EBV-positive methotrexate-associated primary cutaneous lymphoproliferative disorder with features of classical Hodgkin lymphoma in a 58-year-old woman with dermatomyositis

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Clinical History

- The patient was a 58-year-old woman who developed a right arm mass that was treated with rituxan and the mass regressed except for a focal painless non-healing ulcer, which measured 4 x 3 cm and lasted for 3 months before surgical excision.
- Her past medical history was significant for a 6-year history of dermatomyositis treated with methotrexate, mycophenolate mofetil and prednisone.
Clinical Course

• After diagnosis of iatrogenic immunodeficiency-associated cutaneous lymphoproliferative disorder (LPD), further workup revealed neither lymphadenopathy nor hepatosplenomegaly.

• Though the surgical margins were involved, her wound was well-healed following withdrawal of methotrexate.

• However, the lesion recurred locally thirteen months later. A biopsy was performed for pathologic evaluation.
Methods

• The specimens from the initial excision and the following biopsy were both fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned at 3- to 4-μm, and stained with hematoxylin-eosin, counterstained with hematoxylin for immunohistochemistry, or counterstained with Nuclear Fast Red solution for Epstein-Barr virus encoded RNA (EBER) in situ hybridization.

• Immunohistochemical studies and EBER in situ hybridization demonstrated adequate positive and negative controls.
Gross Findings

• The excision specimen was a 4.0 x 2.5 cm ovoid piece of tan skin cut to a depth of 1.0 cm. A central 1.5 x 1.0 cm ulcerated lesion was present, at least 0.5 cm from all surgical margins.

• The biopsy specimen was a 0.7 x 0.7 cm piece of tan skin cut to a depth of 0.2 cm, with a 0.3 x 0.3 cm friable papule abutting the surgical margins.
Histomorphology

• Both specimens showed a dense dermal infiltrate composed of variable numbers of Hodgkin/Reed- Sternberg (HRS) cells and their variants in a background of mixed inflammatory cells including small lymphocytes, plasma cells, neutrophils and rare eosinophils.

• The morphological features were consistent with classical Hodgkin lymphoma. Surgical resection margins were involved in both specimens.
Immunohistochemistry

• The HRS cells and variants were positive for CD30, CD15 and PAX5, but negative for CD45, CD3, CD5, CD20, CD79a, CD43 and Bcl-2.

• Ki-67 revealed a proliferation index of almost 100%.

• Melanoma and carcinoma were ruled out based on negative S-100, melanoma cocktail, cytokeratin cocktail and CAM5.2.
Other Ancillary Studies

• Epstein-Barr virus (EBV) genomes were detected in most of the nuclei of HRS cells and their variants by EBER in situ hybridization analysis.

• Flow cytometry: Not performed

• Cytogenetic study: Not performed
Interesting Features

• This case represents an EBV-positive, iatrogenic immunodeficiency/methotrexate-associated primary cutaneous LPD with features of classical Hodgkin lymphoma in a 58-year-old woman who was on immunosuppressive medications for dermatomyositis for 6 years.

• Withdrawal of methotrexate resulted in complete regression of the lesion. She was then placed on active surveillance with no additional chemotherapy or radiation. The lesion recurred locally thirteen months later.
Discussion

• This is the third case of such iatrogenic primary cutaneous LPD with features of classical Hodgkin lymphoma identified in PubMed, and the only one treated with excision plus withdrawal of immunosuppressant.

• There are no widely-accepted diagnostic criteria and treatment plan for the entity due to its rarity. However, the recurrence of this case suggests that withdrawal of immunosuppressant in addition to surgical excision is insufficient, and additional chemotherapy and/or radiation may be necessary.

• Increased awareness and active investigation with collaboration with treating physicians are important for understanding its clinical behavior and optimizing management.
Proposed Diagnosis

• EBV-positive iatrogenic immunodeficiency /methotrexate-associated primary cutaneous lymphoproliferative disorder with features of Hodgkin lymphoma
References


