Journal of Clinical & Experimental Dermatology Research

Skroza et al., J Clin Exp Dermatol Res 2016, 7:2
DOI: 10.4172/2155-9554.1000335

Short communication Open Access

Psoriasis and Inflammatory Bowel Diseases: Epidemiological, Genetic and Pathogenetic Correlations: A Review of Literature

Skroza N*, Proietti I, La Viola G, Bernardini N, Aquila E and Potenza C

Department of Medical-Surgical Sciences and Bio-Technologies, Dermatology Unit "Daniele Innocenzi", Sapienza University of Rome, Italy

***Corresponding author:** Nevena Skroza, Department of Medical-Surgical Sciences and Bio-Technologies , Dermatology Unit "Daniele Innocenzi", Sapienza University of Rome, Fiorini Hospital ,Via Firenze snc Polo Pontino, 04019 Terracina, Italy, Tel: +39-0773-708531; E-mail: nevena.skroza@uniroma1.it

Received date: January 29, 2016; **Accepted date:** February 20, 2016; **Published date:** February 22, 2016

Abstract

Inflammatory bowel diseases (IBDs) and psoriasis represent two chronic relapsing inflammatory disorders respectively of the gastrointestinal tract and of the skin. The relationship between IBDs and psoriasis has been observed only through epidemiological studies, however starting from 1990s genetic and immunological aspects have been studied in detail. Both conditions share a strong genetic correlation that involves the chromosomal loci 6p22, 16q, 1p31 and 5q33. Polymorphisms of these susceptibility loci are related to the alteration of immune mechanisms in both psoriasis and IBD. Cytokines such as IL-17A, IL-22, TGFβ, IL-6, IL-21 and IL-23 influence the activity of T-Helper 17 Cells (Th17) and T-Regulatory Cells (T-Regs), playing a key role into the inflammatory process and tissue damage. The comparable common course of psoriasis and IBD explains systemic implication seen in both conditions and legitimizes similar therapeutical approach. The aim of this article is to explore the nature of the relationship between inflammatory disease and psoriasis in terms of epidemiology, genetics and pathogenesis.

Keywords: Psoriasis; Inflammatory bowel diseases; IBD

Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are chronic relapsing inflammatory disorders of the gastrointestinal tract and represent two of the most common forms of inflammatory bowel disease (IBD). Psoriasis is a chronic inflammatory immune-mediate condition primarily affecting the skin, associated with a number of cardiovascular, metabolic, and autoimmune diseases co-morbidities. For a long time the relationship IBDs and psoriasis has been observed through only epidemiological studies [1,2]; starting from 1990s genetic and immunological aspects have been studied [3] making clear that both these conditions, IBD and psoriasis, share a common course, an overlapping inflammatory subset with systemic implications and a similar therapeutical approach, that will be discussed in present article.

Epidemiological correlations

The prevalence of psoriasis in the Caucasian population is about 2-3%; almost one-third of patients with psoriasis have a first-degree relative affected by the same disease [4]. The prevalence of CD in the general population is around 7 per 100,000 in the United States [5] with a risk of 3%-5% for the siblings of an affected patient to have the same disease [6]. An increased incidence of IBD among patients with established psoriasis was described in a recent study on 12.502 psoriatic patients and 24.287 controls, that demonstrated that the prevalence of UC was significantly higher in patients with psoriasis compared to those of the control group, respectively 0.5% and 0.3%, with =0.002. Also the prevalence of CD was higher in patients with psoriasis compared to those of the control group, respectively 0.5% and 0.2%, with =0.001. In the same study, multivariate analysis confirmed that psoriasis is associated with CD (OR: 2.49, 95% CI: 1.71 to 3.62) and UC (OR: 1.64, 95% CI: 1.15 to 2.33, and =0.006) [7]. This data shown that psoriasis is strongly associated with CD than UC.

