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EDITORIAL

More Skin in the Game: Screening for Skin Cancer in IBD Patients

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Optimal care of patients with inflammatory bowel disease (IBD), though usually discussed in terms of diagnostic testing, procedures, and therapeutic interventions, also requires close attention to preventive care and health maintenance. Healthcare maintenance is essential since the medications used for treatment of IBD are accompanied by often preventable adverse effects, and also because many IBD patients consider their gastroenterologist to be their primary care provider.

Among all types of cancers, skin cancers appear to among the most increased in incidence in immunocompromised hosts [1]. It is therefore unsurprising that immunomodulatory or immunosuppressive therapies, including thiopurines and biologic (monoclonal antibody-based) anti-tumor necrosis factor (TNF) agents, have increased the probability of developing malignancy, including non-melanoma skin cancer (NMSC) with thiopurine exposure and melanoma with anti-TNF exposure. Long and colleagues reported that anti-TNF use was associated with an increased risk of melanoma, with an odds ratio (OR) of 1.88 (95% CI, 1.08–3.29), and thiopurine use was associated with increased risk of NMSC, with an OR of 1.85 (95% CI, 1.66–2.05) [2]. Although medication use is thought to be a significant contributor to risk of skin cancer in and of itself, IBD alone may confer an increased risk of melanoma. A meta-analysis including 12 studies found that the risk of melanoma in IBD patients was higher in studies performed prior to the introduction of biologic therapies (eight studies, RR 1.52, 95% CI 1.02–2.25) but not in studies performed after 1998 (two studies: RR 1.08; 95% CI, 0.52–1.96). Singh and colleagues determined IBD is associated with an increased risk of melanoma, independent of the use of biologic therapy [3].

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Melanoma rates are increasing annually, with the American Cancer Society estimating there will be 91,270 new cases and 9,320 deaths attributed to melanoma in 2018. NMSC is the most common of all types of cancer, with an estimated 3.3 million Americans diagnosed each year. Eighty and twenty percent are basal cell and squamous cell cancers, respectively. Nevertheless, death from these cancers is not common. About 2000 people die from NMSC in the USA each year [4]. No randomized controlled studies have been conducted to establish the efficacy of skin cancer screening. Although observational studies have not determined that skin cancer screening decreases mortality, they have demonstrated that screening by a clinician was associated with melanoma lesions that were thinner at time of detection, conferring a favorable prognosis. Indeed, lesion thickness may therefore be considered as a surrogate marker for melanoma mortality [5]. Treatment of NMSC detected outside of a formal screening program is almost always curative, with no controlled studies that have shown screening programs to have further improved this outcome [6]. The American College of Gastroenterology (ACG) clinical guideline for preventive care in IBD acknowledges the low level of evidence for screening for melanoma and NMSC, but nevertheless strongly recommends screening for melanoma in all patients with IBD, regardless of medication exposure and screening for NMSC in IBD patients who are treated with thiopurines [7].

In this issue of *Digestive Diseases and Sciences*, Anderson and colleagues conducted a retrospective cohort study employing a prospective IBD research registry in order to investigate the rates of and factors associated with dermatologic care, particularly skin cancer screening [8]. More than half of the cohort of over 2000 patients were female, Caucasian, employed, and in their mid-40s, with over 60% diagnosed with Crohn's disease. In the 7-year study period, only 2.6% had at least one total body skin examination by a dermatologist for skin cancer screening. During the study period, 12 patients were diagnosed with cutaneous squamous cell carcinoma, 15 with basal cell carcinoma, and five with melanoma. A significantly higher proportion of patients

who sought dermatologic care had a family history of skin cancer (18.1 vs 1.9%, $p < 0.001$). Although their utilization of dermatologic care may be related to their greater awareness of risk of skin cancer, it is not clear whether the family history was elicited by their gastroenterologist or during the visit to the dermatologist itself. The authors concluded that IBD patients rarely seek dermatologic care and skin cancer screening and proposed pursuing better understanding of the awareness of and attitudes of both patients and providers toward skin cancer screening guidelines.

