Inflammatory Bowel Disease Treatment and Non-melanoma Skin Cancer: A Case Report

Jacqueline F. De Luca MD; Yun Sun Lee MD; and Douglas Johnson MD

Abstract

Immunosuppressant medications for Inflammatory Bowel Disease can help with both symptoms and disease progression. However, like immunosuppressants used in transplant patients, they are now suspect of contributing to nonmelenoma skin cancer (NMSC). Presented is a case of a 57-year-old Jewish man with Crohn's Disease who was diagnosed with a total of 84 NMSCs. We hope to elucidate the risk of immunosuppressants, particularly the thiopurines, on the development of NMSC.

Keywords

Crohn's Disease, Ulcerative Colitis, Inflammatory Bowel Disease, Thiopurines, Nonmelanoma Skin Cancer

Introduction

Frequent exposure to UVR, fair skin, and reduced immunity are some of the major risk factors for developing nonmelanoma skin cancer (NMSC).[1] While immunosuppressants used in treating patients with inflammatory bowel disease (IBD) have been proven to control symptoms and disease progression, they are also suspected of contributing to iatrogenic NMSC. The association between NMSC and immunosuppressant use has long been documented within transplant patient populations, yet little has been published about patients with IBD until recently. In 2010, Long et al. studied a retrospective cohort with over 50,000 participants with IBD and examined the association between IBD and the development of NMSC. It also included nested case-controls to investigate specific medications that put patients at higher risk for developing NMSC. The incidence of NMSC was significantly higher among patients with IBD compared with controls (IRR, 1.64) and patients with long-term use of thiopurines appeared to be at the highest risk of developing NMSC, followed by anti-TNF medications.[2]

Case Presentation

A 57-year-old Jewish man with Crohn's disease (CD) of the ileum diagnosed at the age of thirteen, presented with multiple nonmelanoma skin cancers (NMSCs); these had developed over the past 16 years coinciding with the initiation of a prolonged course of the thiopurine 6-mercaptopurine (mercaptopurine, 6-MP). He was diagnosed with a total of 84 NMSC: 72 NMSC at our clinic, 12 from other clinics. He was also awaiting biopsy and removal for additional lesions. His CD was initially treated with sulfasalazine and intermittent steroids at diagnosis, but for the past 20 years he had been taking 6-MP daily. In the first ten years after beginning 6-MP he developed 30 NMSC; 14 were squamous cell carcinoma (SCC) and 16 were basal cell carcinoma (BCC). The patient was then treated elsewhere for the subsequent ten years. This past year, however, he returned to the clinic with over 100 new lesions suggestive of malignancy on his torso and extremities. Subsequent to this exam, he had 42 biopsy-proven lesions of NMCS; 20 were SCC and 22 were BCC. In addition, three of the SCCs were moderately differentiated and two were poorly differentiated and some of his larger skin cancers have necessitated Mohs surgery and xenografting. The largest of his lesions was pretibial and measured 64x53 mm (Figure 1). He was awaiting biopsy for many other suspicious lesions.

The patient had Fitzpatrick II skin type and admitted to excessive sun exposure for 25 years in Hawai'i. Early on he did not use sunscreen, and would sail a catamaran during peak sun hours. He also revealed that his mother had one skin cancer lesion removed and denied ever having been a smoker.

Within the past year he discontinued 6-MP and began using mesalamine (Pentasa) and later adalimumab (Humira) hoping to attenuate the progression of NMSC, and continued to have monthly skin exams. Overall, he was hospitalized 16 times for his CD, but never required any intestinal resection. Unfortunately, in his most recent hospitalization he was diagnosed with metastatic adenocarcinoma of the small bowel, and passed away shortly after.

Discussion

Our patient was treated with the thiopurine 6-MP for over 20 years, and was extensively affected with NMSC, necessitating numerous surgeries. In Long's study, persistent thiopurine use, defined as exceeding 365 days, was associated with more than a four-fold increase in risk for developing NMSC.[2] Although the mortality from skin cancer in IBD patients is unknown thus far, it could very well follow the trends seen in transplant patients. More importantly, prolonged 6-MP is considered a significant risk factor for small bowel cancer for patients with CD (OR 10.8, CI 1.1-108.7).[3] Our patient's prolonged course of 6-MP may be implicated in his premature death from metastatic adenocarcinoma of the small bowel. Further studies documenting longer-term exposure to immunosuppressives, in particular, the thiopurines, would be extremely beneficial for our understanding of the risks these medications pose.

