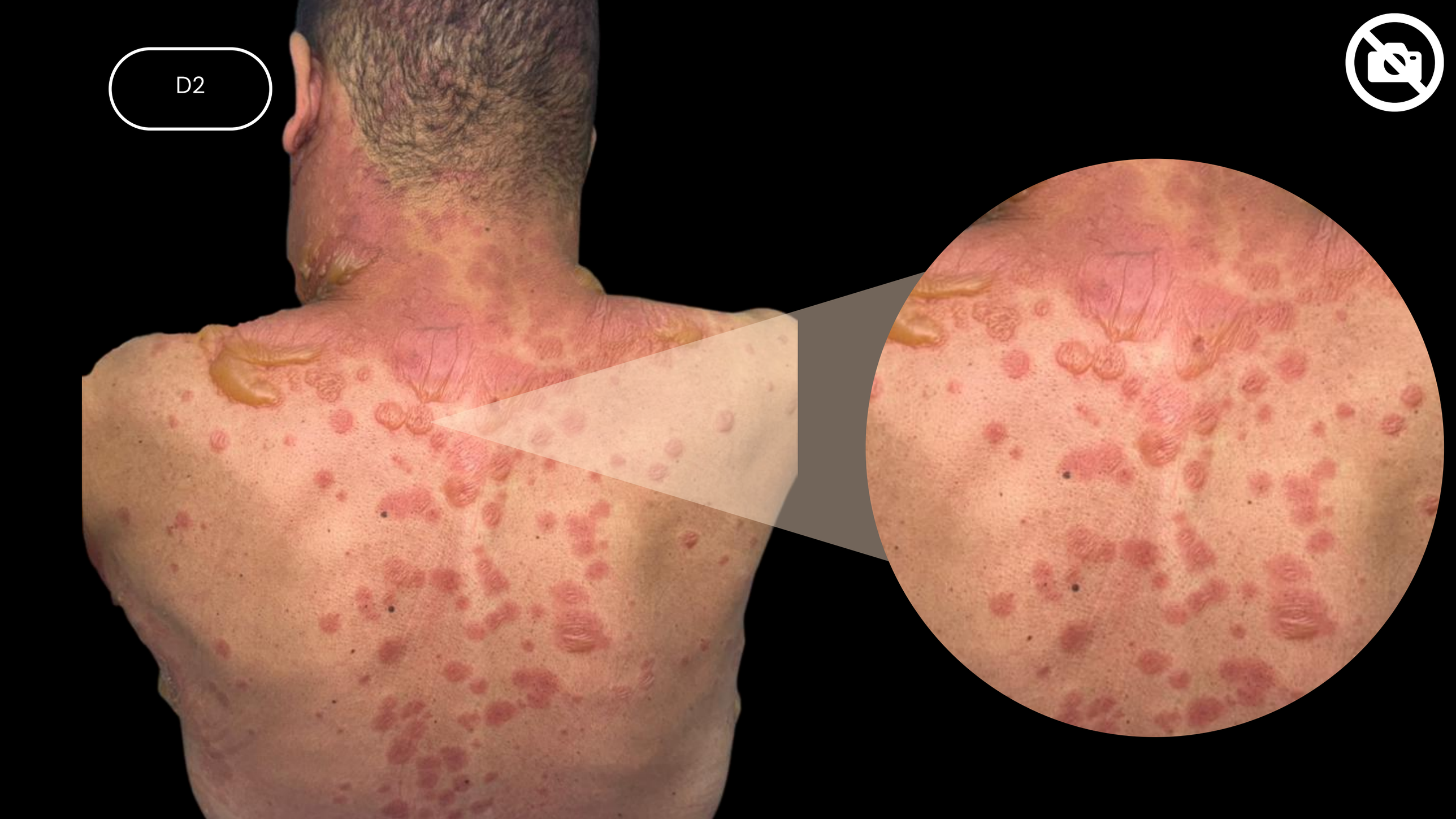


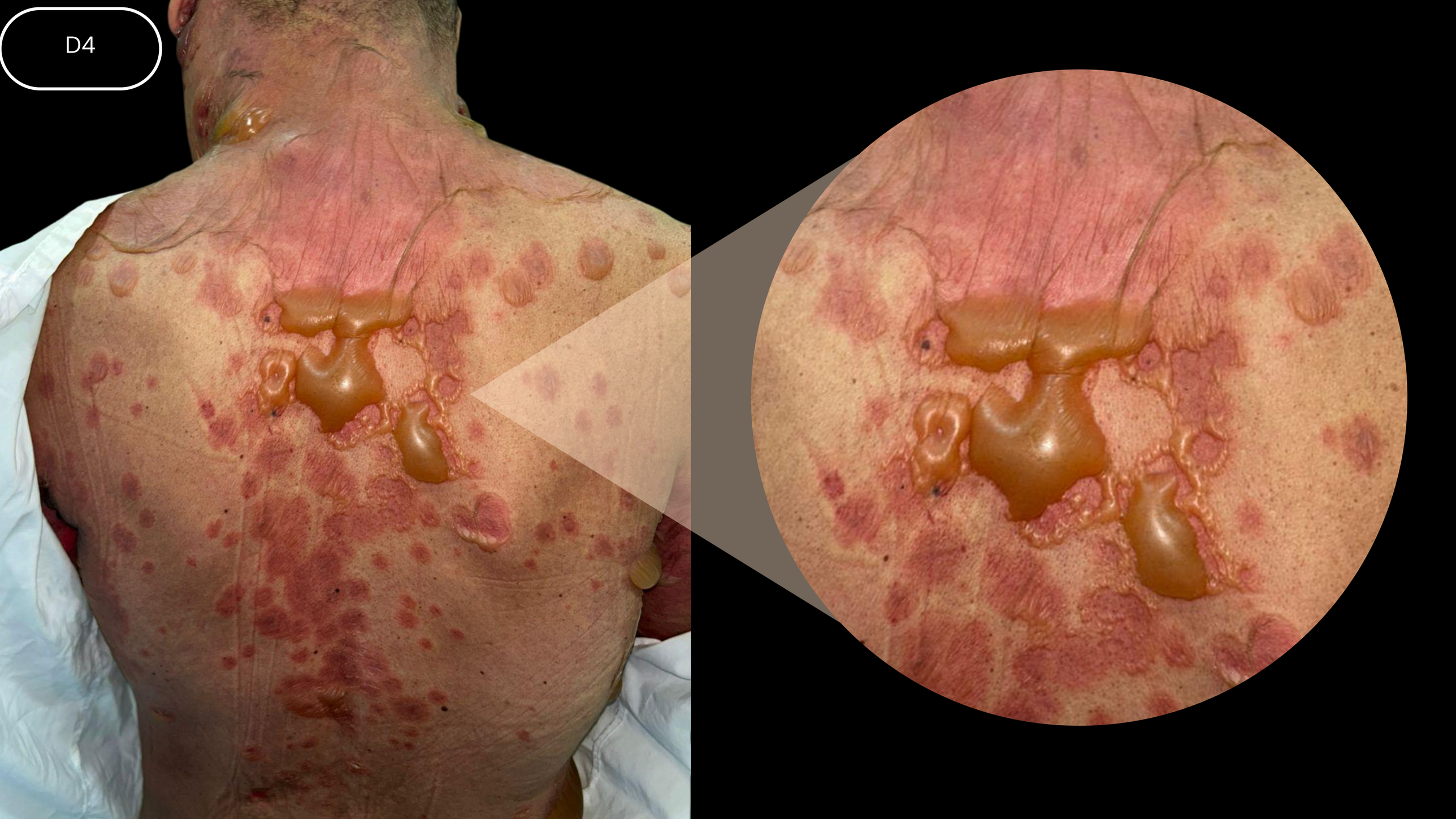


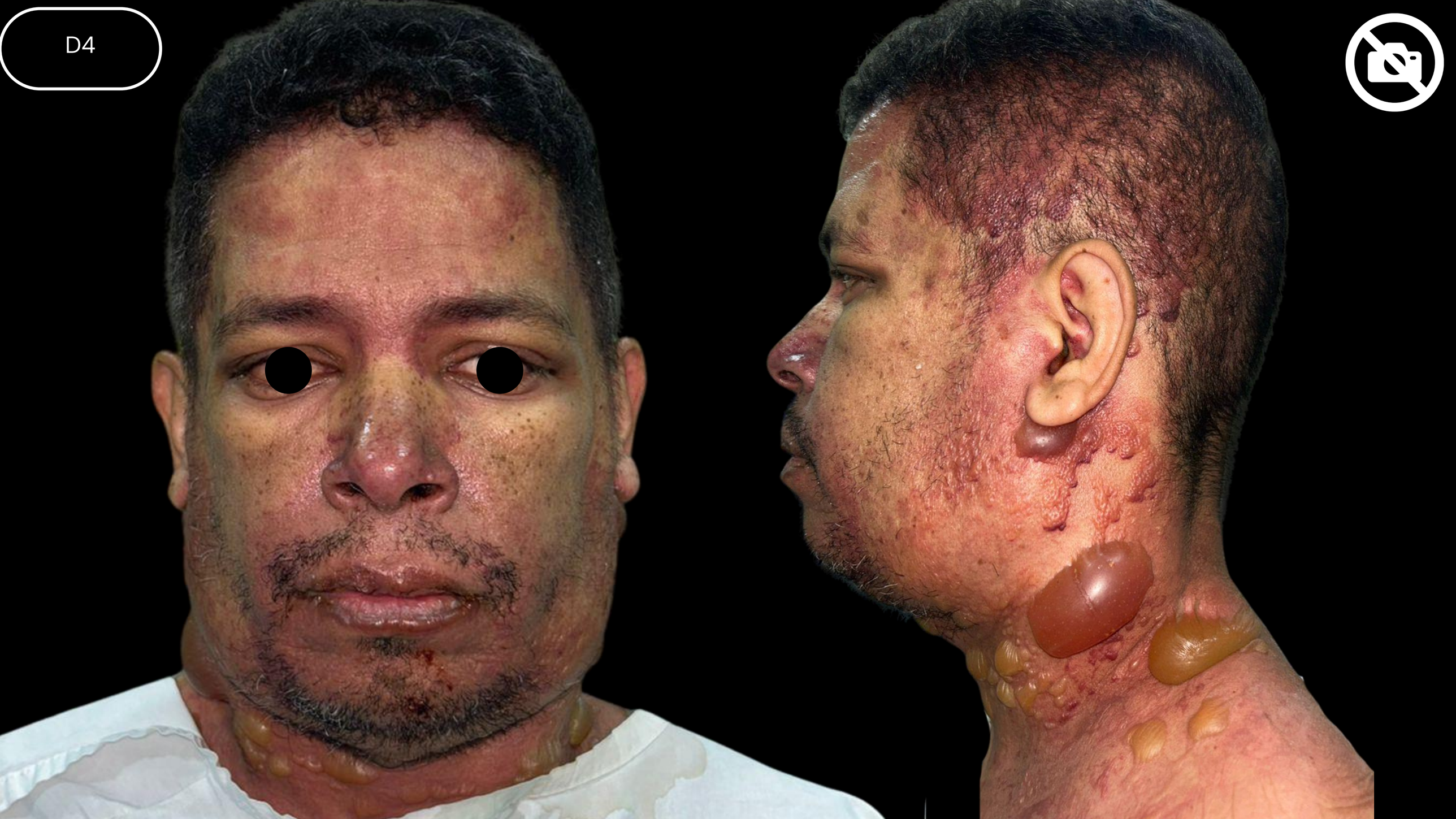





D2

D4




D4

HIPÓTESES DIAGNÓSTICAS

Penfigoide bolhoso

Pênfigo paraneoplásico

SSJ / NET

Dermatose bolhosa por IgA linear

CONDUTA

Biópsias cutâneas

Corticoterapia venosa

Metilprednisolona (equivalente a 1mg/kg/dia de prednisona)

D9

Biópsia de linfonodo

- **Linfoma não hodgkin de células T de alto grau**
- Imuno-histoquímico: CD3 + // CD 10 + // Oncoproteína BCL-2 // MUM1 - //CD 20 - // Ciclina D1 -
- HTLV negativo (exame externo)

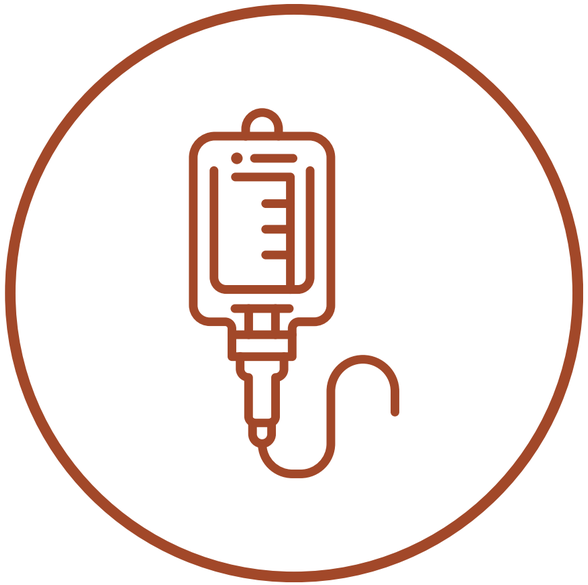
Biópsia de linfonodo

Parecer da hematologia:

