Relapsing Non Melanoma Skin Cancer in a Patient with Ulcerative Colitis Exposed to Long-Term Therapy with Thiopurines: Need for Regular Dermatological Screening

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Abstract
An increase of risk of malignancies such as lymphoma and non-melanoma skin cancer has been reported with the chronic use of immunomodulators in inflammatory bowel disease, particularly thiopurines. A case of a patient with ulcerative colitis after several years in immunosuppressive therapy developing multiple non-melanocytic skin neoplasms is described below.

Keywords
Immunosuppressants, Ulcerative colitis, Malignancies, Nonmelanoma

Introduction
In the management of inflammatory bowel disease (IBD) there are a variety of immunosuppressive drugs that have been shown to achieve control of symptoms and keep patients in remission, which is the primary goal of treatment, thus avoiding the continued use of corticosteroids.

One such Immunomodulators drug is Azathioprine, which is an analog of purines and consequently is incorporated into cellular DNA by the active metabolite, Mercaptopurine. This achieves inhibition of multiple pathways in the biosynthesis of nucleic acids and to a lesser extent causes some “damage” to the DNA through the incorporation of purine thio-analogues. Chronic use of Immunomodulator drugs has been reported to increase the risk of developing some tumors, which in turn increases the risk per se of IBD patients having other malignancies.

Clinical Case
A 78-year-old male farmer (he has worked for over 40 years), frequent smoker with the following personal history: arterial hypertension, cerebrovascular disease, pacemaker since 2010, chronic obstructive pulmonary disease and esophagectomy due to perforation because of a foreign body.

The patient was diagnosed with ulcerative colitis in 1997. Since then, he was treated with Azathioprine 100 mg/24 hours and Mesalazine 3g with success; however he stopped attending check-ups at the Digestive Department.

Since 2011 the patient’s case was followed at the department of Dermatology due to keratotic and ulcerated skin lesions in the facial, head region and elbows (Figure 1 and Figure 2). He was prescribed with surgical resection and occasional treatment with cryotherapy on lesions proving to be basal cell carcinomas and squamous.

In May 2014 also an exophytic tumor lesion on the dorsum of the...
higher risk of non-melanoma skin tumors such as squamous cell carcinoma in patients taking these drugs, as indeed in our case.

In this case several risk factors for developing malignancies were observed, such as: IBD, smoking, continuous sun exposure and chronic use of immunomodulators. In this patient the treatment of skin lesions was removing the involved drug, cryotherapy and surgical resection with good response. Unfortunately, the patient died months later due to underlying conditions.

Therefore, it is important to monitor patients with IBD receiving immunomodulators therapy for skin lesions, especially if they also have additional risk factors like in this case, with a history of smoking and sun exposure. So that, it is of utmost importance to advise patients on Immunomodulator therapy to examine themselves and use sunscreen, avoiding unnecessary UV exposures.

Finally, it is also necessary to share this knowledge to other professionals upon detecting skin lesions associated with the use of Immunomodulators in IBD patients. In this regard an article has recently been published by Okafor et al. [6] concluding that all patients with inflammatory bowel disease with or without immunosuppressants must undergo annual skin cancer screening as a cost-effective intervention.

### References


### Table 1: Risk of cancer with immunomodulator treatment.

<table>
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<tr>
<th></th>
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<td>↑</td>
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<tr>
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<td>Basal cell carcinoma</td>
<td>↑</td>
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* ↑ = It is not clearly established

**Figure 2:** Tumor lesion of 4.5 cm and shaped crater, with large central hyperkeratotic horn fills the nasal dorsum.