Risk of Melanoma and Nonmelanoma Skin Cancer Among Patients With Inflammatory Bowel Disease

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Gastroenterology, 143 (2): 390-399.el. Epub 2012 May 11

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Introduction

Inflammatory bowel disease (IBD) is characterized by a dysregulated immune system. Immunomodulating therapies (e.g. thiopurines and anti-tumor necrosis factor α (anti-TNF) agents) are widely used in treatment of both Crohn's disease (CD) and ulcerative colitis (UC). Patients with immune dysfunction and immunosuppressive therapies are at increased risk of developing neoplasia. Thiopurine use, especially long term, has been associated with increased risk of non-melanoma skin cancer (NMSC), including in patients with IBD [1, 2]. Anti-TNF therapy often is used in combination with thiopurines to treat IBD, leading to an even more immunocompromised state. Little is known about the potential of anti-TNF drugs to promote malignancy when used alone or in combination with other immunosuppressants. Whether, anti-TNF agents are associated with NMSC and melanoma is unclear. Some cases of basal cell carcinoma and melanoma have recently been reported in IBD patients treated with biologics [3, 4]. NMSC incidence was raised in patients with CD on adalimumab therapy [5], especially, those on prolonged treatment regimens [2]. However, long term safety report for adalimumab has shown that overall malignancy rates were comparable to the general population [5].

What is this paper about?

A retrospective cohort study design was used to determine the overall risk of melanoma and NMSC compared in an IBD to a non-IBD population. Secondly, a nested-case control study assessed the effect of different medications used in IBD treatment on skin neoplasia.

Patients with IBD, particularly with CD had increased risk of melanoma (IRR 1.29, 95% CI 1.09-1.53; and IRR 1.45, 95% CI 1.13-1.85, respectively) but not those with UC (IRR 1.13, 95% CI 0.89-1.42). However, both disease subtypes had increased risk of developing NMSC (IRR 1.64, 95% CI 1.54-1.74 and IRR 1.34, 95% CI 1.26-1.42, respectively).

It has to be stated that thiopurines and biologics were used more frequently among CD patients compared to UC (15% with CD were treated with thiopurines vs. 6.3% with UC; 5% of CD individuals received anti-TNF drugs vs. only 0.7% UC).

Furthermore, from 1997 to 2009 a slight risk elevation of developing melanoma was observed among IBD patients (IRR from 1.1 increased to 1.5), simultaneously with increasing use of biologics.

With a nested case-control study the authors assessed:

(1) The association of skin cancer with medication use and
(2) If the risk associated with medication use was related to therapy duration.

They revealed that IBD patients with melanoma had an increased use of anti-TNF drugs, as well as, that biologics were associated with developing melanoma for both CD and UC (OR 1.94, 95% CI 1.03-3.68 and OR 1.73, 95% CI 0.53-5.63 respectively). Use of thiopurines was not linked to melanoma. Regarding NMSC, the use of thiopurines was related to increased risk in both CD and UC subgroups (OR 1.99, 95% CI 1.73-2.27 for CD patients and OR 1.63, 95% CI 1.36-1.94 - for UC). This cancer type was not linked to biological therapy. Both skin neoplasias were not associated with 5-ASA treatment.

Concerning length of therapy, long term treatment with immunosuppression and/or biologics was associated with increased risk of skin cancer: risk of melanoma was related to prolonged anti-TNF use (OR 3.93, 95% CI 1.82-8.50); the greatest risk of NMSC was associated with combined thiopurine and biological treatment (OR 3.89, 95% CI 2.33-6.46), followed by thiopurine single use (OR 2.72, 95% CI 2.27-3.26) and biologics use alone (OR 1.63, 95% CI 1.12-2.36).

Conclusion

This study shows an increased risk of melanoma among CD patients, as well as an increased risk of NMSC in both CD and UC patients. The increased risk of melanoma is related to anti-TNF drugs use and the risk of NMSC is associated with thiopurine therapy. The greatest risk for NMSC are the long-term and combined treatment regimens with immunosuppressants and anti-TNF medications. Some further questions to be clarified are: (1) whether older age in combination with immunomodulating therapy contributes to risk elevation in skin neoplasias; (2) if there are some common genetic mutations for IBD and skin cancer; (3) is human papilloma virus infection a co-factor in the risk of NMSC in immunosuppressed patients; (4) if patients with IBD are at increased risk for skin malignancies due to the immunomodulating medications alone, or the immune dysfunction of the disease itself, or a combination of both factors.

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