Sugestivo de Linfoma T **Angioimunoblástico**

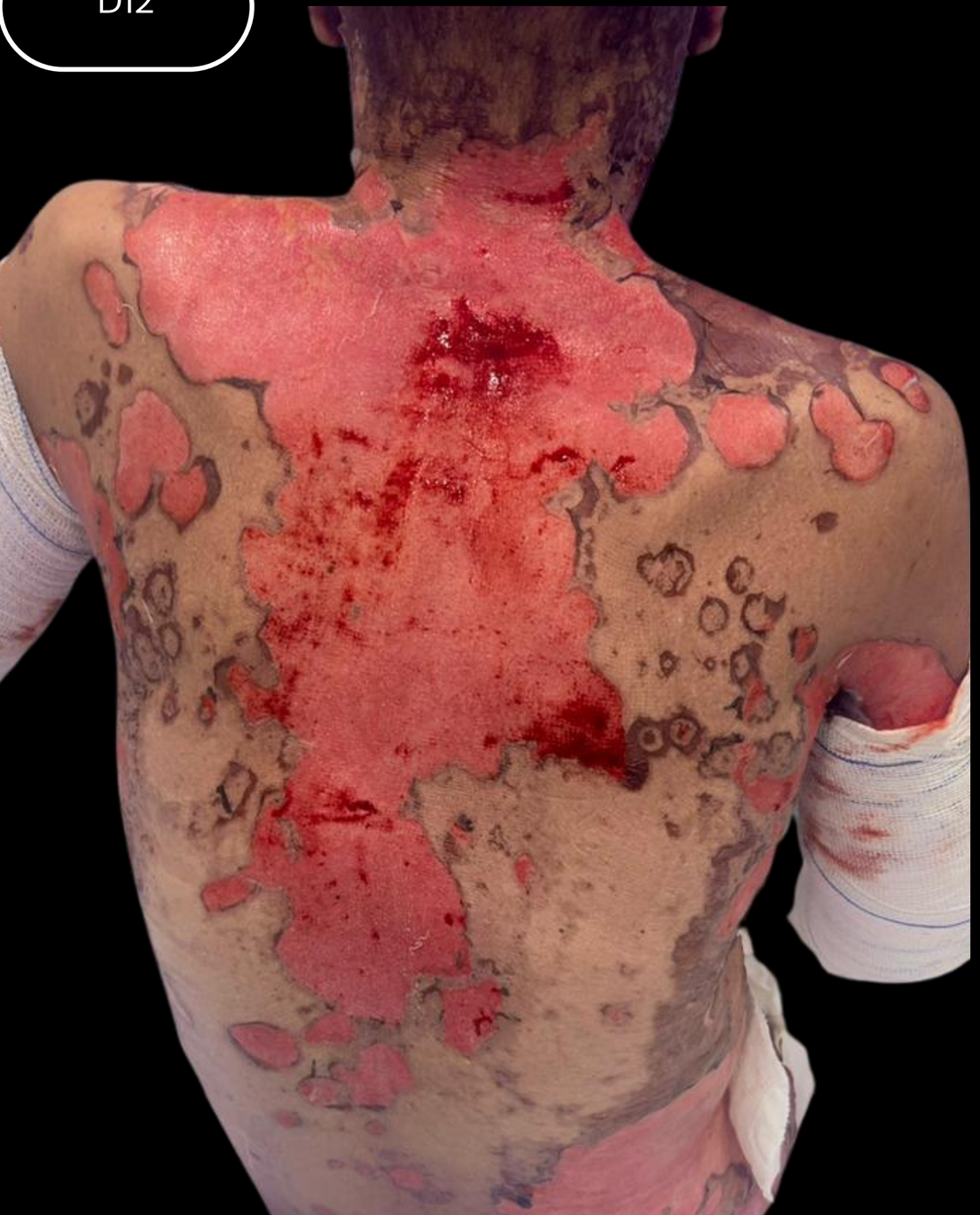
D10

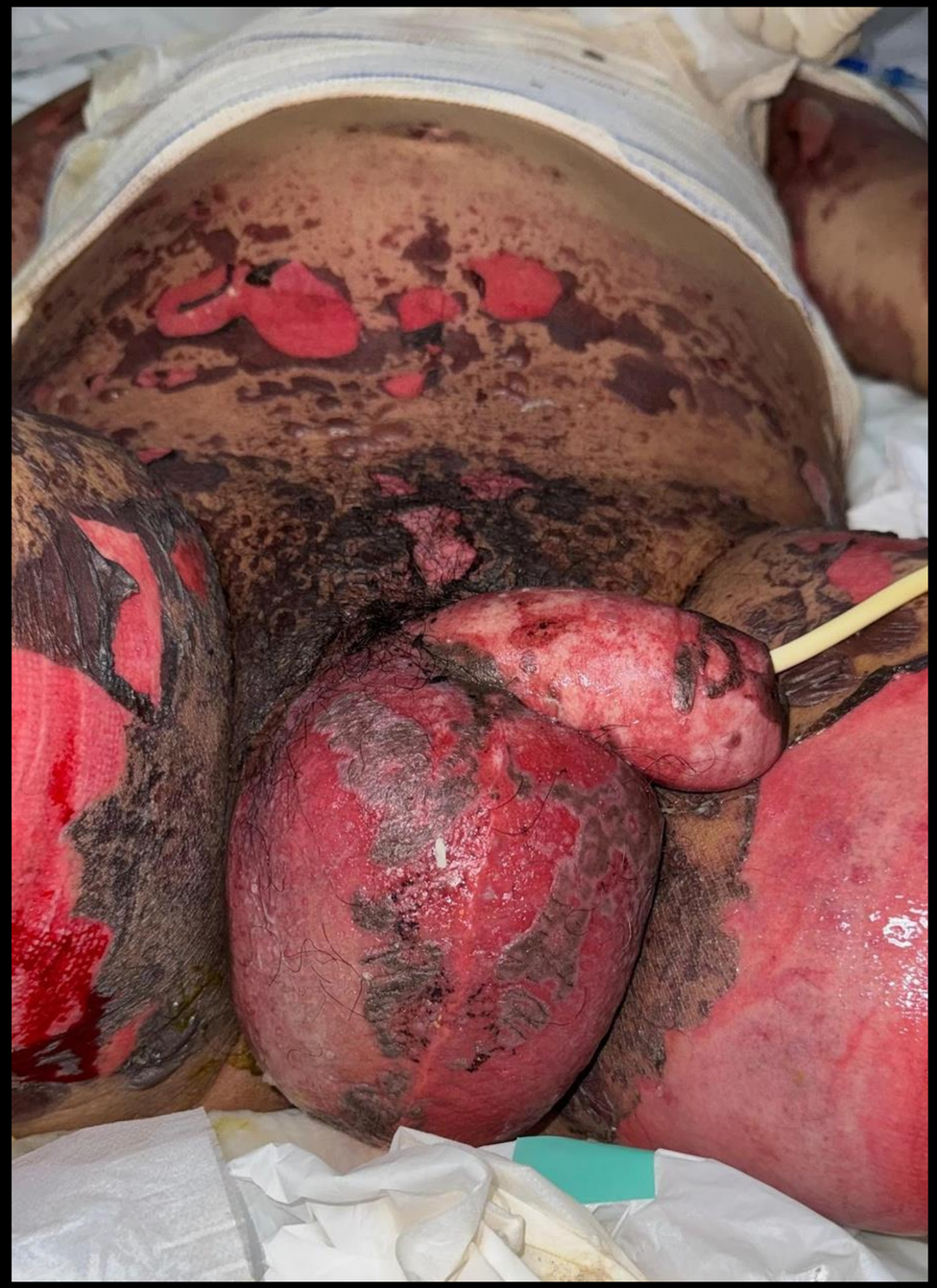
Iniciado esquema CHOP



Ciclofosfamida + Doxorrubicina + Vincristina + Prednisona

D12





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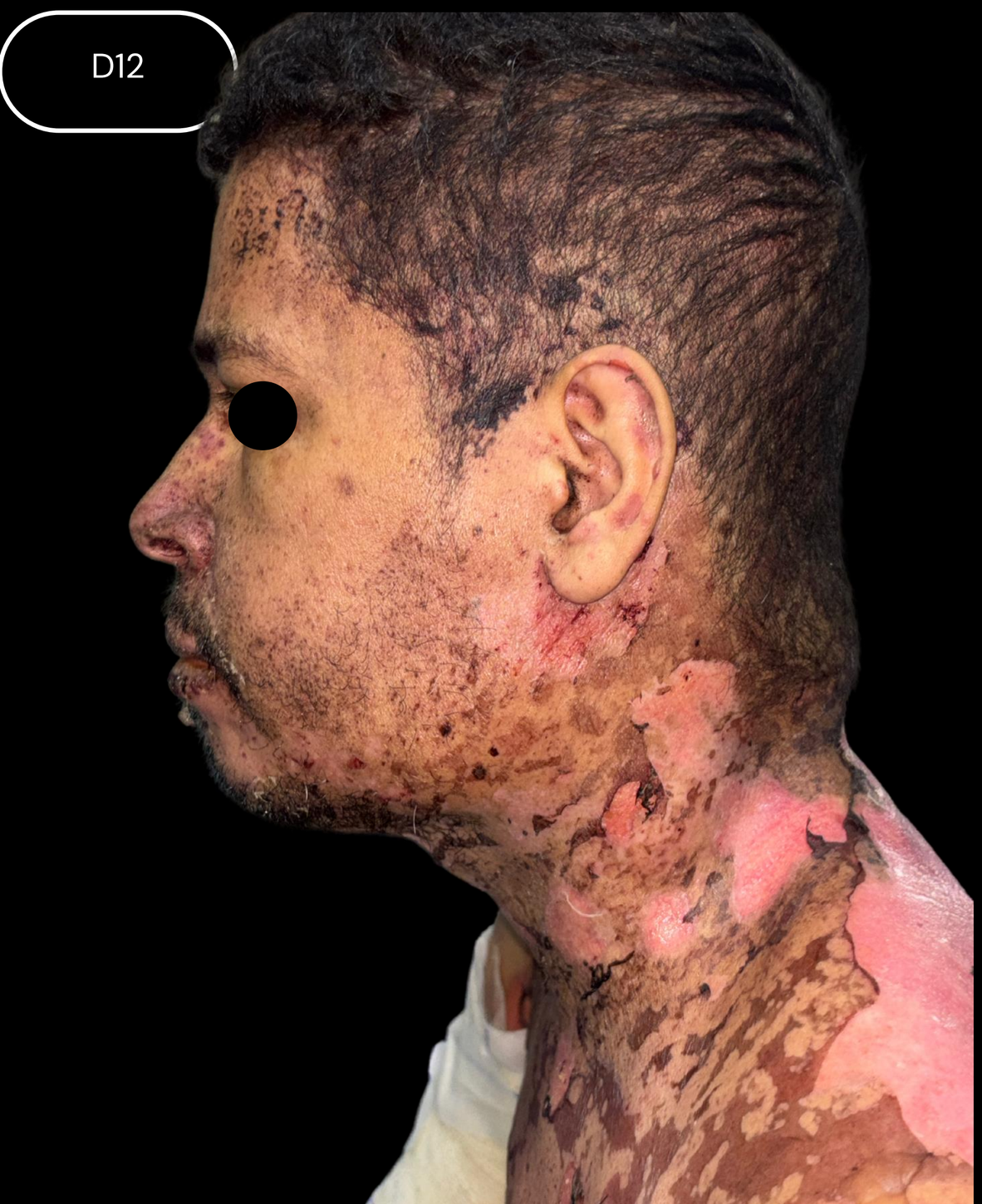