The authors were uniquely positioned to address this important clinical issue as they have access to a large, longitudinal research registry with multiple years of follow-up. Studies that incorporate use of International Classification of Disease (ICD) codes for identification of clinical outcomes can be fraught with misclassification bias that was likely mitigated in this study as the dermatologists themselves entered the ICD codes. Yet, a few limitations of this study still exist which may affect the interpretation and applicability of the findings. Notably, since the cohort studied is from a tertiary referral academic center specializing in IBD, it is likely that patients in the registry are not representative of IBD patients in the community. It is likely that patients were more often treated with immune suppressants and/or biologic therapies which would influence the risk of skin cancer and perhaps prompt referral for skin cancer screening. The population included in this study was predominately Caucasian with an inherently higher risk of skin cancer than in other populations. Further, inclusion of patients from only one geographic area does not account for the differences in awareness of skin cancer risk and the adherence to skin cancer screening guidelines. Nonetheless, the results are likely applicable to a predominately Caucasian population with moderate–severe IBD. There is also a possibility that the authors underestimated the rate of skin cancer screening through ascertainment bias. Despite use of an electronic medical record, it is likely that some patients did receive dermatologic care at other medical facilities, reducing the likelihood of capturing skin cancer screening from outside providers.

Continued efforts like those of Anderson and colleagues can increase awareness of the importance of skin cancer screening in the IBD population. Further investigation into the knowledge and interpretation of the guidelines for skin cancer screening among gastroenterologists and primary care providers can help determine whether more intensive education of providers would significantly increase rates of screening. As access to dermatologic care is essential to addressing this issue, efforts should be made to better connect patients with dermatologists. The ideal strategy would be to regularly incorporate a dermatologist into an IBD subspecialty practice (i.e. IBD Medical Home) to conduct skin cancer screening, in addition to addressing many other dermatologic concerns of IBD patients. Still, the majority of IBD patients do not receive care within an integrated IBD subspecialty practice. Referral of all IBD patients to a dermatologist for screening examinations can be considered, preferably an initial consultation followed by an individualized plan for further screening based on risk factors including skin type, geographic location, personal and family history of skin cancer, and medications. Utilization of advance practice providers (APP), nurse navigators, and highly trained medical technicians to create and implement preventive care such as skin cancer screening is certainly feasible in most practices.

Regardless of the model used, implementation of skin cancer screening requires adequate access to a dermatologist and additional office visits for the patient. Adequate and timely access to a dermatologist can be a significant issue. While the density of dermatologists in the USA has increased over the last decade, it is still outstripped by growing demands of an aging population, compounded by the unequal geographic distribution of dermatologists, which can further restrict access [9]. Incorporation of dermatologic APPs could ameliorate this problem [10], since APPs could help bridge the gap in access. Teledermatology offers an additional opportunity to increase access to skin cancer screening. Although a 2017 systematic review confirmed that teledermatology reduces wait times and improves patient satisfaction, it also concluded that the diagnostic accuracy of face-to-face dermatology consultation was superior to that of teledermatology [11]. Routine skin self-examination (SSE) may also be an important opportunity for early detection of skin cancer. A 2010 review including 15 studies determined that SSE has a low sensitivity (25–93%), with a high specificity (83–97%). Nonetheless, it also found educational interventions can improve the diagnostic accuracy of SSEs and improve the individual's ability to make appropriate decisions regarding the need to seek professional care [12].

The substantial health consequences of melanoma and non-melanoma skin cancers are indisputable, and the risk of developing these cancers is clearly increased in patients with IBD, particularly those treated with immune suppressants and anti-TNF biologics. Gastroenterologists can make a vital contribution to the prevention of skin cancer in patients with IBD. The path to optimizing skin cancer screening in the IBD population should include increased education of patients about the risk of skin cancer, development of health prevention pathways that can be implemented by support staff, improving access to dermatologists and trained APPs, and utilization of additional tools like teledermatology and self-examinations.

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