

Multifocal paraganglioma, mycosis fungoides, and monoclonal B-cell lymphocytosis in association with *RAD51C* mutation



Amrita Goyal, MD, Kevin Gaddis, MD, and Kimberly Bohjanen, MD
Minneapolis, MN

Key words: biopsy; chronic lymphocytic leukemia; histopathology; mycosis fungoides; paraganglioma; *RAD51C*.

INTRODUCTION

Mycosis fungoides is a rare, generally indolent non-Hodgkin T-cell lymphoma that typically presents with persistent, pruritic, scaly patches and plaques in sun-protected areas. Few genetic mutations have been consistently identified as being associated with mycosis fungoides. In this case report, we identify a patient with mycosis fungoides, multifocal paragangliomas, and a monoclonal B-cell lymphocytosis with a germline mutation in the *RAD51C* gene, a pathogenic mutation associated with breast, ovarian,¹ pancreatic,² and prostate cancers.³

CLINICAL CASE

A 76-year-old woman with a history of multifocal paraganglioma, who had resection and radiation therapy 1 year prior, myocardial infarction, hyperlipidemia, hypertension, chronic kidney disease, gastroesophageal reflux, duodenal ulcer, and diverticulitis, presented with a 4- to 5-year history of a pruritic erythematous slightly papular, scaly, and somewhat poikilodermatous eruption over the right breast (Fig 1). This rash was persistent despite use of desonide 0.05% ointment daily. Because of persistence of the eruption, a punch biopsy was performed.

Histopathology found a predominantly dermal lymphoid infiltrate of small and medium-sized hyperchromatic lymphocytes, positive for CD3 with a CD4/CD8 ratio of approximately 5:1. Epidermal lymphocytes were CD4⁺. Scattered intraepidermal lymphocytes were suspicious for early mycosis fungoides (Fig 2). T-cell receptor (TCR) gene



Fig 1. Erythematous, papular, slightly poikilodermatous eruption on the right breast present for 4 to 5 years.

rearrangement studies were positive for clonal rearrangement of the TCR γ chain. Given the clinical history, the patient's presentation was consistent with early mycosis fungoides. Triamcinolone 0.1% ointment was prescribed with improvement in the rash.

Peripheral blood flow cytometry found a population of CD5⁺ λ -monotypic B cells (6%), consistent with the immunophenotype of chronic lymphocytic leukemia/small lymphocytic lymphoma. Based on a white blood cell count of 7.5×10^9 cells per milliliter, low-count monoclonal B-cell lymphocytosis was favored. Computed tomography of the chest, abdomen, and pelvis found right-sided abdominal/retroperitoneal enhancing masses: one 5.5- $\times$ 4.9-cm invading the caudate lobe of the liver

From the Department of Dermatology, University of Minnesota.

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Amrita Goyal, MD, 420 Delaware St. SE, Minneapolis, MN 55401. E-mail: Amrita.goyal@gmail.com.

JAAD Case Reports 2019;5:240-1.

2352-5126

© 2019 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2019.01.007>

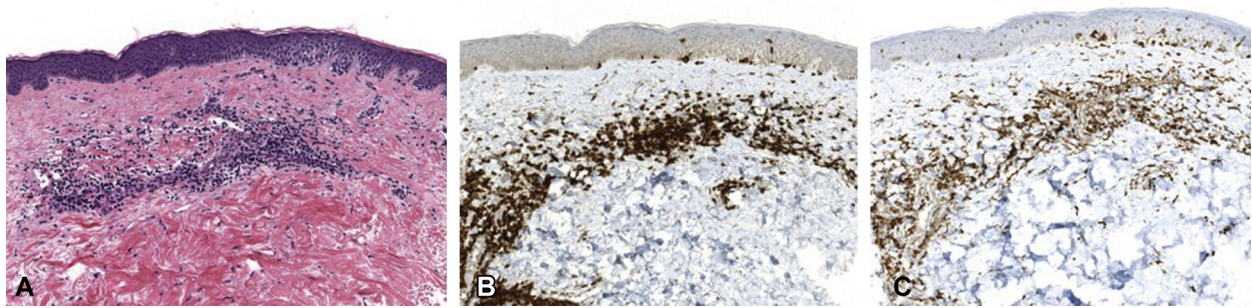


Fig 2. Mycosis fungoides. **A**, Lichenoid and epidermotropic infiltrate of small-to-medium sized lymphocytes with crenelated nuclei. **B**, Preponderance of T cells in the infiltrate and along the dermoepidermal junction. **C**, Staining for CD4 reveals mostly CD4⁺ cells along the dermoepidermal junction and in the epidermis. (**A**, Hematoxylin-eosin stain; **B**, CD3 stain; original magnifications: **A** and **B**, x100.)