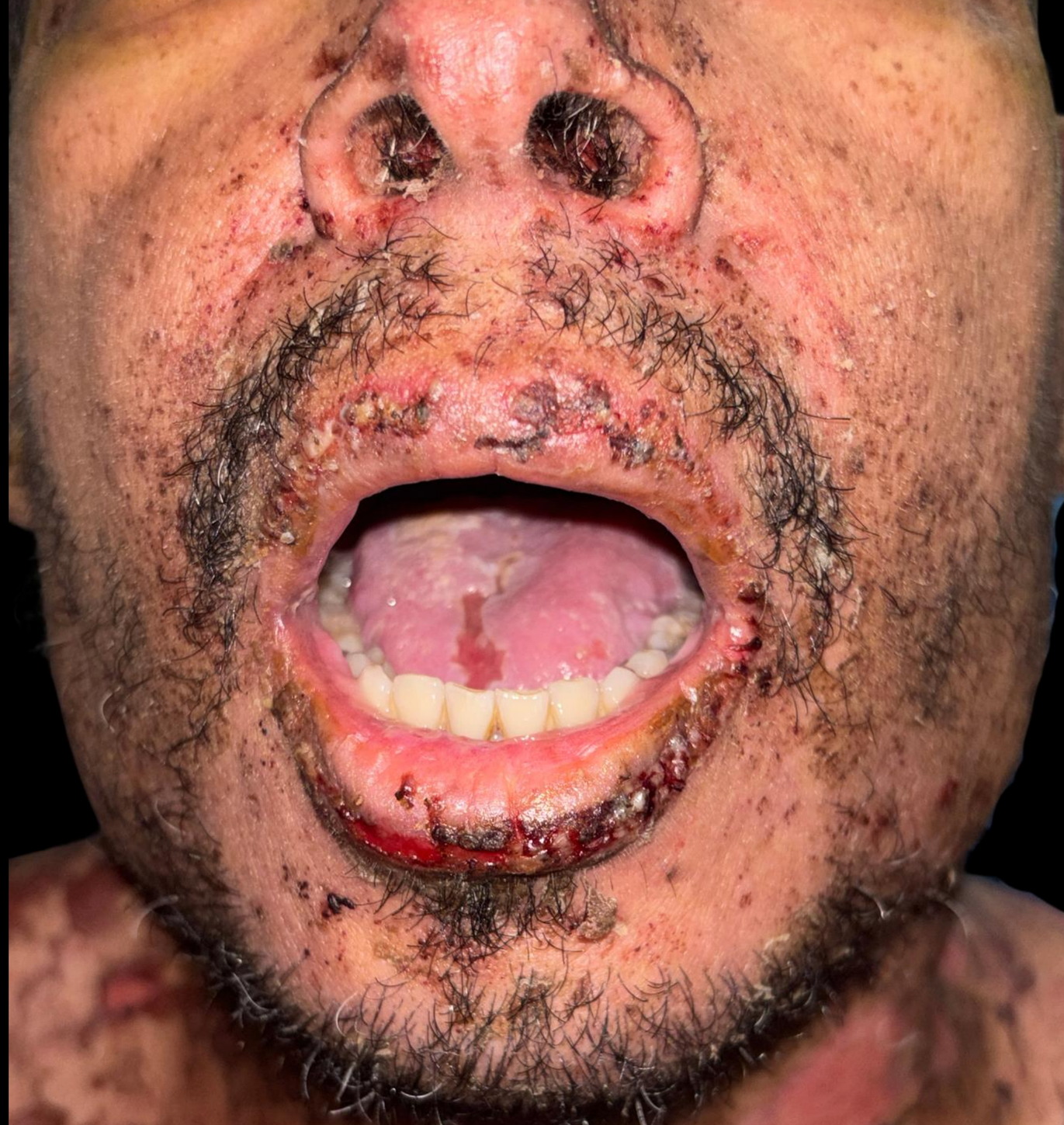

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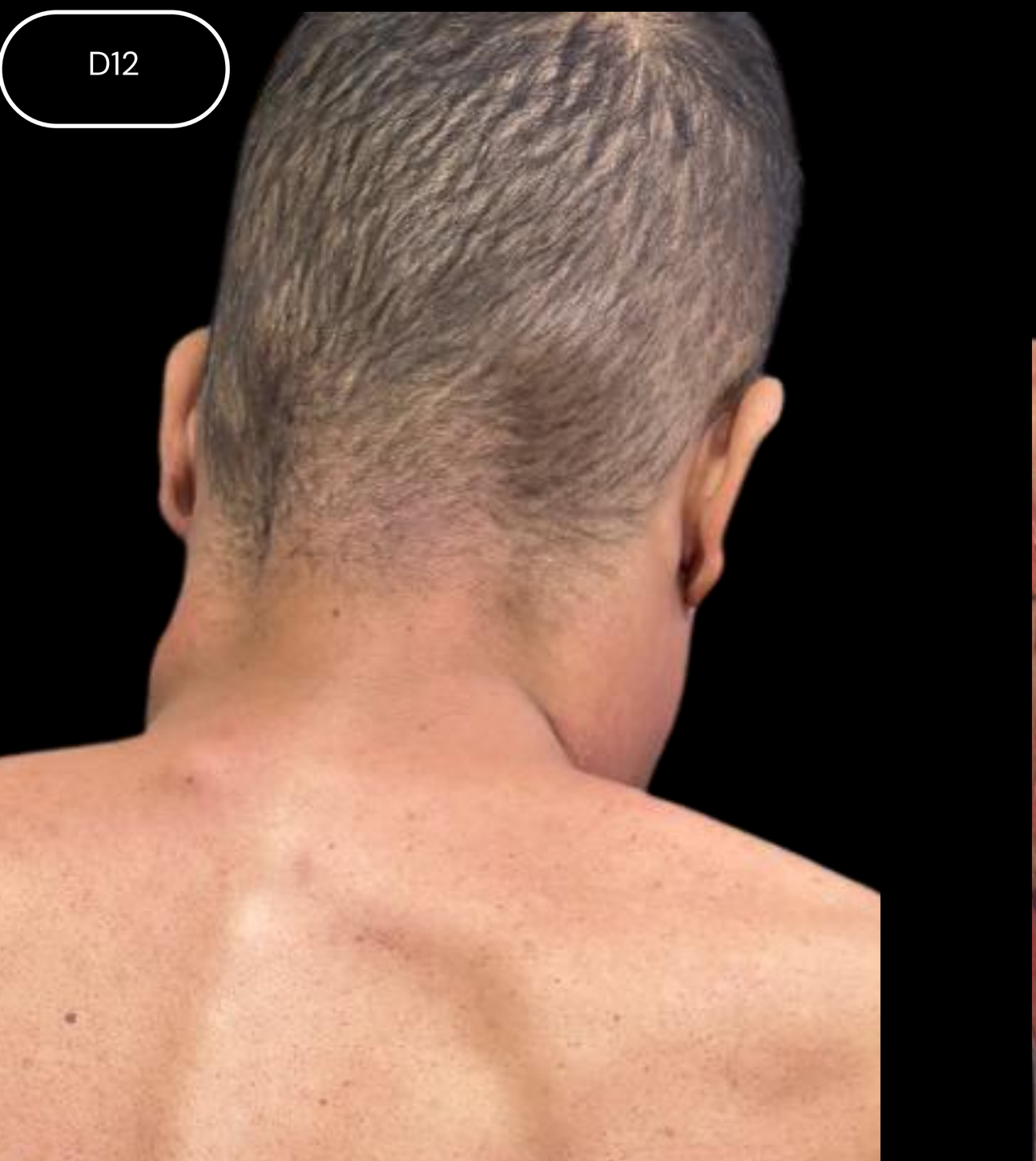