Genetic correlation

Genome wide association (GWA) studies have proven a correlation between psoriasis and IBD, identifying 13 psoriasis susceptibility loci (called PSORS1-13) and 28 IBD susceptibility loci (called IBD1-28). The stronger correlations involve the chromosomal loci 6p22, 16q, 1p31, and 5q33 that will be further analyzed.

A single nucleotide polymorphism (SNP: rs6908425) in locus 6p22 was related to CD in WTCCC study in 2007 [8]; later in 2008 Walf found an association of 6p22 with psoriasis compared with healthy controls (OR: 1.26, 95%CI: 1.12 to 1.42 and =0.00015) [9].

Locus 16q corresponds to PSORS8 and IBD3. NOD2/CARD is a gene located on chromosome 16; three polymorphisms (G2722C; C2104T; 3020insC) of this gene are strongly related to CD but not to psoriasis [10]. A 2012 meta-analysis by Zhu of nine studies, confirmed the absence of association between psoriasis, psoriatic arthritis, and common polymorphisms of NOD2/CARD15; however the authors emphasized the importance of the protein encoded by this gene in the pathogenesis of psoriasis and psoriatic arthritis and the presence of conflicting results among the studies analyzed [11].

The IL-23R has a fundamental pathogenetic role both in IBD (IBD17) and in psoriasis (PSORS7). This important gene is located on locus 1p31.1. More studies shown a correlation between two SNPs (rs7530511 [L310P] and rs11209026 [R381Q]) of IL-23R and psoriasis [12,13]. In IBD risk variants different from psoriasis have been identified (rs7517847 and rs11805303). So, while IBD and psoriasis share the same protective polymorphism, rs11209026 (R381Q), the risk variants, rs7517847 and rs11805303, were different.

The association of psoriasis (PSORS11) and IBD (IBD19) with locus 5q33.1 is widely documented, especially with the polymorphisms of IL12B gene (i.e., IL-23B, or p40). In IBDs the risk alleles identified were rs6556416 and rs6887695 that were found in psoriasis too [14,15].

Moreover, locus 6p21 and locus 5q31 appear to be more important in IBD and psoriasis pathogenesis but these correlations should be evaluated by further research.

Pathogenetic correlation

Pathogenetic mechanisms of psoriasis and IBDs have been individually investigated but there's lack of studies on patients who suffer concurrently from both these diseases. Based on current knowledge, psoriasis and IBDs pathogenesis have two different moments, the first related to the innate immunity triggered by unknown stimuli, the second as a consequence of the adaptive immunity caused by the cytokines released from innate immune cells (mainly dendritic ones).

Cytokines influence the activity of T-Helper 17 Cells (Th17) and T-Regulatory Cells (T-Regs) that play a key role into the inflammatory processes and tissue damage in both Psoriasis and IBDs. Th17 are a sub-population of T-Helper cells related to chronic conditions such as psoriasis, juvenile diabetes, celiac disease, rheumatoid arthritis and Crohn's disease [16-18]. The main cytokines that stimulate the Th17 differentiation from T-Helper naïve cells are TGFβ, IL-6, IL-21 and IL-23 (the last one produced by dendritic cells). Th17, in turn, produce IL-17 and IL-21 [19,20]. The IL-17 promotes the chemotaxis of neutrophils and monocytes and the migration and activation of T lymphocytes and neoangiogenesis. Furthermore it also induces other cytokines such as IL-6, GMCFS, IL-1β, TGF and TNFα and chemokines (e.g. IL-8, GRO-α, MCP-1) and prostaglandins (e.g. PGE2) by different cells. Augmented levels of IL-23 and IL-17 in the inflamed mucosa of patients suffering of IBDs suggest an alteration of Th17. Likewise, biopsies of psoriatic patients show a high number of Th17 and high levels of TGFβ1, IL-6, IL-15, IL-22 and IL-23 [21,22]. In skin diseases Th17 promotes acanthosis, hyperkeratosis and parakeratosis due to the synthesis of inflammatory molecules within dermis and epidermis [23,24].

