Aggressive tumors in a patient with HIV-induced immunosuppression

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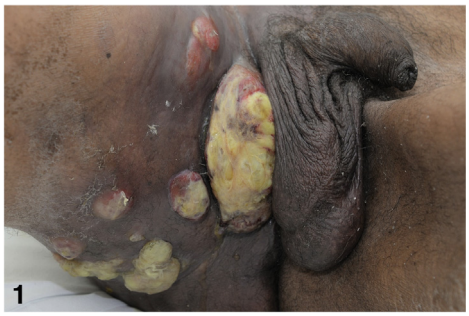

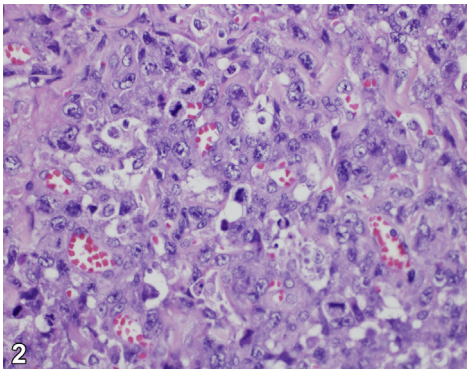

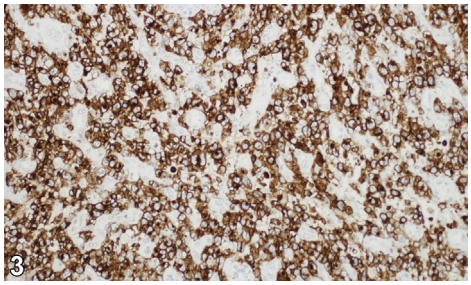

A 59-year-old man with a 2-year history of acquired immunodeficiency syndrome, who was adherent to highly-active antiretroviral therapy, developed tumors in his right inguinal region over one month. He reported loss of appetite, local pain, and fever, soon followed by tumor onset. Physical examination revealed an erythematous-to-violaceus plaque extending from the right inguinal region to the inner thigh with underlying multiple friable violaceus tumors and adherent lymph nodes (Fig 1). The CD4 count was 138 cells/mm^3 with undetectable viral load. Skin biopsy, histopathological exam (Fig 2), and immunostainings were performed, including epithelial membrane antigen (EMA), anaplastic lymphoma kinase (ALK) and CD markers (Fig 3). Imaging exams revealed no systemic involvement.

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Question 1: What is the most likely diagnosis?

A. Angiosarcoma

B. HIV-associated plasmablastic lymphoma

C. Primary cutaneous anaplastic large-cell lymphoma (PCALCL)

D. Squamous cell carcinoma (SCC)

E. Atypical mycobacteriosis

Answers:

A. Angiosarcoma—Incorrect. Clinically possible, but usually, cases occur following radiotherapy, and histopathology would reveal a network of dermal vascular canals varying in size from small capillaries to sinusoid spaces interspersed by normal endothelium,[1] which were not observed in this case.

B. HIV-associated plasmablastic lymphoma—Incorrect. This is a distinct subtype of non-Hodgkin B-cell lymphoma, originally described with a strong predilection to the human oral cavity.[2]

C. Primary cutaneous anaplastic large-cell lymphoma (PCALCL)—Correct. Diagnosis of PCALCL is based on key morphological features, especially the presence of "hallmark" cells, which are large pleomorphic cells with abundant cytoplasm and eccentric nuclei, which are "horseshoe or kidney"-shaped, and which often contain multiple small basophilic nucleoli. Immunohistochemistry is essential for the confirmation of diagnosis and excluding other malignancies with anaplastic morphology.[3] The general immunophenotype reported in HIV-positive patients is positivity for CD30 and EMA.[4] Common sites of involvement are the face, trunk, extremities, and buttocks.[3] PCALCL commonly presents with solitary nodules, which may ulcerate.[4] In this case, immunostainings were positive for both EMA and CD30.

D. Squamous cell carcinoma (SCC)—Incorrect. Clinically, the two types of lesions are not compatible. Also, the histology of SCC usually shows enlarged tumor cells with hyperchromatic, variably pleomorphic nuclei showing prominent mitotic activity. Atypical mitoses are present as well as the horny pearls,[5] which were not observed in this case.

E. Atypical mycobacteriosis—Incorrect. Although this conditions exhibits heterogeneous manifestations, this patient had no compatible histopathology and acid-fast staining for bacilli was negative.

Question 2: Which immunohistochemical marker is associated with this type of lymphoma?

A. CD31

B. CD20

C. S100

D. ALK

E. Cytokeratin AE1/AE3

Answers:

A. CD31—Incorrect. Usually tumors of vascular origin, *e.g.*, angiosarcoma, are positive for CD31.

B. CD20—Incorrect. CD20 is a marker for type B lymphocytes.

C. S100—Incorrect. S100 is a marker for melanoma.

D. ALK—Correct. ALK is a kinase specific to PCALCLs. In this patient, ALK was negative.

E. Cytokeratin AE1/AE3—Incorrect. Cytokeratin AE1/AE3 is usually found in tumors such as carcinomas and sarcomas.

Question 3: Which of the following is true regarding this condition?

A. PCALCLs are a group of B-cell lymphomas composed of large anaplastic lymphoid cells exhibiting diffuse CD30 positivity.

B. Anaplastic large-cell lymphomas (ALCLs) include three entities: Systemic ALK-positive ALCLs, systemic ALK-negative ALCLs, and primary cutaneous ALCL (PCALCL), which are often ALK-negative.

C. In HIV patients, PCALCLs manifest almost exclusively with extranodal involvement and exhibit a good clinical course.

D. Different from aggressive B-cell non-Hodgkin lymphoma, the risk of developing PCALCL is decreased in the setting of HIV infection.

E. Positivity for CD30 is specific for ALCL.

Answers:

A. Incorrect. ALCs are a group of T-cell lymphomas.[3]

B. Correct. ALCLs are usually classified into these three entities.[3]

C. Incorrect. These lymphomas exhibit an extremely aggressive clinical course.[4]

D. Incorrect. Like aggressive B-cell non-Hodgkin lymphoma, the risk of developing PCALCL is also increased in the setting of HIV infection.[4]

E. Incorrect. Positivity for CD30 is not specific for ALCL. It can be expressed by Hodgkin and Reed/Sternberg cells and a subset of B- and T-cell lymphomas.[3]

Abbreviations used:

ALCL: anaplastic large-cell lymphoma
ALK: anaplastic lymphoma kinase
EMA: epithelial membrane antigen
HIV: human immunodeficiency virus
PCALCL: primary cutaneous anaplastic large-cell lymphoma
SCC: squamous cell carcinoma

Conflicts of interest
None disclosed.

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