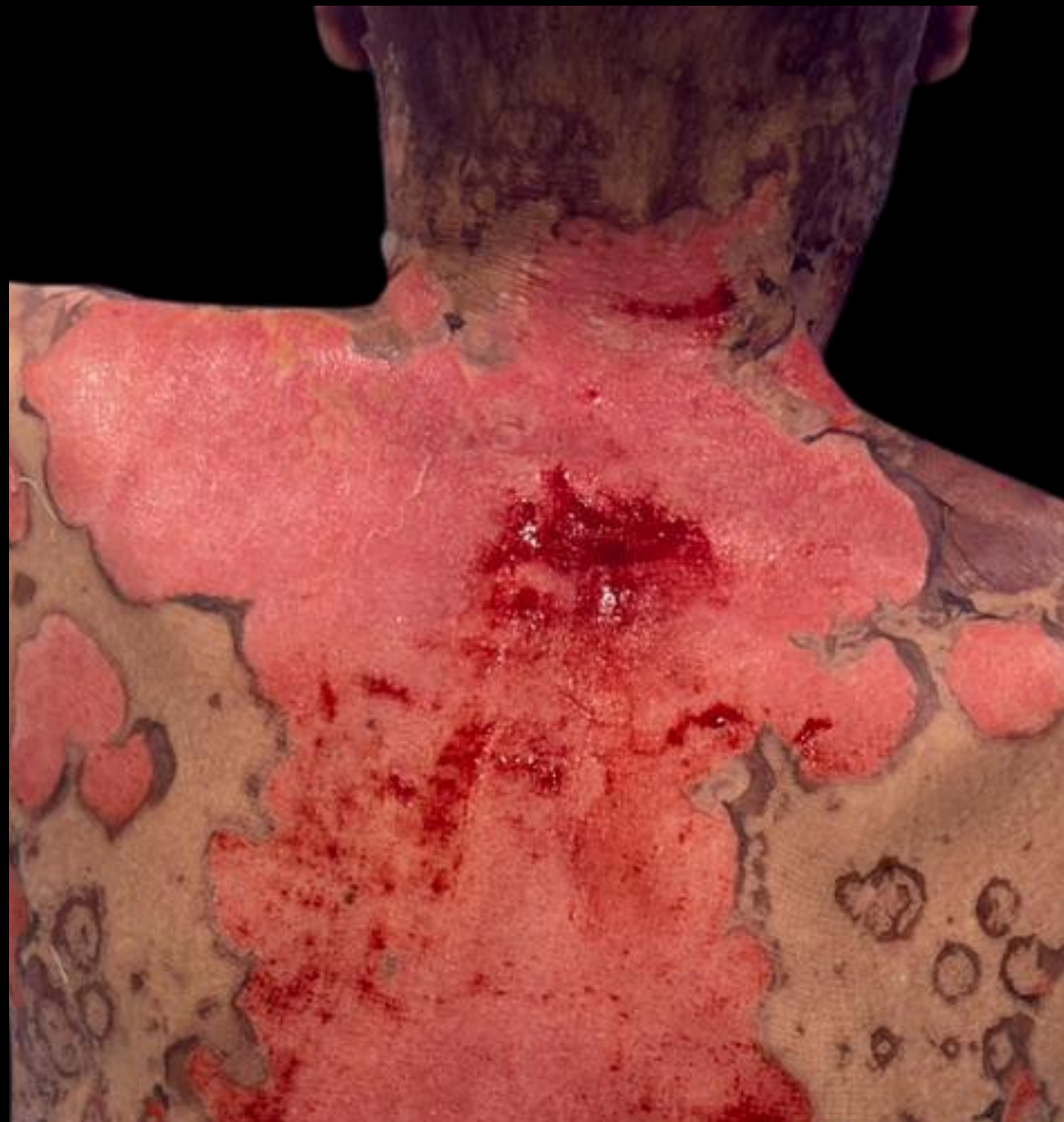

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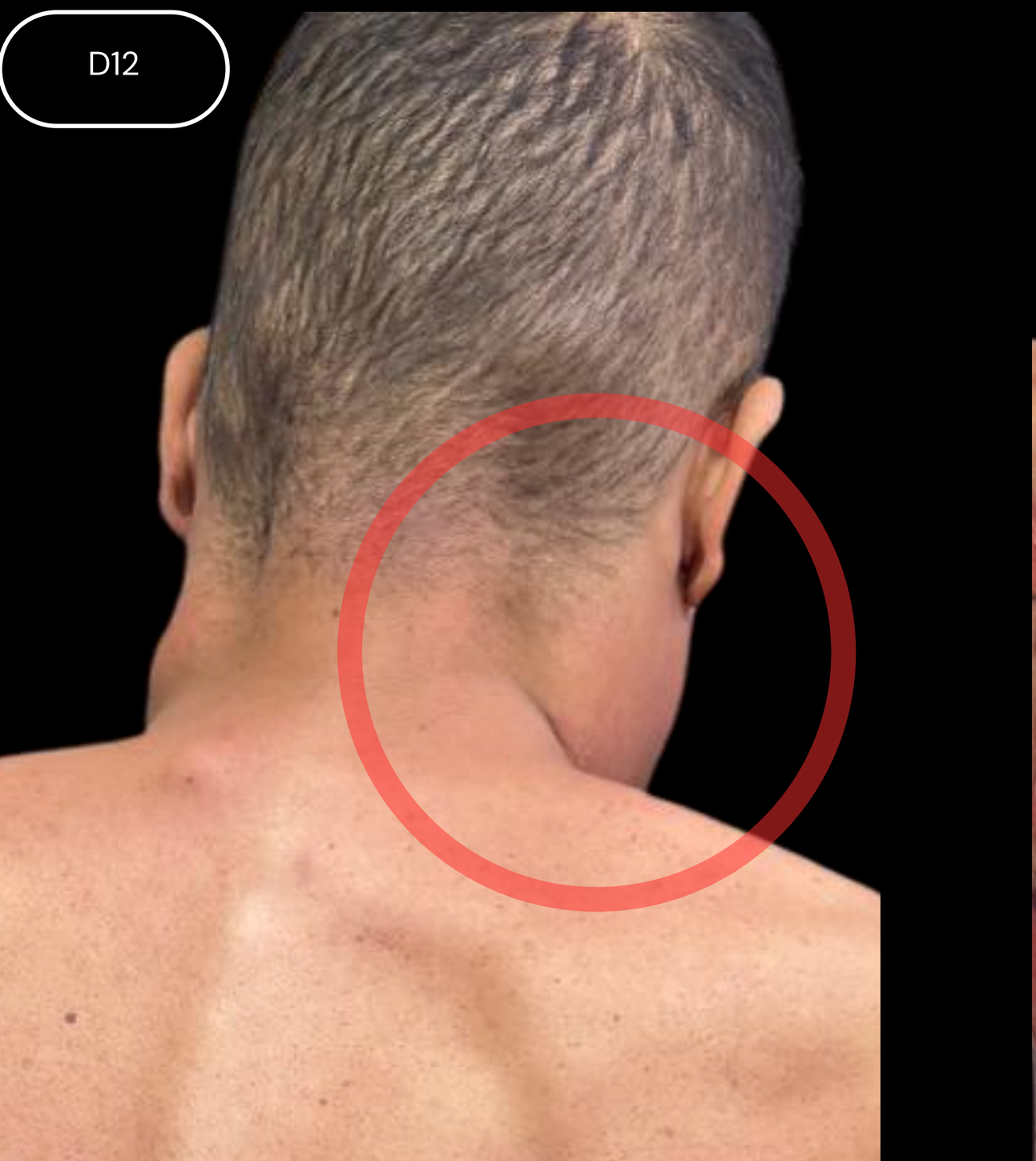
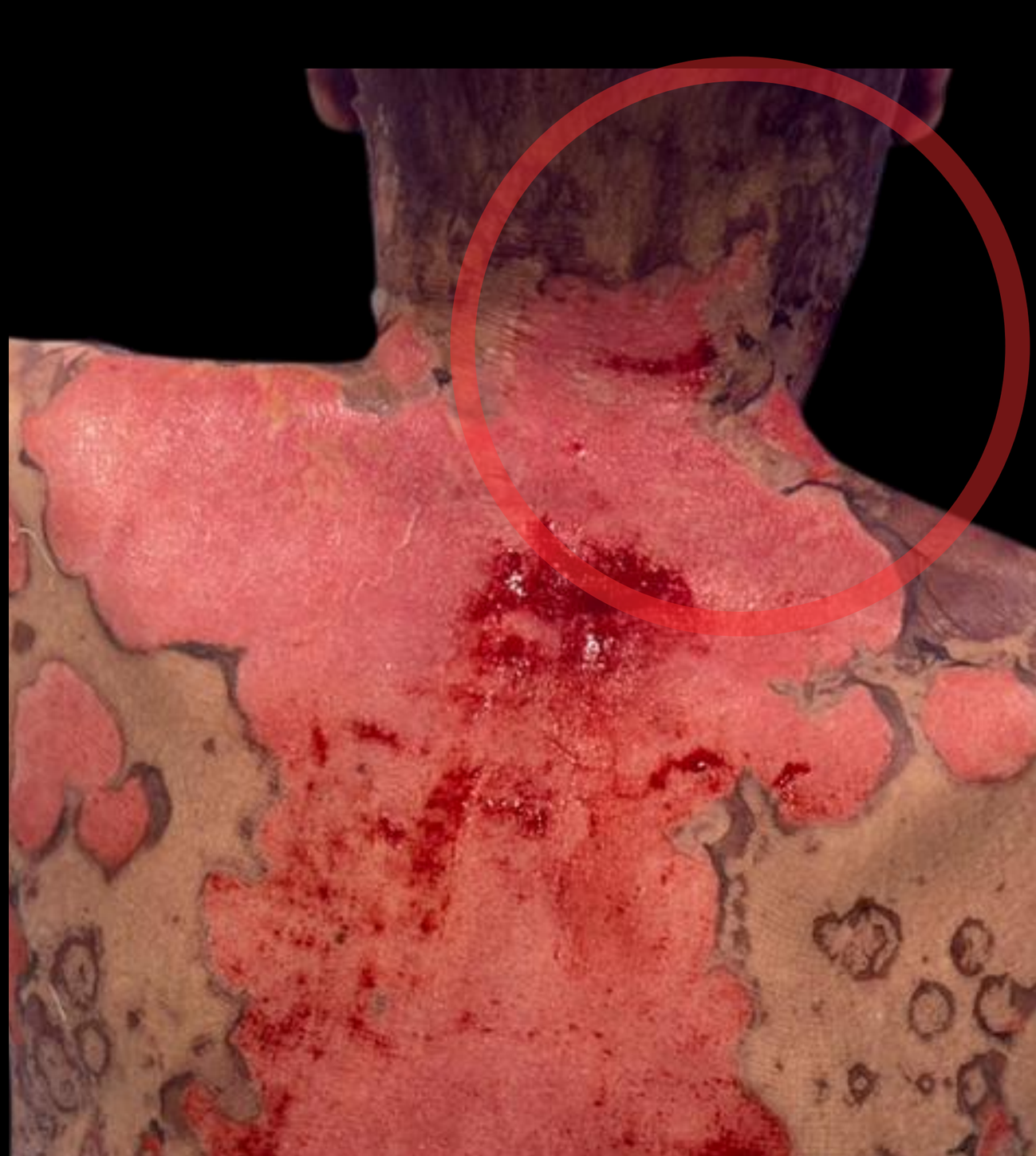
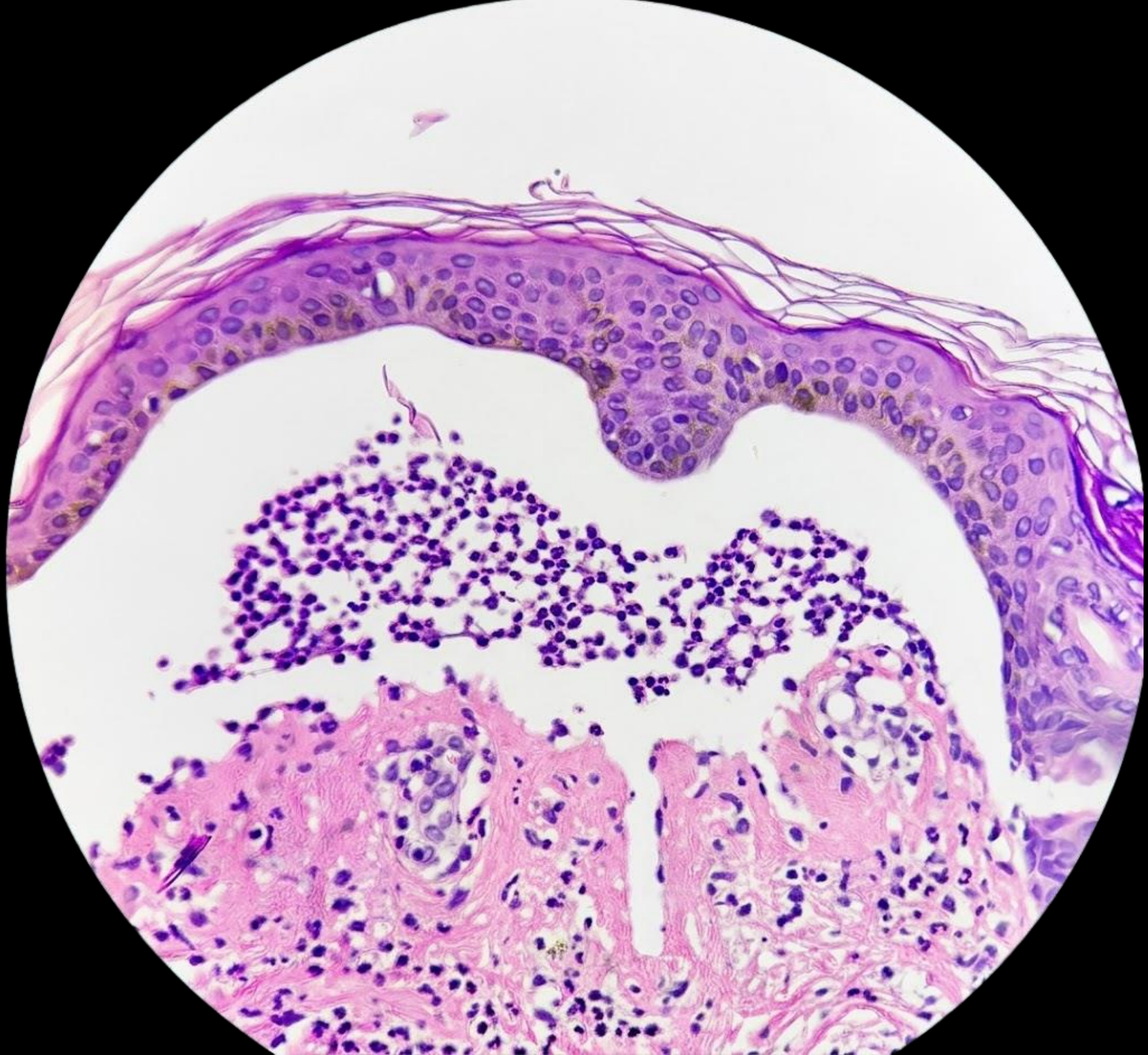
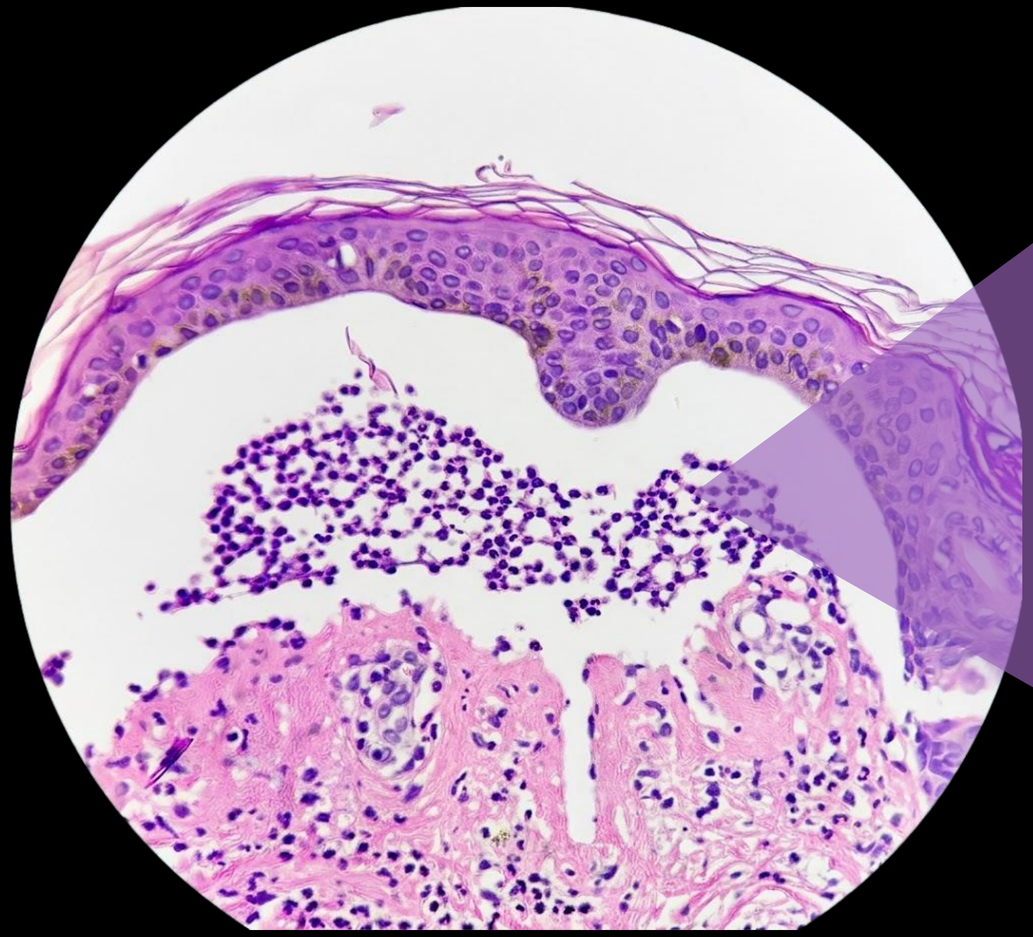
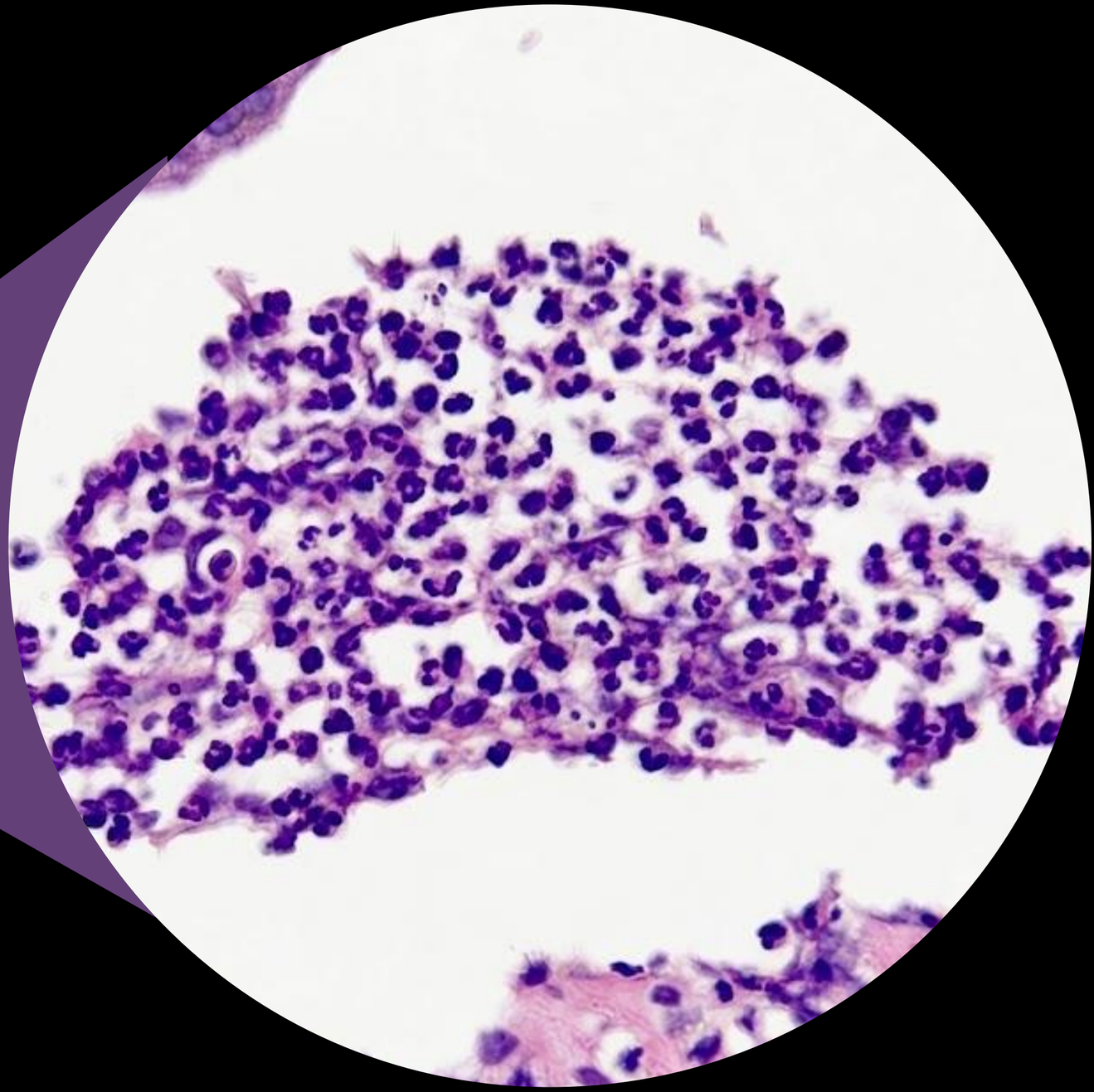