Disclosure

The authors have no affiliation with or significant financial involvement in any organizations or entity with a direct financial interest in the subject matter or materials discussed in this manuscript. This includes employment, honoraria, consultancies, or relevant stock ownership.

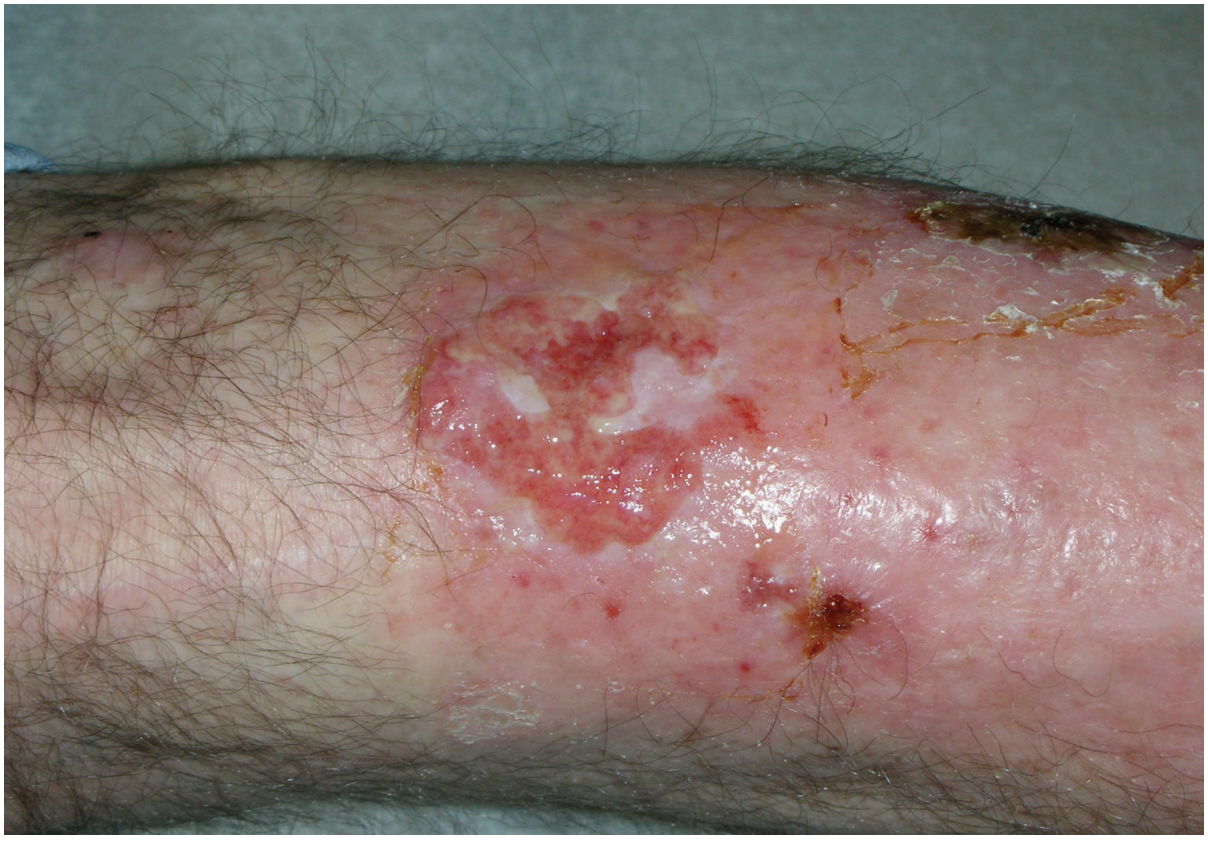

Figure 1. Left Lower Leg

Authors' Affiliation:
- University of Hawai'i Transitional Residency Program, Honolulu, HI (JFDC)
- University of California, Irvine, Department of Dermatology, Irvine, CA (YSL)
- University of Hawai'i, John A. Burns School of Medicine, Honolulu, HI (DJ)

Correspondence to:
Douglas Johnson MD, 1380 Lusitana Street, Suite 401,
Honolulu HI 96813; Ph: (808) 531-7541; Email: dwjohnson@pol.net

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