T-Regs also called T-suppressor are a sub-population of T-Cells specialized in suppressing of abnormal activation of the immune system in different organs including intestine and skin [25]. Abnormalities in the number and function of these cells have been found in psoriasis and other several autoimmune diseases [26,27]. In patients with CD and UC the number of T-Regs in peripheral blood and in inflamed intestinal mucosa is reduced if compared to controls [28,29]. Similarly, functional and numerical abnormalities of T-Regs have been described in patients with psoriasis, both in peripheral blood and superficial dermis [30].

The relationship between Th17 and T-Regs have been postulated and defined through the discovery of TGFβ. This cytokine is responsible of the induction of both lymphocytes subtypes. Recent evidences show that TGFβ participates in the induction of T-Regs but in the presence of IL-6 contributes to the induction of Th17 [31].

Conclusion

Skin and bowel represent barrier and connection between inner and outer sides of the body. In these organs immune system has a fundamental role in maintaining homeostasis. Therefore the alteration of immune processes is related to development of both psoriasis and IBDs, and explains their relationship in terms of epidemiology, genetic subset and pathogenetic mechanisms.

References

1. Rudikoff D, Baral J, Lebwohl M (1999) Psoriasis and Crohn's disease. Mt Sinai J Med 66: 206.
2. Hoffmann R, Schieferstein G, Schunter F, Jenss H (1991) Re: Increased occurrence of psoriasis in patients with Crohn's disease and their relatives. Am J Gastroenterol 86: 787-788.
3. Skroza N, Proietti I, Bernardini N, La Viola G, Nicolucci F, et al. (2013) Efficacy of food supplement to improve metabolic syndrome parameters in patients affected by moderate to severe psoriasis during anti-TNFa treatment. G Ital Dermatol Venereol 148: 661-665.
4. Oestreicher J, Walters I, Kikuchi T, Gilleaudeau P, Surette J, et al. (2001) Molecular classification of poriasis disease-associated genes through pharmacogenomic expression profiling. Pharmacogenomics J 1: 272-287.
5. Friedman S, Blumberg RS, Braunwald G, Fauci AS, Kasper DL, et al. (2001) Inflammatory bowel disease in Harrison's Principles of Internal Medicine. McGraw-Hill, New York, NY, USA VII Eds: 1679-1686
6. Yang H, Plevy SE, Taylor K, Tyan D, Fischel-Ghodsian N, et al. (1999) Linkage of Crohn's disease to the major histocompatibility complex region is detected by multiple non-parametric analyses. Gut 44: 519-526.
7. Cohen AD, Dreiher J, Birkenfeld S (2009) Psoriasis associated with ulcerative colitis and Crohn's disease. J Eur Acad Dermatol Venereol 23: 561-565.
8. Wellcome Trust Case Control Consortium (2007) Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature 447: 661-678.
9. Wolf N, Quaranta M, Prescott NJ, Allen M, Smith R, et al. (2008) Psoriasis is associated with pleiotropic susceptibility loci identified in type II diabetes and Crohn disease. J Med Genet 45: 114-116.
10. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, et al. (2001) A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature 411: 603-606.
11. Zhu K, Yin X, Tang X, Zhang F, Yang S, et al. (2012) Meta-analysis of NOD2/CARD15 polymorphisms with psoriasis and psoriatic arthritis. Rheumatol Int 32: 1893-1900.
12. Cargill M, Schrodi SJ, Chang M, Garcia VE, Brandon R, et al. (2007) A large-scale genetic association study confirms IL12B and leads to the identification of IL23R as psoriasis-risk genes. Am J Hum Genet 80: 273-290.
13. Smith RL, Warren RB, Eyre S, Ho P, Ke X, et al. (2008) Polymorphisms in the IL-12beta and IL-23R genes are associated with psoriasis of early onset in a UK cohort. J Invest Dermatol 128: 1325-1327.
14. Capon F, Di Meglio P, Szaub J, Prescott NJ, Dunster C, et al. (2007) Sequence variants in the genes for the interleukin-23 receptor (IL23R) and its ligand (IL12B) confer protection against psoriasis. Hum Genet 122: 201-206.
15. Nair RP, Ruether A, Stuart PE, Jenisch S, Tejasvi T, et al. (2008) Polymorphisms of the IL12B and IL23R genes are associated with psoriasis. J Invest Dermatol 128: 1653-1661.
16. Stockinger B, Veldhoen M (2007) Differentiation and function of Th17 T cells. Curr Opin Immunol 19: 281-286.
17. Steinman L (2007) A brief history of T(H)17, the first major revision in the T(H)1/T(H)2 hypothesis of T cell-mediated tissue damage. Nat Med 13: 139-145.
18. Skroza N, Proietti I, Bernardini N, Giorgio LV, Mancini MT, et al. (2014) Skin manifestations in course of celiac disease: case report and review of the literature. Curr Pharm Des 20: 1136-1138.
19. Manel N, Unutmaz D, Littman DR (2008) The differentiation of human TH-17 cells requires transforming growth factor-?? And induction of the nuclear receptor RORγT Nature Immunol 9: 641–649.