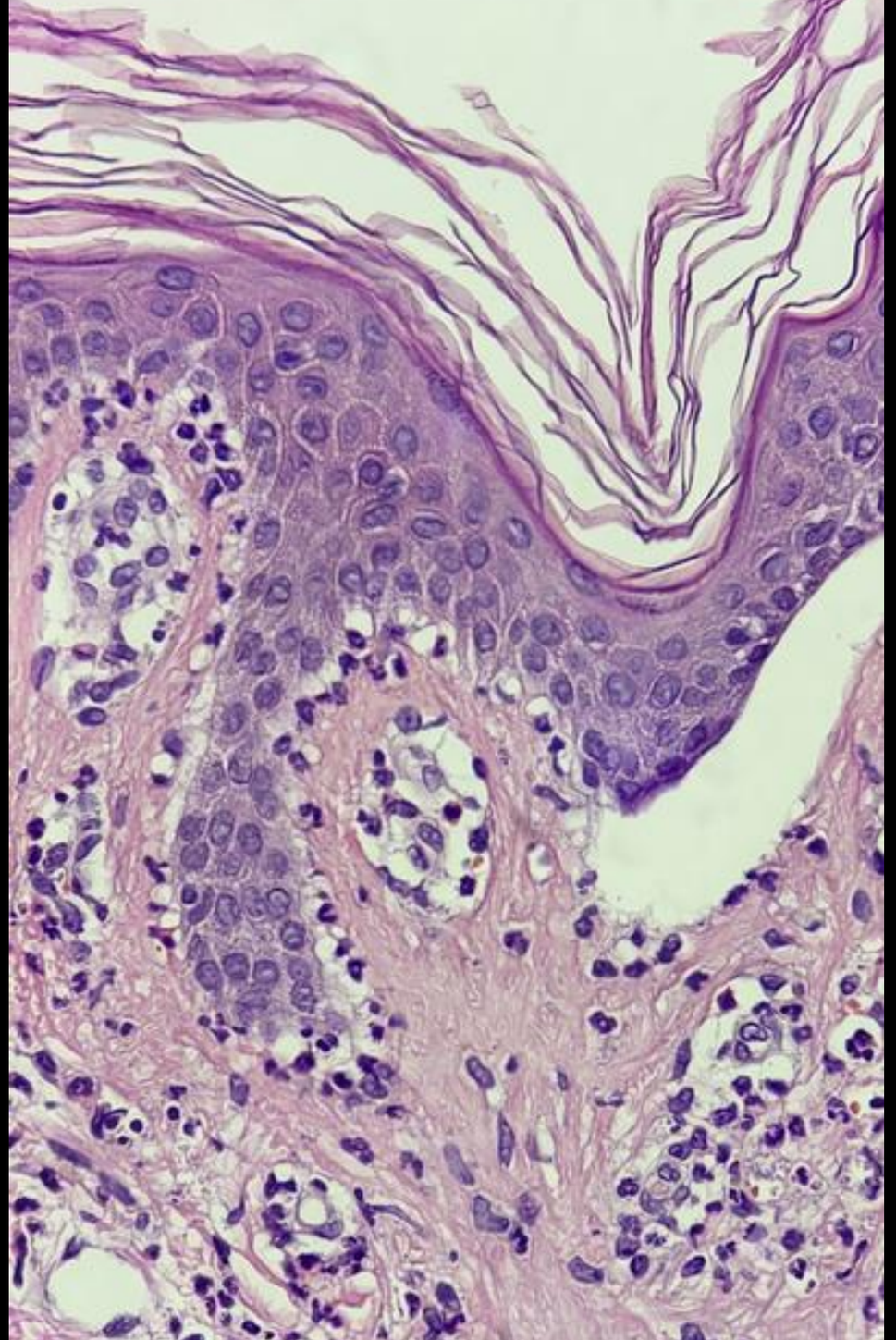


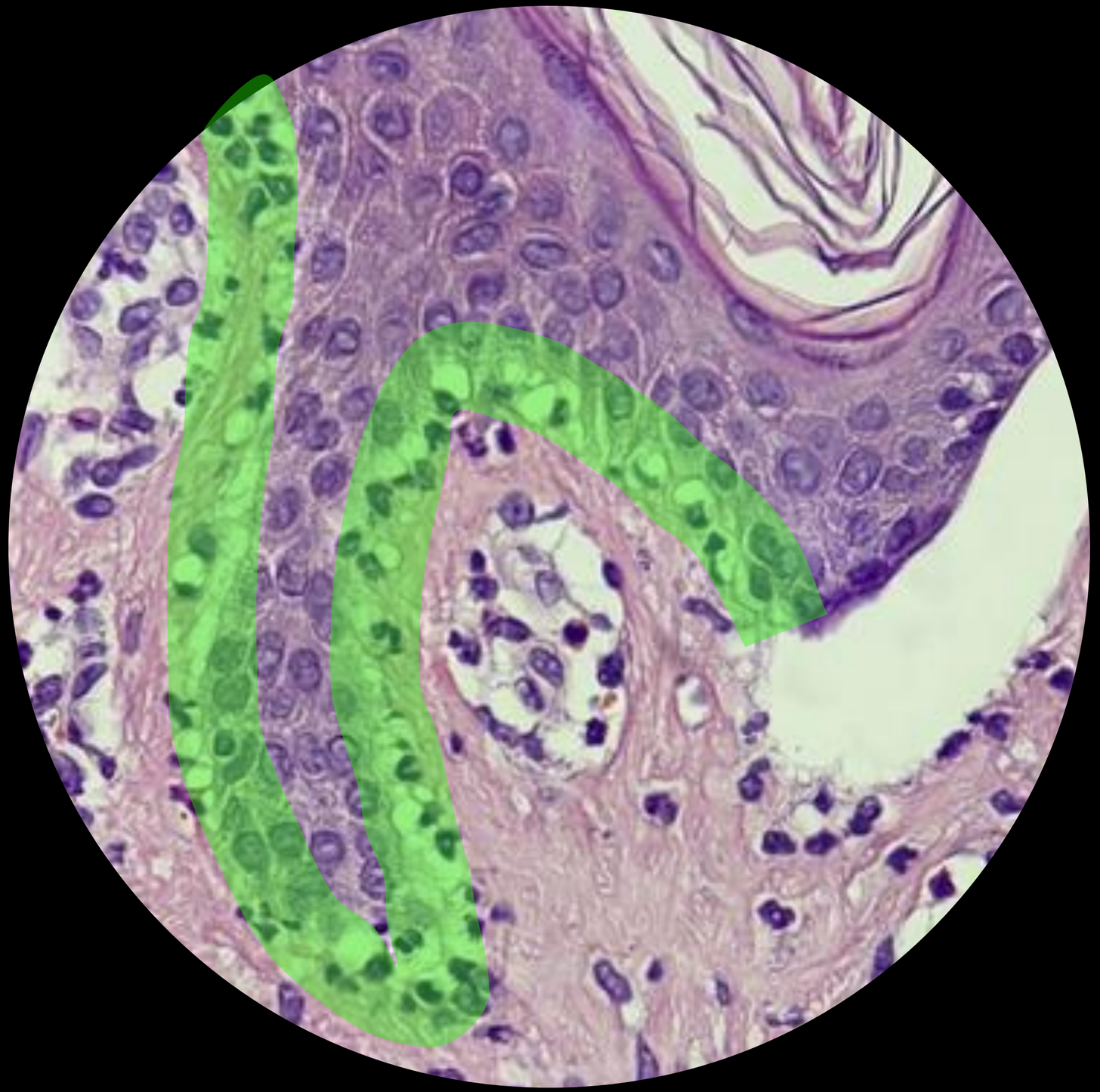
HISTOPATOLOGIA











RACIOCÍNIO DIAGNÓSTICO

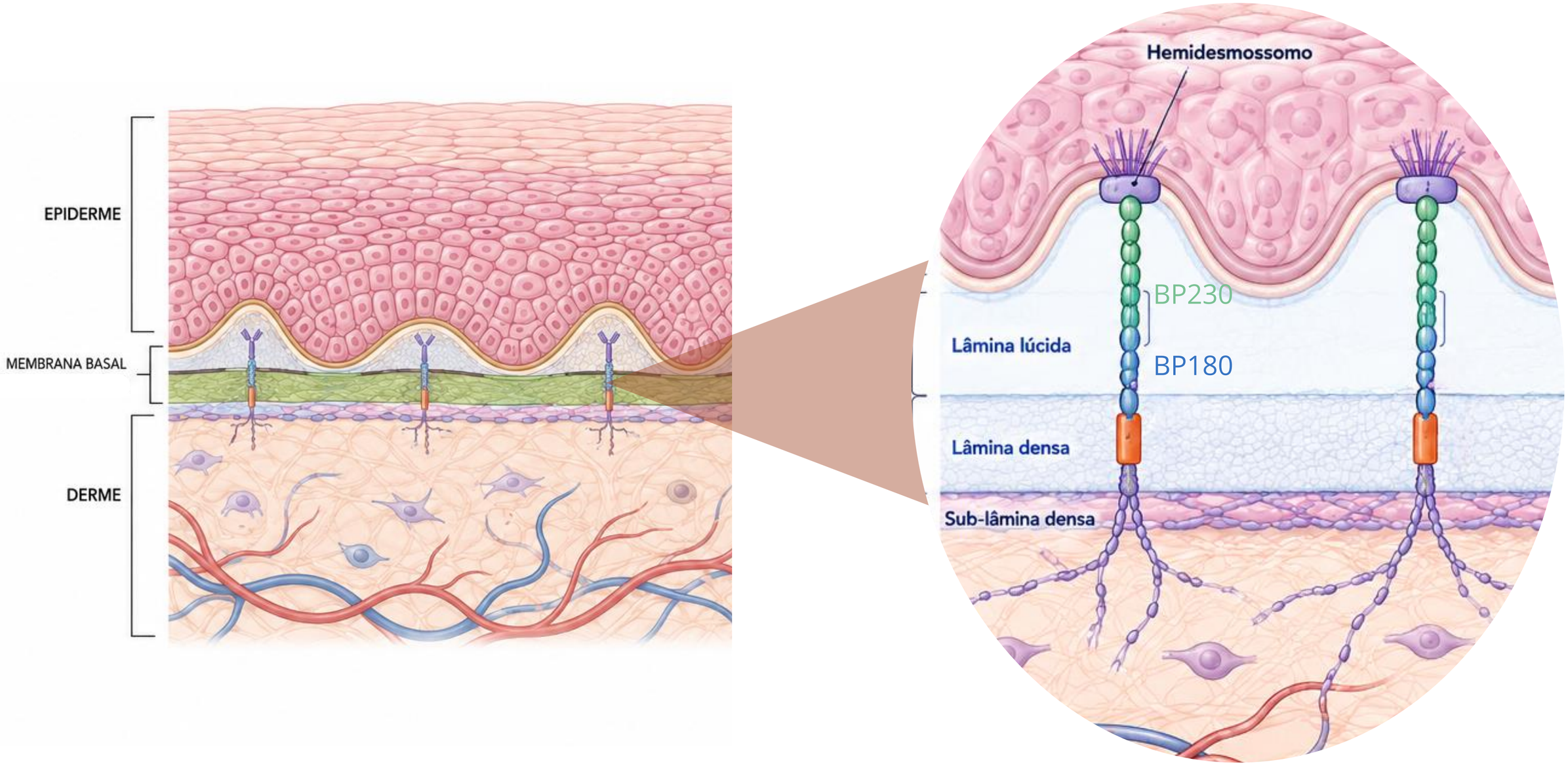
Bolha subepidérmica

Infiltrado neutrofílico

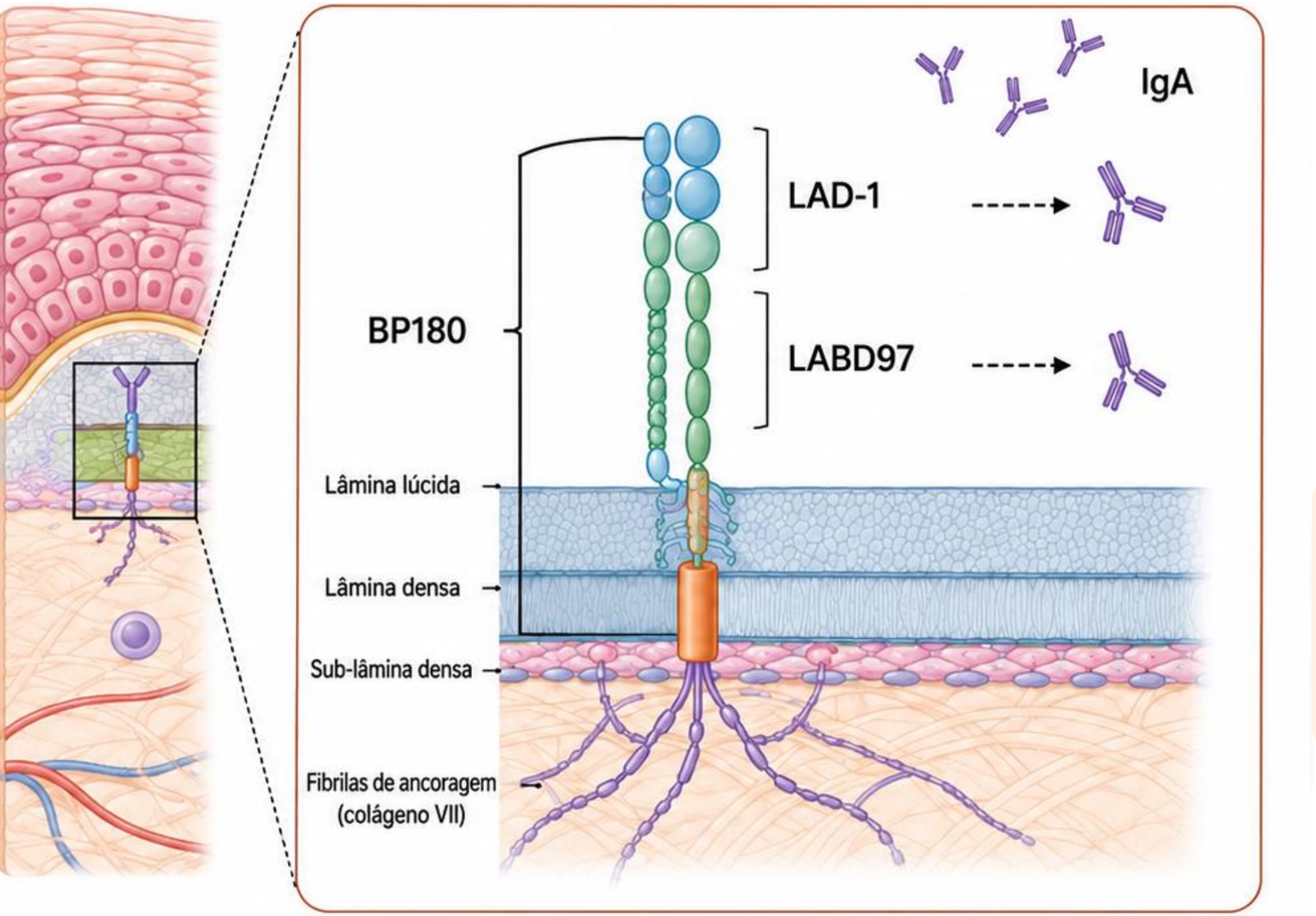
Disposição linear de neutrófilos

Dermatose Bolhosa por IgA Linear

FISIOPATOLOGIA



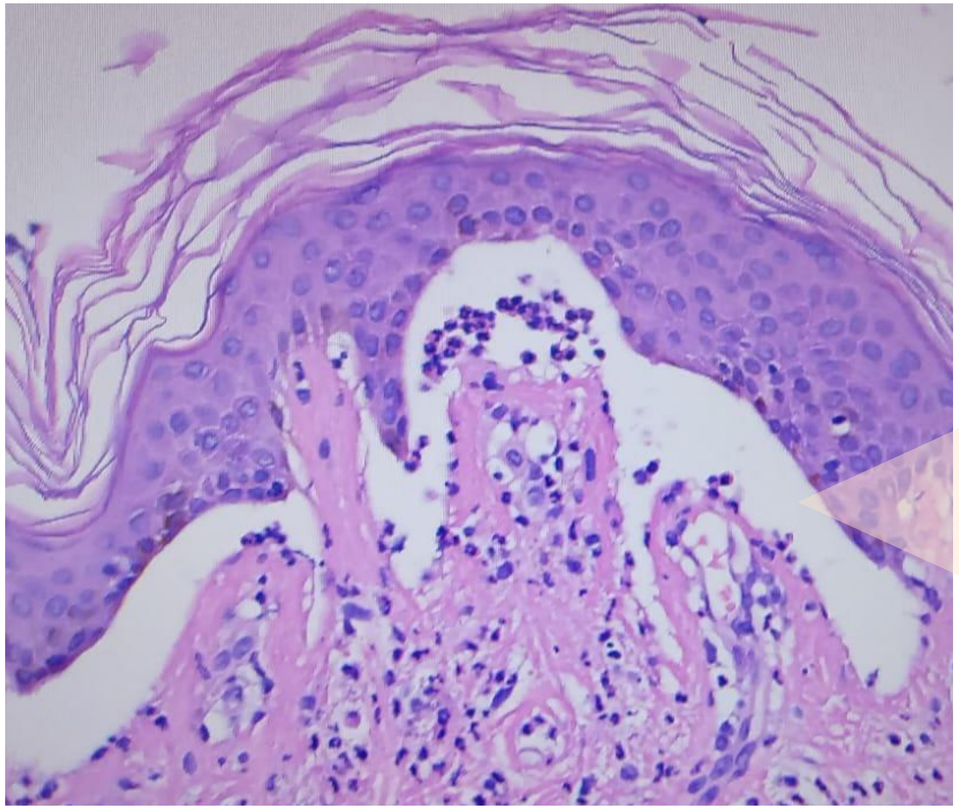
FISIOPATOLOGIA

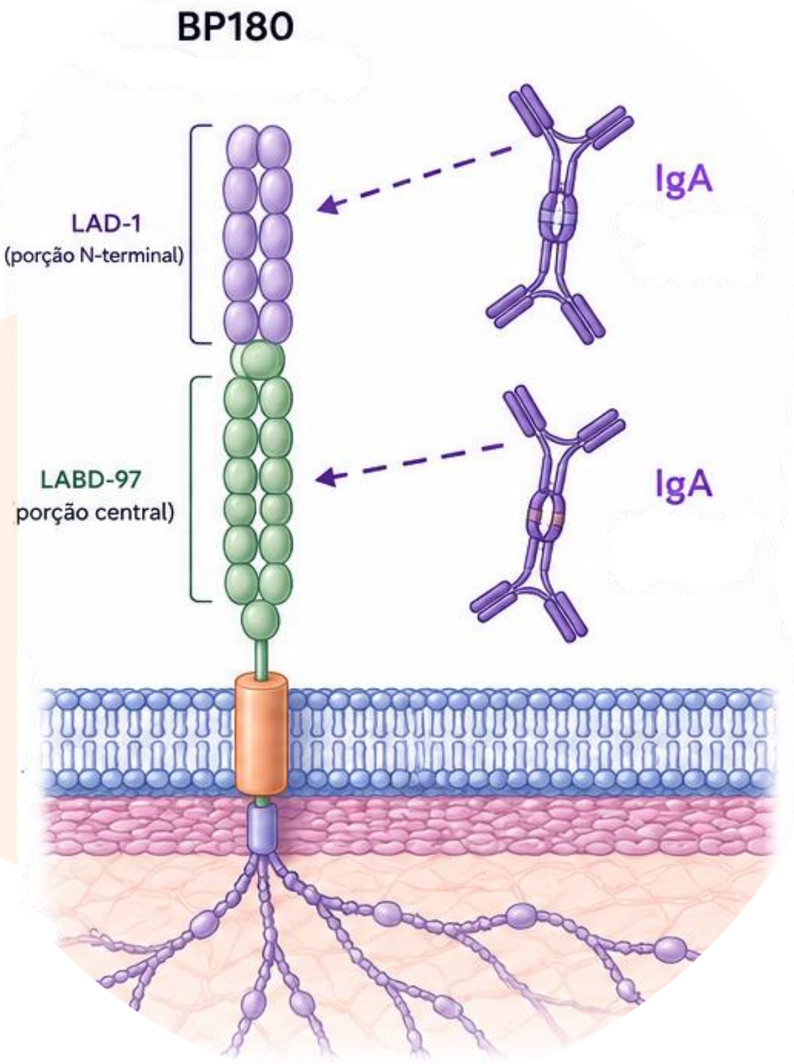


Anticorpos IgA contra os antígenos LABD97 e LAD-1

Fragmentos do antígeno BP180

FISIOPATOLOGIA





Existem associações da dermatose bolhosa por IgA linear com linfomas?