and effacing the portal vein, and one 5.2- × 4.2-cm mass anterior to the inferior vena cava, consistent with enlargement of her known malignant multifocal paragangliomas. The patient opted to treat her intraabdominal paragangliomas and her monoclonal B-cell lymphocytosis with observation. Given the diagnosis with 2 malignancies and a monoclonal B-cell lymphocytosis, as well as a family history of ovarian and colon cancer, genetic testing was performed via the CustomNext (PGLNext and OvaNext) panel (Ambry Genetics). She was found to be positive for the *RAD51C* c.577C>T (p.R193*) mutation.

DISCUSSION

In this case report, we identify the first association between mycosis fungoides and a germline *RAD51C* mutation. Gene mutations previously associated with mycosis fungoides have included *TNFRSF1B*,⁴ *Janus kinase 3* (*JAK3*),⁵ *TP63*,⁶ *PLCG1*,⁷ and *CDKN2A-CDKN2B*,⁸ among others.

The *RAD51C* gene product is involved in the homologous recombination and repair of DNA. It interacts with other *RAD51* paralogs and is important in Holliday junction resolution during genetic recombination.⁹ *RAD51C* mutation has been associated with familial cancer syndromes involving breast, ovarian,¹ pancreatic,² and prostate cancers.³ Mutations have also been associated with a Fanconi anemia-like syndrome.¹⁰

The coexistence of 2 malignancies and 1 premalignancy in the setting of a known oncogenic gene mutation is suggestive of causality but certainly not definitive. It will be important to identify additional patients with this same mutation. Of note, *RAD51C* has variably been reported as not being associated with chronic lymphocytic leukemia.¹¹

This is the first report, to our knowledge, of a patient with a pathogenic *RAD51C* mutation in

conjunction with mycosis fungoides, paragangliomas, and a B-cell lymphocytosis.

REFERENCES

1. Golmard L, Castéra L, Krieger S, et al. Contribution of germline deleterious variants in the *RAD51* paralogs to breast and ovarian cancers. *Eur J Hum Genet*. 2017;25:1345-1353.
2. Yurgelun MB, Chittenden AB, Morales-Oyarvide V, et al. Germline cancer susceptibility gene variants, somatic second hits, and survival outcomes in patients with resected pancreatic cancer. *Genet Med*. 2018. <https://doi.org/10.1038/s41436-018-0009-5>.
3. Paulo P, Maia S, Pinto C, et al. Targeted next generation sequencing identifies functionally deleterious germline mutations in novel genes in early-onset/familial prostate cancer. *PLoS Genet*. 2018;14:e1007355.
4. Ungewickell A, Bhaduri A, Rios E, et al. Genomic analysis of mycosis fungoides and Sézary syndrome identifies recurrent alterations in *TNFR2*. *Nat Genet*. 2015;47:1056-1060.
5. McGirt LY, Jia P, Baerenwald DA, et al. Whole-genome sequencing reveals oncogenic mutations in mycosis fungoides. *Blood*. 2015;126:508-519.
6. Chavan RN, Bridges AG, Knudson RA, et al. Somatic rearrangement of the *TP63* gene preceding development of mycosis fungoides with aggressive clinical course. *Blood Cancer J*. 2014;4:e253.
7. Vaqué JP, Gómez-López G, Monsálvez V, et al. *PLCG1* mutations in cutaneous T-cell lymphomas. *Blood*. 2014;123:2034-2043.
8. Laharanne E, Chevret E, Idrissi Y, et al. *CDKN2A-CDKN2B* deletion defines an aggressive subset of cutaneous T-cell lymphoma. *Mod Pathol*. 2010;23:547-558.
9. Rodrigue A, Coulombe Y, Jacquet K, et al. The *RAD51* paralogs ensure cellular protection against mitotic defects and aneuploidy. *J Cell Sci*. 2013;126:348-359.
10. Jacquinet A, Brown L, Sawkins J, et al. Expanding the FANCO/*RAD51C* associated phenotype: cleft lip and palate and lobar holoprosencephaly, two rare findings in Fanconi anemia. *Eur J Med Genet*. 2018;61:257-261.
11. Sellick G, Fielding S, Qureshi M, Catovsky D, International Familial CLL Consortium, Houlston R. Germline mutations in *RAD51*, *RAD51AP1*, *RAD51B*, *RAD51C*, *RAD51D*, *RAD52* and *RAD54L* do not contribute to familial chronic lymphocytic leukemia. *Leuk Lymphoma*. 2008;49:130-133.