20. Ouyang W, Kolls JK, Zheng Y (2008) The biological functions of T helper 17 cell effector cytokines in inflammation. Immunity 28: 454-467.
21. Lee E, Trepicchio WL, Oestreicher JL, Pittman D, Wang F, et al. (2004) Increased expression of interleukin 23 p19 and p40 in lesional skin of patients with psoriasis vulgaris. J Exp Med 199: 125-130.
22. Sabat R, Philipp S, Höflich C, Kreutzer S, Wallace E, et al. (2007) Immunopathogenesis of psoriasis. Exp Dermatol 16: 779-798.
23. Fitch E, Harper E, Skorcheva I, Kurtz SE, Blauvelt A (2007) Pathophysiology of psoriasis: recent advances on IL-23 and Th17 cytokines. Curr Rheumatol Rep 9: 461-467.
24. Asarch A, Barak O, Loo DS, Gottlieb AB (2008) Th17 cells: a new paradigm for cutaneous inflammation. J Dermatolog Treat 19: 259-266.
25. Sakaguchi S, Powrie F (2007) Emerging challenges in regulatory T cell function and biology. Science 317: 627-629.
26. Fattorossi A, Battaglia A, Buzzonetti A, Ciaraffa F, Scambia G, et al. (2005) Circulating and thymic CD4+ CD25+ T regulatory cells in myasthenia gravis: effect of immunosuppressive treatment. Immunology 116: 134–141.
27. Lindley S, Dayan CM, Bishop A, Roep BO, Peakman M, et al. (2005) Defective suppressor function in CD4(+)CD25(+) T-cells from patients with type 1 diabetes. Diabetes 54: 92-99.
28. Saruta M, Yu QT, Fleshner PR, Mantel PY, Schmidt-Weber CB, et al. (2007) Characterization of FOXP3+CD4+ regulatory T cells in Crohn's disease. Clin Immunol 125: 281-290.
29. Yu QT, Saruta M, Avanesyan A, Fleshner PR, Banham AH, et al. (2007) Expression and functional characterization of FOXP3+ CD4+ regulatory T cells in ulcerative colitis. Inflamm Bowel Dis 13: 191-199.
30. Bovenschen HJ, van Vlijmen-Willems IM, van de Kerkhof PC, van Erp PE (2006) Identification of lesional CD4+ CD25+ Foxp3+ regulatory T cells in Psoriasis. Dermatology 213: 111-117.
31. Bettelli E, Carrier Y, Gao W, Korn T, Strom TB, et al. (2006) Reciprocal developmental pathways for the generation of pathogenic effector TH17 and regulatory T cells. Nature 441: 235-238.