Linfoma T angioimunoblástico e dermatose bolhosa IgA linear

Sim, especialmente com o linfoma T angioimunoblástico

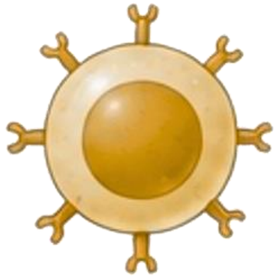
Relatos de **outras doenças** relacionadas ao IgA: vasculite leucocitoclástica e nefropatia

Melhora das lesões frequentemente relacionada com o controle da neoplasia

Andriano TM et al., J Cutan Pathol, 2023. Linear IgA bullous dermatosis in the setting of angioimmunoblastic T-cell lymphoma.
Harada Y et al., Intern Med. 2017. Angioimmunoblastic T-cell Lymphoma Associated with IgA Nephropathy
Colmant C, et al., J Cutan Pathol, 2020. Linear IgA dermatosis in association with angioimmunoblastic T-cell lymphoma infiltrating the skin: A case report with literature review.

FISIOPATOLOGIA

Células TFH

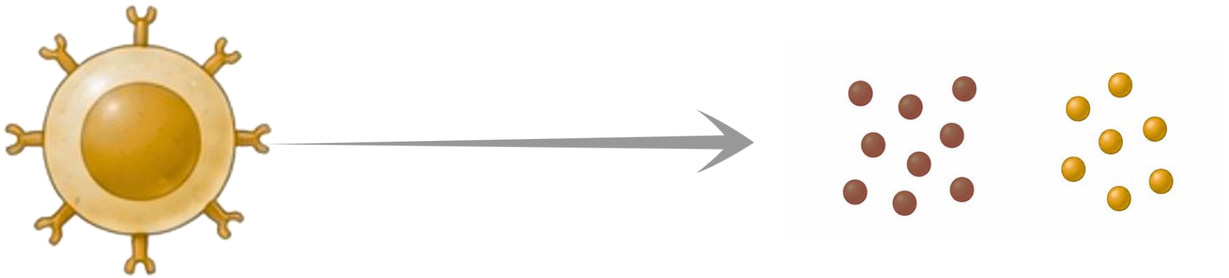


Função fisiológica:
promover a diferenciação e proliferação de células B dentro dos centros germinativos

Colmant C, et al. Linear IgA dermatosis in association with angioimmunoblastic T-cell lymphoma infiltrating the skin: A case report with literature review. J Cutan Pathol. 2020

FISIOPATOLOGIA

Células TFH



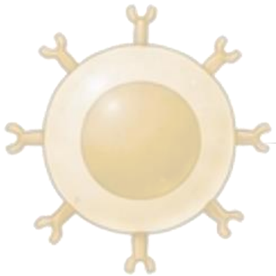
IL-6 e IL-21

Promovendo intensa ativação policlonal dos linfócitos B

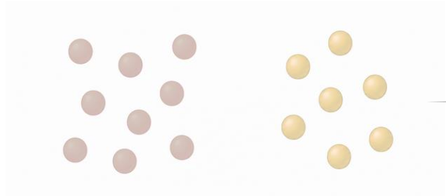
Colmant C, et al. Linear IgA dermatosis in association with angioimmunoblastic T-cell lymphoma infiltrating the skin: A case report with literature review. J Cutan Pathol. 2020

FISIOPATOLOGIA

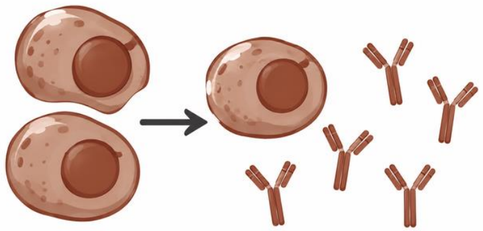
Células TFH



IL-6 e IL-21



Plasmócitos



Expansão Policlonal de Plasmócitos produtores de IgA

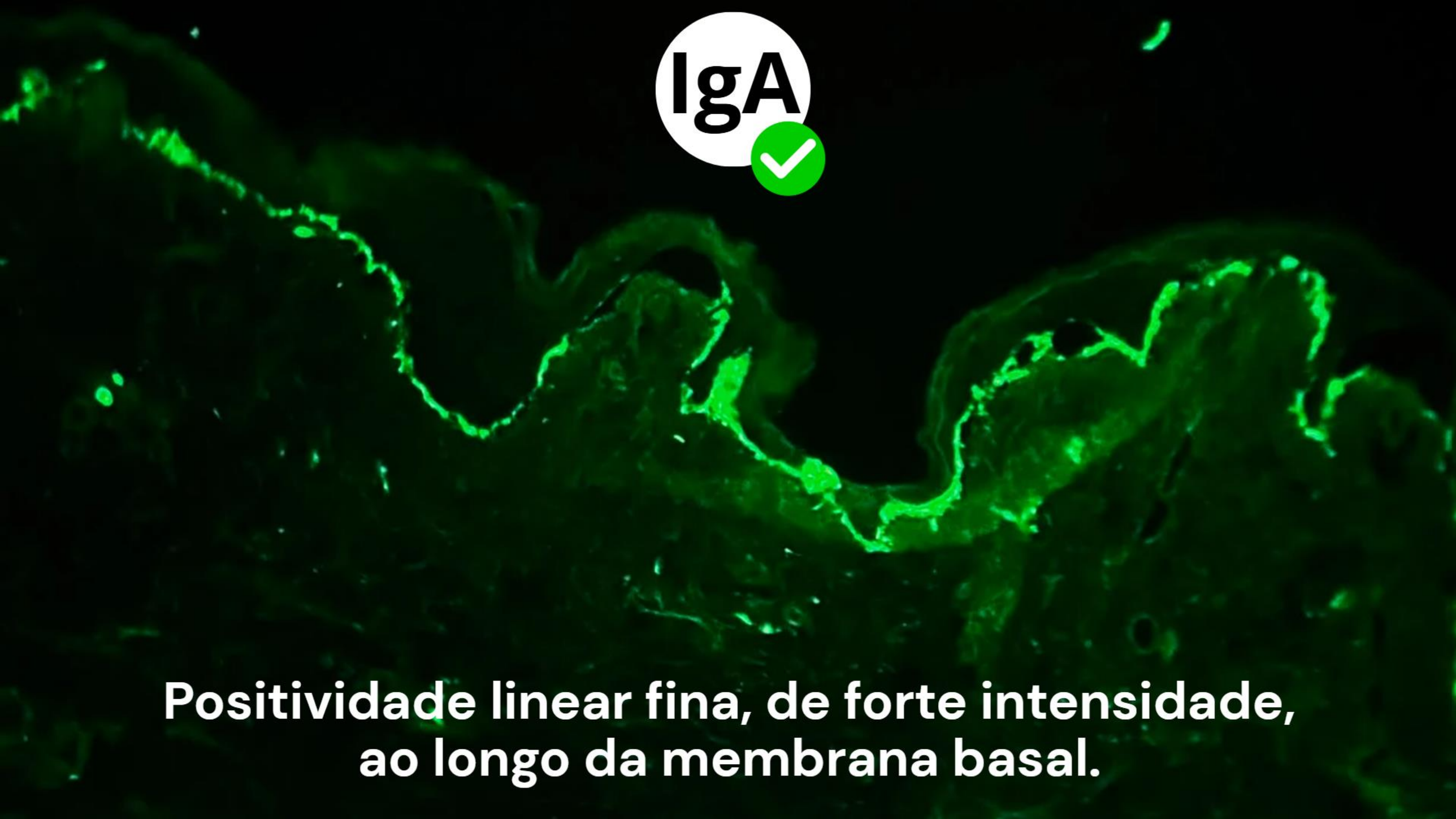
Colmant C, et al. Linear IgA dermatosis in association with angioimmunoblastic T-cell lymphoma infiltrating the skin: A case report with literature review. J Cutan Pathol. 2020

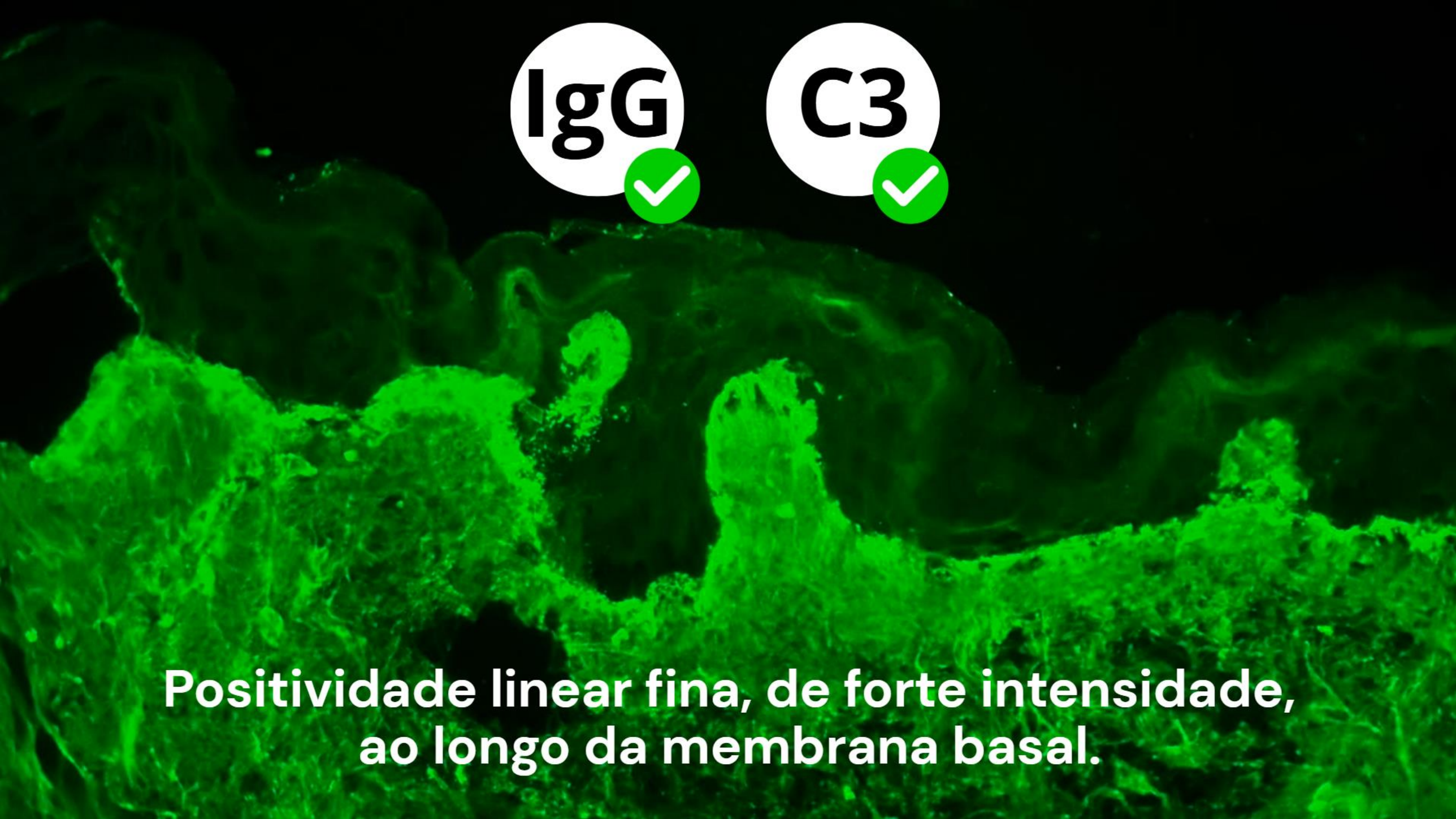
FISIOPATOLOGIA

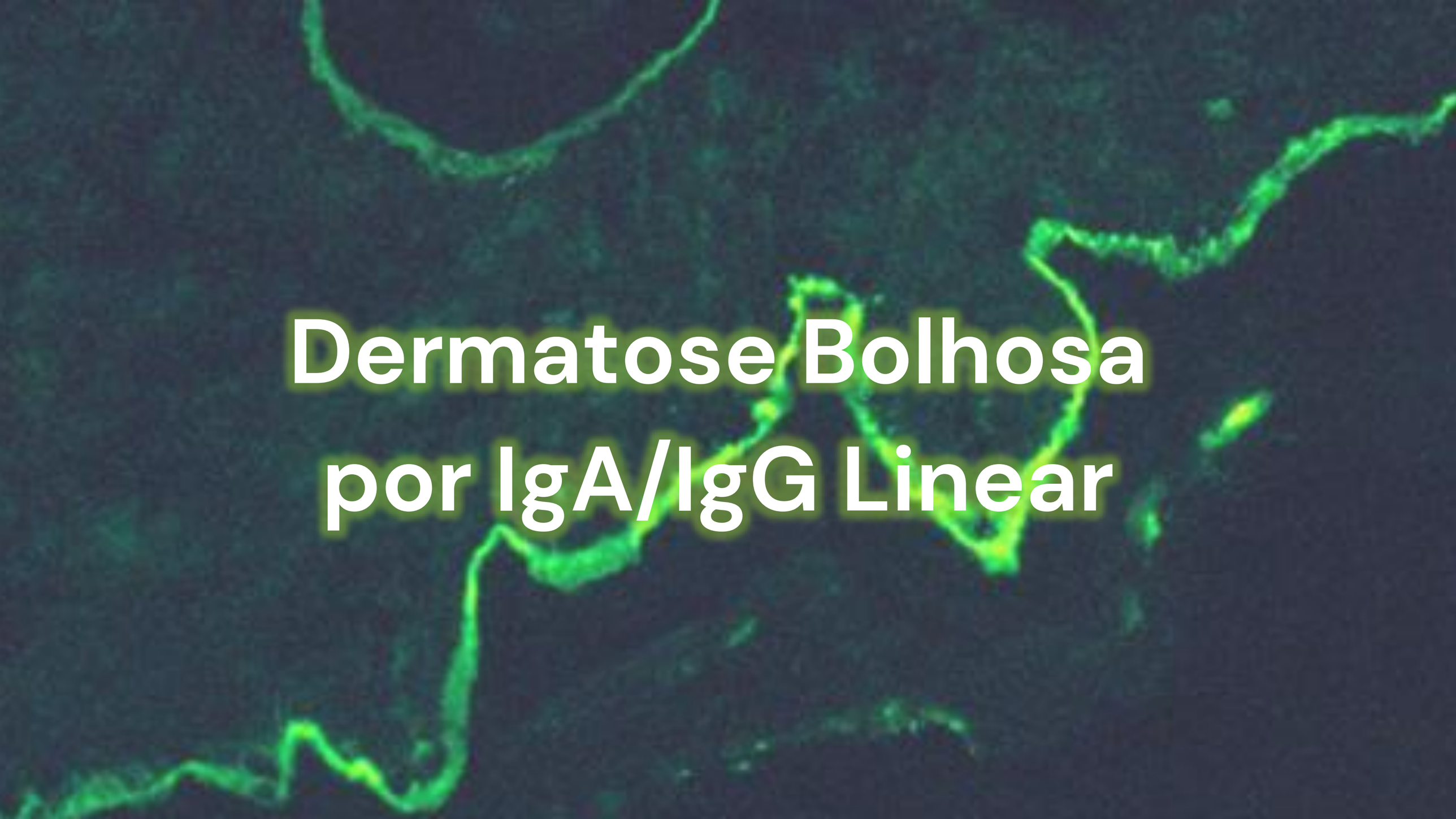
Depositam-se linearmente na junção dermoepidérmica, iniciando todo o processo inflamatório responsável pela formação das bolhas

