An enlarging subcutaneous nodule on the hand

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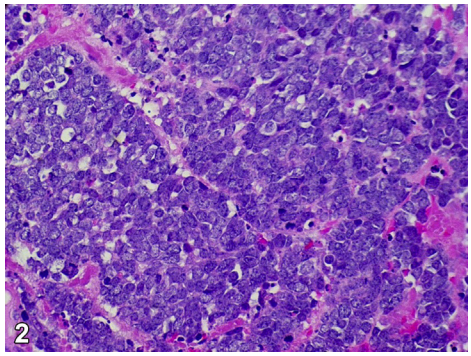

A 48-year-old woman with a 15-year history of an atypical spongiotic dermatitis was treated previously with topical corticosteroids, calcipotriene, tacrolimus, tar preparations, narrow-band ultraviolet B therapy, and methotrexate and was ultimately well controlled for 3 years on mycophenolate mofetil, 1 g twice a day. During routine follow-up, she mentioned a 3-month history of a slowly enlarging, tender growth on the right hand (Fig 1). Physical examination found a well-circumscribed 1.5- × 0.6-cm mobile, skin-colored to blue subcutaneous nodule with overlying erythema on the dorsoulnar aspect of the right hand. A biopsy was done, and definitive surgery was performed after histopathologic review (Fig 2).

Question 1: Which virus is associated with this form of skin cancer?

A. Human polyomavirus

B. Epstein-Barr virus (EBV)

C. Hepatitis B virus

D. Human herpes virus-8

E. Human papillomavirus (HPV)

A. Human polyomavirus — Correct. The best clinicopathologic correlation is a Merkel cell carcinoma (MCC). The hematoxylin-eosin stain of MCC shows small basophilic cells in solid sheets and clusters, typically with areas of necrosis and "crushing" artifact. MCC is best identified by the typical histology found on Hematoxylin-eosin staining paired with immunohistochemistry results. Multiple studies documented an association of MCC with the human polyomavirus, also known as the Merkel cell polyomavirus.[1]

B. EBV — Incorrect. EBV has been associated with the development of several different types of cancers including, but not limited to, nasopharyngeal carcinoma, gastric carcinoma, Burkitt lymphoma, non-Hodgkin lymphoma, and Hodgkin lymphoma. EBV has not been associated with MCC.[2]

C. Hepatitis B virus — Incorrect. Hepatitis B virus has been associated with the development of

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hepatocellular carcinoma; it has not been associated with MCC.[2]

D. Human herpes virus-8 — Incorrect. Human herpes virus-8 has not been associated with the development of MCC; however, it has been associated with the development of Kaposi sarcoma.[2]

E. HPV — Incorrect. HPV has been associated largely with cervical cancer and cancers of the vulva, vagina, penis, anus, and oropharynx. HPV has not been associated with MCC.[2]

Question 2: Which is a risk factor for this form of skin cancer?

A. Alcohol ingestion

B. Black race

C. Female gender

D. HIV infection

E. HPV infection

A. Alcohol ingestion — Incorrect. Alcohol ingestion has not been specifically associated with MCC. It has been associated with certain cancers of the head and neck, esophagus, liver, breast, colon, and rectum.[3]

B. Black race — Incorrect. The risk of MCC development is highest in white individuals and lowest in black individuals.[4]

C. Female gender — Incorrect. MCC is more commonly seen in males.[4]

D. HIV infection — Correct. The patient discussed in this case was on chronic mycophenolate mofetil, an immunosuppressive medication and had also received narrowband ultraviolet B therapy. The incidence of MCC is increased in immunosuppressed patients including HIV-infected patients, those on immunosuppressive medications, those with B-cell malignancies, organ transplant recipients, and those with chronic ultraviolet exposure.[4]

E. HPV infection — Incorrect. HPV has been associated largely with cervical cancer and some cancers of the vulva, vagina, penis, anus, and oropharynx.[2]

Question 3: Which of the following immunohistochemistry staining profiles is characteristic of this tumor?

A. $CK20^-$, $CD45^-$, thyroid transcription factor-1 $(TTF\text{-}1)^-$, $SOX10^-$, neuron-specific enolase $(NSE)^-$, $S100^+$

B. $CK20^-$, $CD45^+$, $TTF\text{-}1^-$, $SOX10^-$, NSE^-, $S100^-$

C. $CK20^+$, $CD45^-$, $TTF\text{-}1^-$, $SOX10^-$, NSE^+, $S100^-$

D. $CK20^-$, $CD45^-$, $TTF\text{-}1^+$, $SOX10^-$, NSE^-, $S100^-$

E. $CK20^-$, $CD45^-$, $TTF\text{-}1^-$, $SOX10^+$, NSE^-, $S100^-$

A. $CK20^-$, $CD45^-$, $TTF\text{-}1^-$, $SOX10^-$, NSE^-, $S100^+$ — Incorrect. The S100 stain is often used to help distinguish melanocytic from nonmelanocytic lesions. Most melanomas are $S\text{-}100^+$, whereas, MCC is $S\text{-}100^-$.[5]

B. $CK20^-$, $CD45^+$, $TTF\text{-}1^-$, $SOX10^-$, NSE^-, $S100^-$ — Incorrect. CD45 is an antigen present in most lymphomas except lymphoblastic lymphoma and is typically absent in MCC.[5]

C. $CK20^+$, $CD45^-$, $TTF\text{-}1^-$, $SOX10^-$, NSE^+, $S100^-$ — Correct. NSE is positive in most neuroendocrine tumors, including MCC; hence, it is not specific for MCC. However, when combined with $CK20^+$ staining in a paranuclear dot pattern, which is specific for MCC, a diagnosis of MCC can be made. Other markers of MCC include positive staining with chromogranin and synaptophysin.[5]

D. $CK20^-$, $CD45^-$, $TTF\text{-}1^+$, $SOX10^-$, NSE^-, $S100^-$ — Incorrect. TTF-1 is classically positive in metastatic small cell carcinoma of the lung and is negative in MCC.[5]

E. $CK20^-$, $CD45^-$, $TTF\text{-}1^-$, $SOX10^+$, NSE^-, $S100^-$ — Incorrect. SOX10 is a nuclear transcription factor useful for differentiating Schwann cells and melanocytes. It is expressed in all types of nevi and melanoma. It is not present in MCC.[5]

Abbreviations used:

EBV: Epstein-Barr virus
HPV: human papillomavirus
MCC: Merkel cell carcinoma
NSE: neuron-specific enolase
TTF-1: thyroid transcription factor-1

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