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

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## 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 rearrangement studies were positive for clonal rearrangement of the TCR $\gamma$ 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.

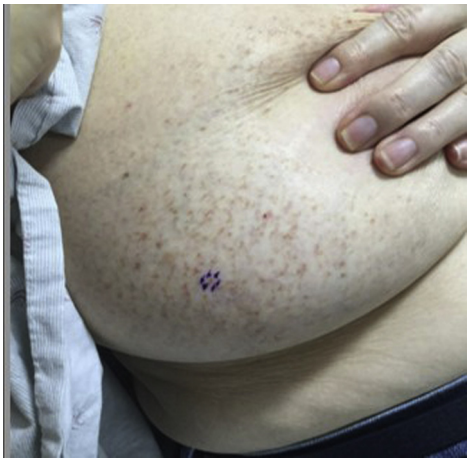

**Fig 1.** Erythematous, papular, slightly poikilodermatous eruption on the right breast present for 4 to 5 years.

Peripheral blood flow cytometry found a population of $CD5^+$ $\lambda$-monotypic B cells (6%), consistent with the immunophenotype of chronic lymphocytic leukemia/small lymphocytic lymphoma. Based on a white blood cell count of $7.5 \times 10^9$ 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- × 4.9-cm invading the caudate lobe of the liver

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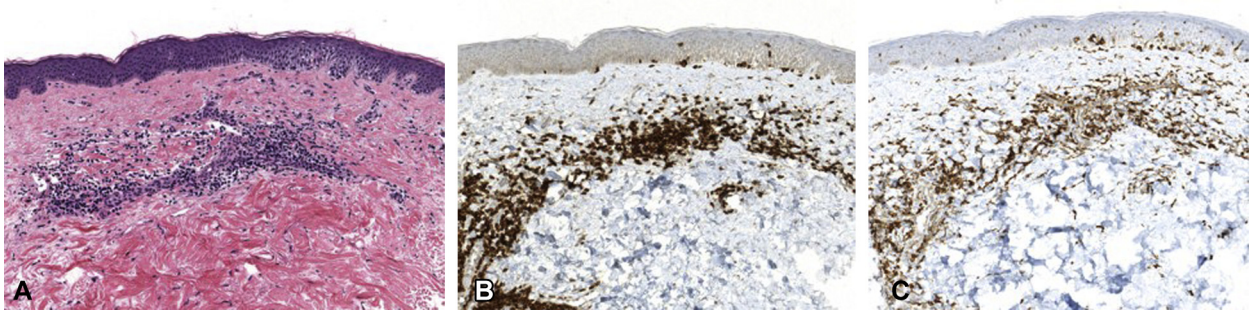


**Fig 2.** Mycosis fungoides. **A,** Lichenoid and epidermotropic infiltrate of small-to-medium sized lymphocytes with crenelated nuclei. **B,** Preponderance of T cells in the infiltrate and along the dermoepidermal junction. **C,** Staining for CD4 reveals mostly $CD4^+$ cells along the dermoepidermal 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.

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