Frente a hipótese de Dermatose bolhosa por IgA linear

Realizada imunofluorescência direta


IgA
Positividade linear fina, de forte intensidade,
ao longo da membrana basal.


IgG
C3
Positividade linear fina, de forte intensidade,
ao longo da membrana basal.


Dermatose Bolhosa
por IgA/IgG Linear

Dermatose Bolhosa IgA e IgG Linear

CONCEITO

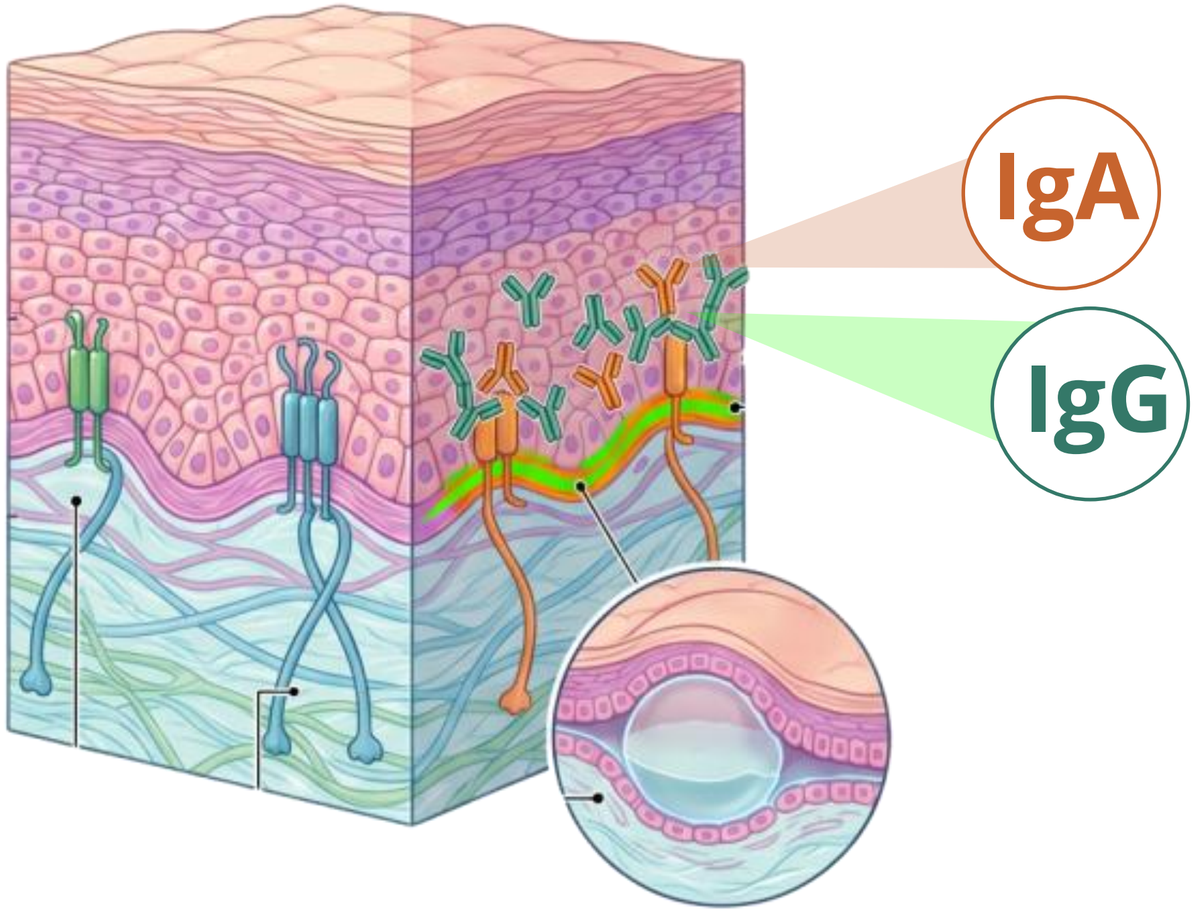
Deposição linear na mesma intensidade de autoanticorpos IgA e IgG ao longo da zona da membrana basal.

FATORES DE RISCO

Medicamentos (vancomicina), infecções, doenças autoimunes e distúrbios linfoproliferativos.

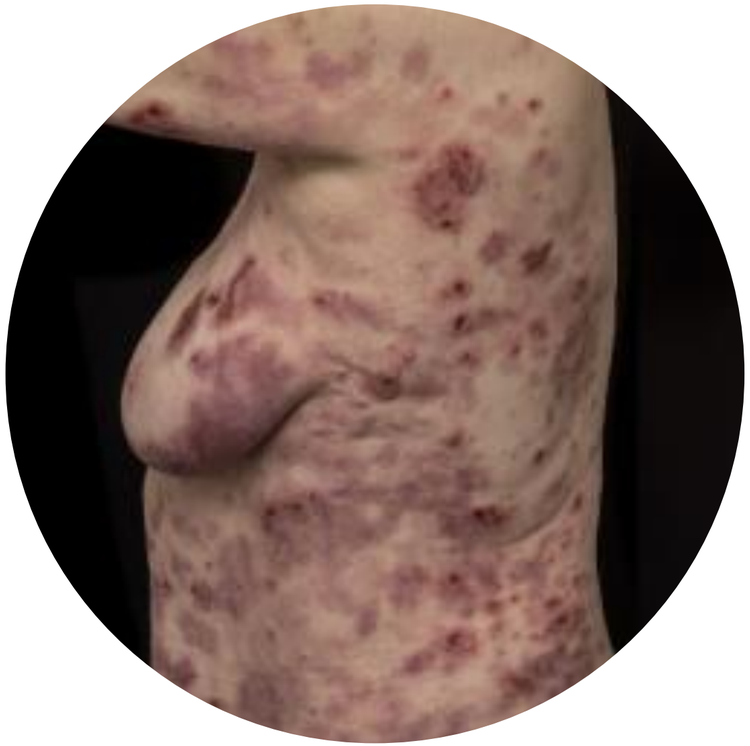
ANTÍGENOS-ALVO

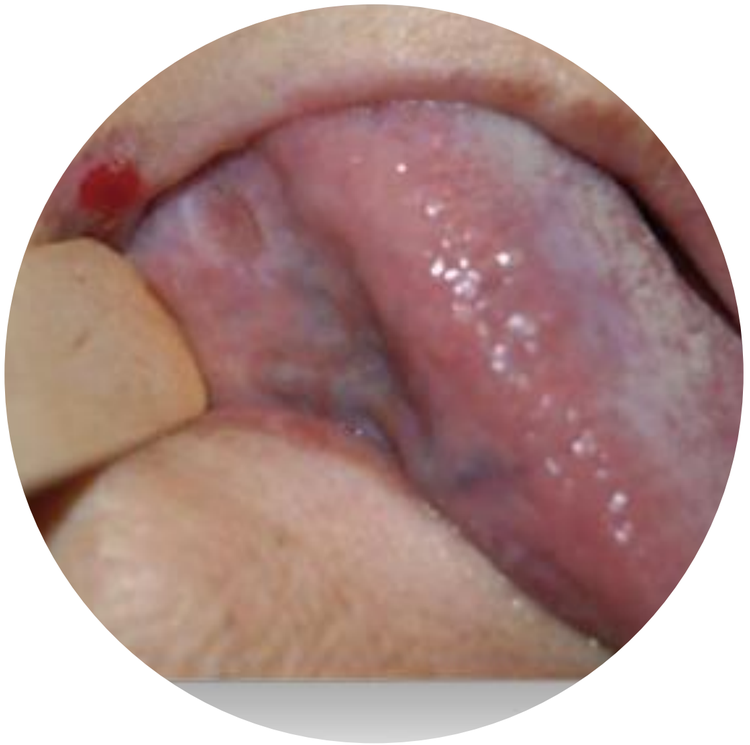
LABD-97, LAD-1
laminina-332, BP180, BP230, colágeno VII

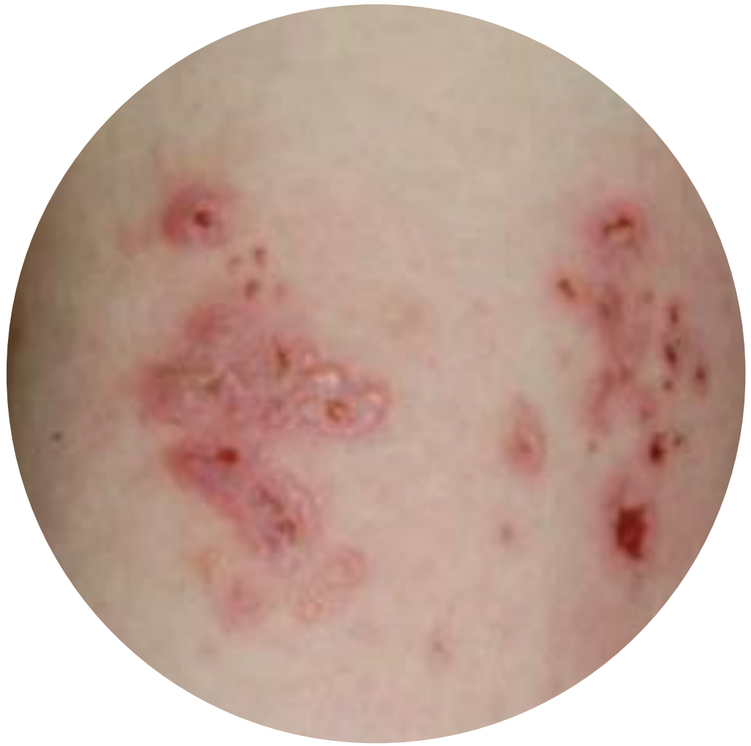


Fernandes KA, Vargas TJ et al. Linear IgA and IgG bullous dermatosis. An Bras Dermatol. 2016

CLÍNICA







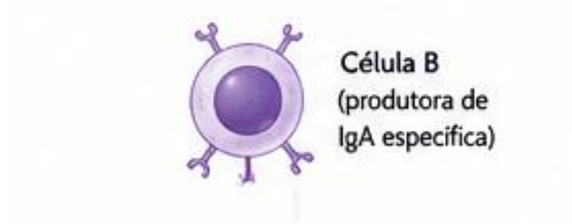
A maioria dos casos apresenta características clínicas que se assemelham ao Penfigoide bolhoso e a Dermatose bolhosa por IgA linear.

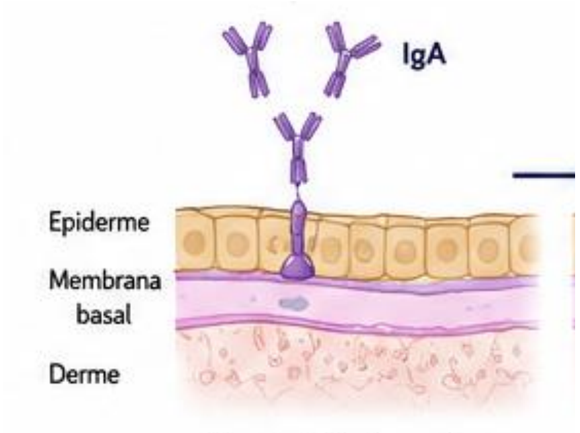
Sakaguchi M, et al. Três casos de dermatose bolhosa linear IgA/IgG apresentando reatividade de IgA e IgG com múltiplos antígenos, particularmente laminina-332. JAMA Dermatol. 2013

Como explicar positividade de IgA e IgG

?

