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Editorial

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Psoriasis and Inflammatory Bowel Disease: Two Sides of the Same Coin?

Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBDs) that share common pathogenesis and clinical behaviour.[1] Both innate and adaptive immunity appear to play a key role in triggering and maintaining chronic inflammation in IBD. The involvement of both these arms of the immune system is common to other immune-mediated diseases (IMIDs), such as rheumatoid arthritis, ankylosing spondylitis and psoriasis, hence the use of similar therapeutic strategies, including the use of steroids, immunomodulators and monoclonal antibodies in all these diseases.[2] In particular, psoriasis can be associated with IBD as an independent concomitant IMID, or can be a manifestation of underlying IBD, or even a paradoxical adverse event of anti-tumour necrosis factor (TNF) therapy.[3,4] Such an association could be related to shared genetic abnormalities, common cytokine-driven inflammation [such as the interleukin 23 (IL-23) and Th17 pathway] or environmental factors. However, the link between psoriasis and IBD is currently far from clear. It is known that psoriasis is observed at a frequency about eight times higher among patients with CD than in the general population.[5]

In addition, families with psoriasis or CD are at higher risk of developing other inflammatory diseases. Lee *et al.*[6] showed that 10% of patients with CD have a first-degree relative with psoriasis, compared with only 3% of control subjects.

Lolli *et al.*[7] conducted a study to investigate whether IBD is associated with specific psoriasis phenotypes in patients developing both conditions. In the present issue, the results of their case–control prospective study, performed at the University of Tor Vergata in Rome, are presented and discussed. The authors aimed to assess the severity and phenotype of psoriasis in a prospective cohort of patients with IBD versus matched non-IBD controls with psoriasis (defined as the non-IBD group), followed up regularly from 2011 to 2013 by a multidisciplinary team including gastroenterologists and dermatologists. Dermatological assessment was required for suspected psoriasis in 251 IBD patients, the majority of whom had CD rather than UC. Psoriasis was detected in 25% of patients, with a significantly higher familiarity rate for psoriasis in the IBD group, but with milder severity than the non-IBD group. Plaque type psoriasis was the most common phenotype in both study groups, but the frequency of plaque type and nail psoriasis and psoriatic arthritis was significantly lower in IBD patients than in non-IBD patients. No further correlation was found between psoriasis and characteristics of patients, such as age, sex, concomitant medication, smoking habits or surgical history.

These results give additional information about the complex correlation between IBD and psoriasis. Psoriasis had a relatively high incidence, occurring in about 25% of patients referred to dermatologists for skin lesions. Although this is not enough to recommend routine dermatological screening for psoriasis in IBD patients, this incidence rate suggests the need for early referral to dermatologists if any skin lesion occurs in patients with IBD. Such referral would aid early diagnosis and initiation of effective therapies for both IBD and psoriasis within the window of opportunity for maximal therapeutic effectiveness. The relationship between IBD and psoriasis may be independent of the severity of psoriasis, given that severity was lower in IBD patients than in non-IBD patients.

There is evidence that T-helper cells of type 1 (Th1) and type 17 (Th17) and regulatory T-cells (T-regs) and the consequent cytokine pathway mediated by these cell populations [such as TNF-α, interleukin (IL)-1, IL-12/23 and IL-6] act at a systemic level, and can affect the intestine and the joints, metabolic pathways and the cardiovascular system.[2] Looking beyond the severity of skin and gut lesions, such systemic involvement may need a systemic approach, particularly with the use of monoclonal antibodies directed against TNF or the IL-12/23 p40 subunit. Moreover, the high correlation between psoriasis and IBD observed in the study may support the hypothesis that intestinal microbiota, together with the skin bacterial flora, could act as a trigger for psoriasis, since the loss of tolerance at the skin and gut level may share the same mechanisms through innate and adaptive immunity,[8] and might be facilitated by the increased intestinal permeability observed in IBD.[9,10] This aspect was not evaluated by Lolli *et al.*, but it would be an intriguing future avenue of investigation and may help in elucidating the role of microbes in both diseases (Figure 1).

The role of genetics in concomitant IMID is also a challenging topic. Lolli *et al.* found that IBD patients had significantly more frequent familiarity for psoriasis, although no genetic investigation was performed in the study population. It is known that the most important susceptibility locus for psoriasis is located on chromosome 6 (p21), very close to IBD-3 (p23), which is implicated in CD pathogenesis, and also very close to the gene encoding TNF-α.[11] Moreover, a recent study of a Hungarian cohort affected by CD, UC and psoriasis found that IL-23R polymorphisms may play a crucial role in the risk of development of such diseases.[12] This finding might explain the correlation between IBD and psoriasis, and provides a further avenue to explore regarding genetic predictive factors for the association between psoriasis and IBD, and also for identifying subjects who may respond to selective monoclonal antibodies, such as IL-23 inhibitors, for both conditions.

In conclusion, the study by Lolli *et al.* provides a new perspective in terms of understanding the complex mechanisms underlying IMID and, in general, the immune system. Further studies are needed to evaluate the combined role of genes, environmental factors, microbes and cytokine expression in patients with IBD and

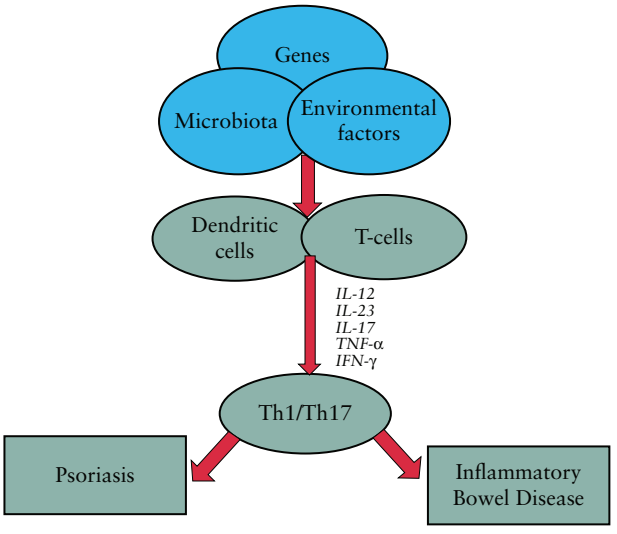

Figure 1. Proposed common mechanism in the pathogenesis of psoriasis and inflammatory bowel disease.

concomitant psoriasis or other autoimmune diseases. Such further studies may lead to the discovery of new methods for early diagnosis and new tailored therapeutic agents for the control and restoration of a healthy immune system in patients with IMID.

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Conflict of Interest

Gionata Fiorino has served as a consultant and member of the Advisory Board for AbbVie, MSD and Janssen Pharmaceuticals; Paolo Omodei has no conflicts to declare.

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Author contributions

Gionata Fiorino drafted the manuscript and figures; Paolo Omodei critically revised the manuscript; both authors approved the final version of the manuscript.

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