Alastramento de epítopos

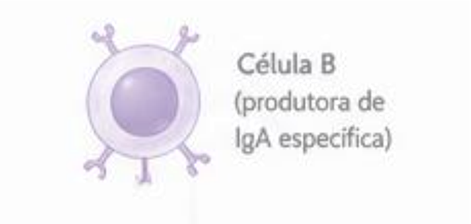


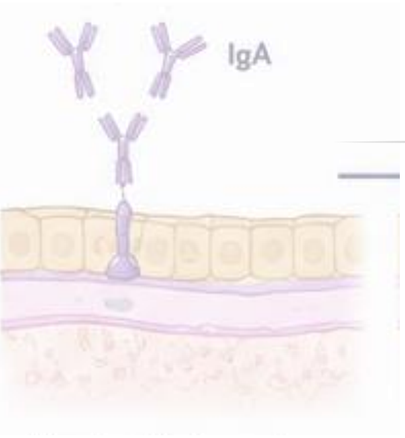


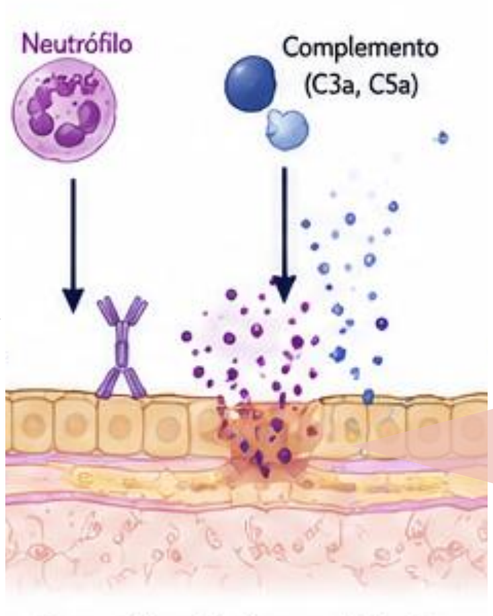
Ligação de IgA ao epítopo inicial (ex: LABD97)

Didona D, et al Humoral Epitope Spreading in Autoimmune Bullous Diseases. Front Immunol. 2018 Apr

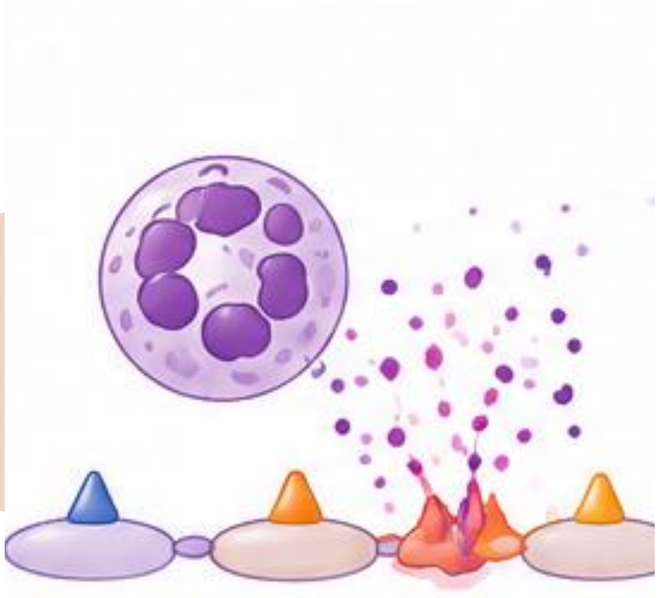
Alastramento de epítopos





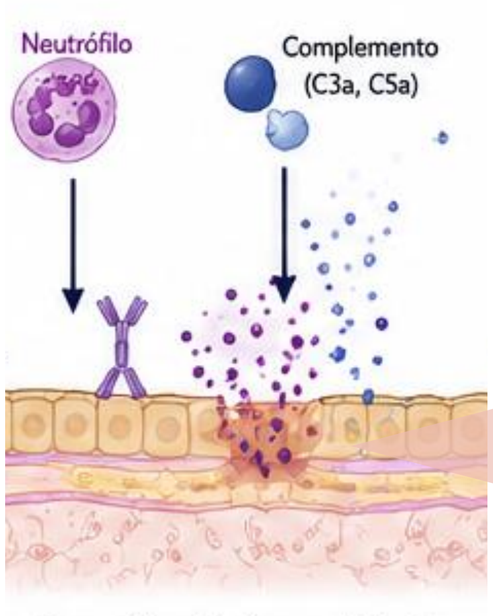


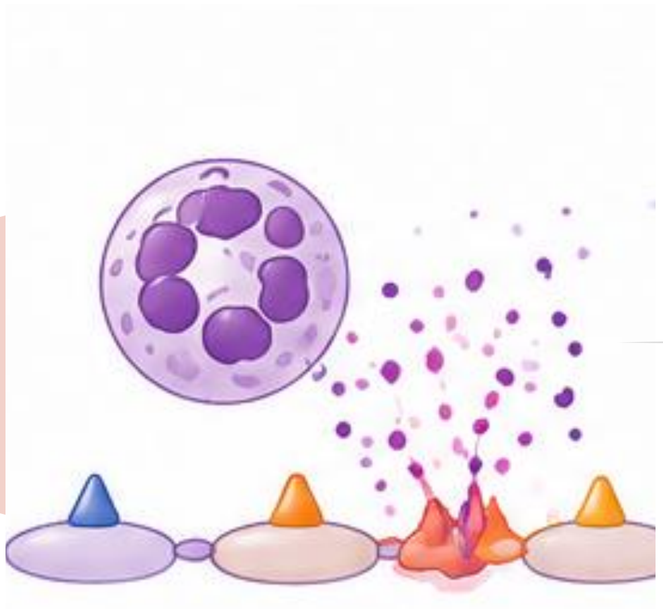
Dano a junção dermoepidérmica

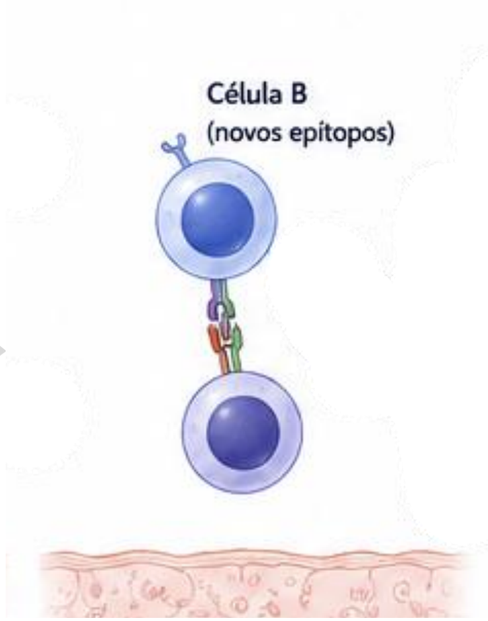


Liberação de novos epítopos

Alastramento de epítopos

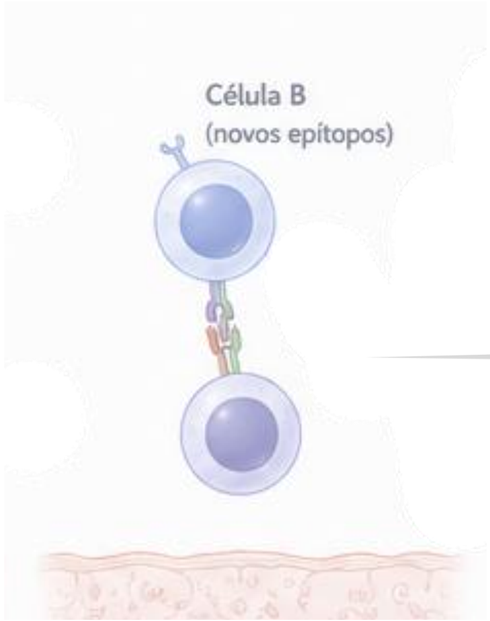


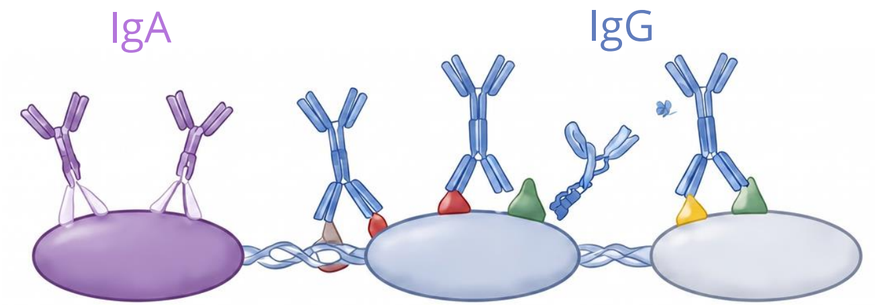




Ativação de novos clones de linfócitos B

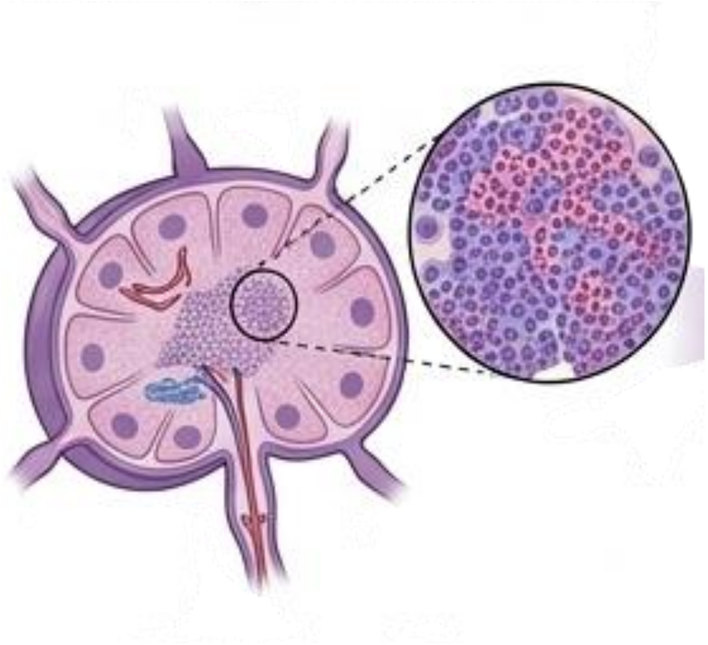
Alastramento de epítopos





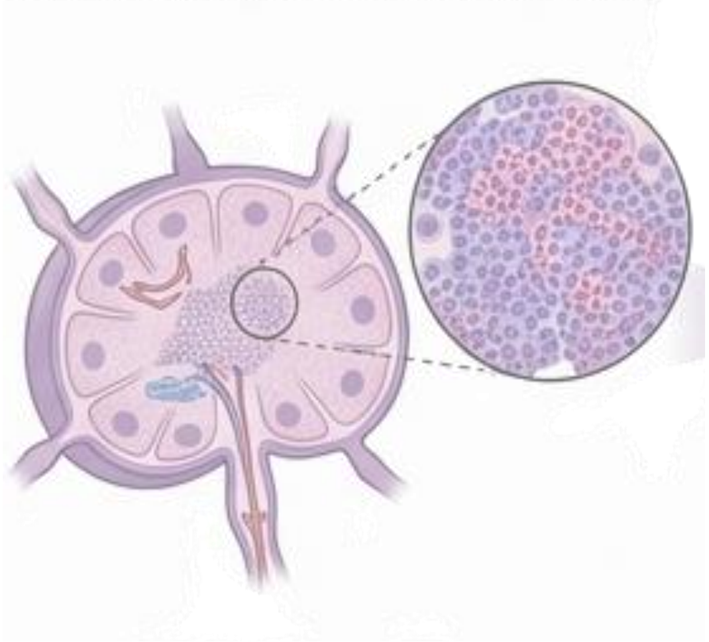
Produção de IgG e manutenção de IgA contra múltiplos epítopos

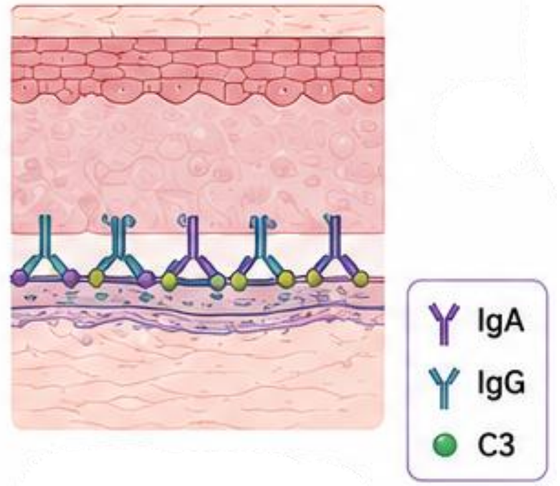
Conclusão



Desregulação imunológica promovida pelo linfoma T angioimunoblástico

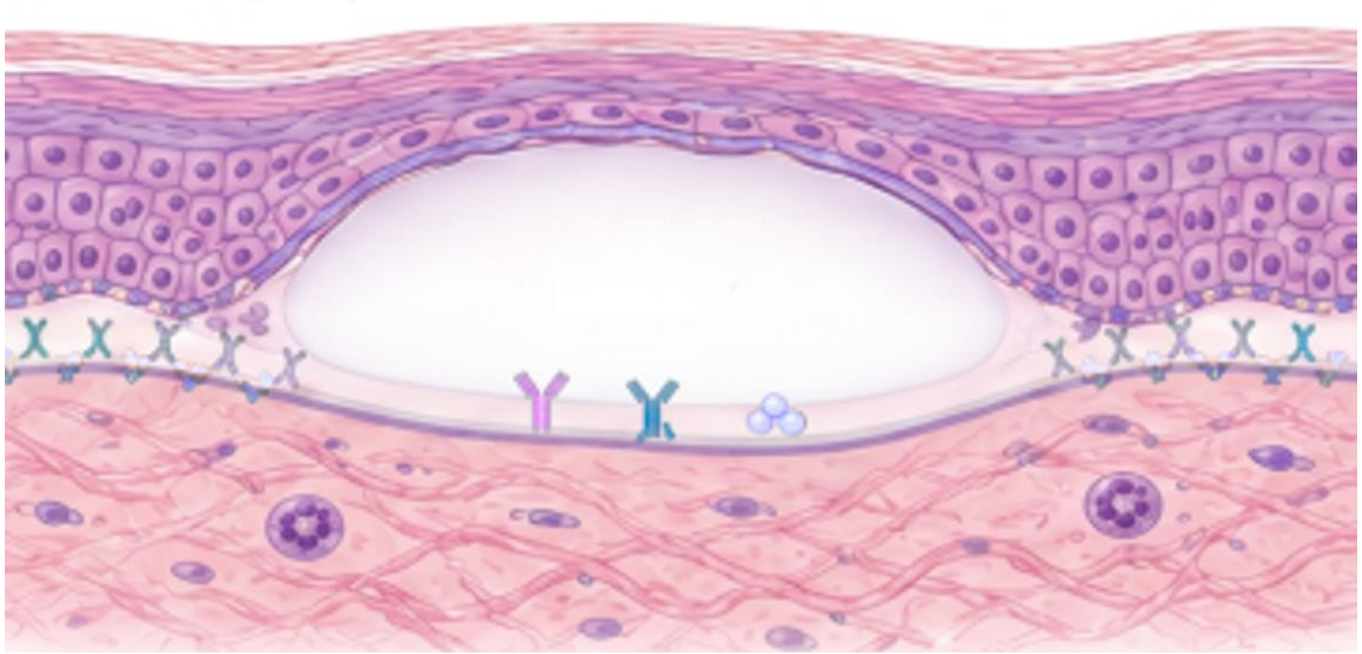
Conclusão





Produção de autoanticorpos e alastramento de epítopos

Conclusão



Dermatose Bolhosa por IgA/IgG Linear

VOLTANDO AO CASO

Após a quimioterapia

Evolução com sepse de foco pulmonar
em contexto de neutropenia

Extensa cobertura antibiótica

Óbito

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OBRIGADA!

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