We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Psoriasis and Skin Comorbidities

Florentina Silvia Delli and Elena Sotiriou

Abstract

Psoriasis is a heterogeneous skin disease with many clinical presentations in patients with different medical backgrounds. Medical specialties such as rheumatology, pathology, and cardiology focus lately on the systemic inflammation nature of the psoriatic disease. From the Dermatologist's point of view, the revolution of therapeutic spectrum in many autoimmune skin diseases, as well as the progression noted in physiopathological mechanism, the skin comorbidities became an important issue regarding therapeutic choice.

Keywords: psoriasis, vitiligo, alopecia areata, autoimmune bullous skin diseases

1. Introduction

Psoriasis is not a merely skin disease but rather a multisystemic inflammatory disorder. As such, comorbidities, including but not limited to cardiovascular diseases and metabolic syndrome, play a significant role in therapeutic decision-making. Even though skin comorbidities in patients with psoriasis are common, they are usually neglected. The epidemiology studies and therapy-related literature dominate the recently published relevant data. The pathogenesis of comorbid diseases, either systemic or dermatologic, in patients with psoriasis remains unknown; however, shared inflammatory pathways, cellular mediators, genetic susceptibility, and common risk factors are hypothesized to be contributing elements.

Patients with psoriasis are more likely to have at least one other autoimmune disease [1], including vitiligo [2], alopecia areata [1], and autoimmune bullous diseases [3].

The clinical implications of the most frequent comorbid skin diseases associated with psoriasis are discussed in this chapter.

2. Psoriasis and skin comorbidities

2.1 Psoriasis and vitiligo

Vitiligo is the most common disorder of pigmentation. Although the association of psoriasis and vitiligo has been described since 1890, the interrelationship between the two dermatoses remains debatable. Most of the studies found that 6% of patients with vitiligo develop psoriasis [4, 5] and 2% of patients with psoriasis suffer from vitiligo [4]. Furthermore, a clinical and even dermoscopic challenge is to distinguish vitiligo from the occurrence of hypopigmentation in areas of previously affected psoriatic

skin [6]. Healing of psoriatic lesions often leaves hypopigmentation that could simulate vitiligo. There have been cases reported in the literature of psoriatic plaques and guttate lesions strictly localized to the vitiliginous patches (**Figure 1**), and the two dermatoses occurring together without strict colocalization of lesions. In many cases, it is difficult to say which disease starts first, vitiligo, or psoriasis, or may occur at the same time. A retrospective study found that almost 47% of patients having both diseases had separated lesions [7], while, in another study, 34% of patients' psoriatic plaques covered the vitiligo patches [8].

Many hypotheses tried to explain the pathogenesis of vitiligo. These hypotheses consider the role of neural implication, microvascular anomalies, melanocyte degeneration from oxidative stress, defects in melanocyte adhesion, autoimmunity, somatic mosaicism, and genetic influences [9]. Genetic and immunological factors are present in both diseases, psoriasis and vitiligo. A study in China found that both skin diseases share a common genetic locus in the major histocompatibility complex (MHC) [10]. Precisely, the rs. 9468925 in HLA-C/HLA-B is associated with both psoriasis and vitiligo, providing the first substantial evidence that two different skin diseases share a common genetic locus in the MHC. In the molecular etiopathogenesis mechanism of both diseases, Th1 cytokines play a key role. Vitiligo and psoriasis are both chronic inflammatory Th1 type autoimmune diseases with increased TNF- α and interferon γ levels [8]. Otherwise, both share the activation of the Th17 pathway [11]. Even more,

Figure 1.
A typical elbow psoriatic plaque on vitiligo area. Photo from personal collection.

the memory cells might be a link between psoriasis and vitiligo. Recent translational research shows the presence in psoriatic skin of memory CD8⁺ T cells directed against the melanocyte-derived protein ADAMTSL5 [12], a protein that may favor the development of vitiligo in a predisposed patient. The tissue-resident memory T (T_{RM}) cells are also vital in the recurrence of chronic inflammatory skin disorders, including psoriasis and vitiligo, under pathological or uncontrolled conditions [13].

An interesting phenomenon is the case of vitiligo induced by biological drugs used for psoriasis treatment. The anti-TNF- α (etanercept, infliximab) is one of the most cited groups of biological drugs that induce new-onset vitiligo or progression of pre-existence vitiligo in psoriatic patients [14]. Even anti-IL12/23 [15] and anti-IL17 [15, 16] class can induce a progression of pre-existing vitiligo, while, to date, no cases are reported in the literature considering anti-IL23 drugs. It is difficult to understand how molecules that block cytokines involved in both diseases' pathogenesis can trigger the mechanisms underlying this phenomenon. However, a new type of medication that functions by inhibiting the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2), thereby interfering with the JAK-STAT signaling pathway, have been approved for psoriatic therapy and are also a promising novel therapy for vitiligo.

In conclusion, the paucity of data on the link between psoriasis and vitiligo underlines the gaps of knowledge on this topic. To highlight the pathogenetic mechanisms underlying the two diseases are strongly needed further studies.

2.2 Psoriasis and alopecia areata

Psoriatic lesions of the scalp are sometimes associated with symptomatic hair loss and alopecia. The type of alopecia can be, in most cases, characterized using the dermatoscope.

Alopecia areata (AA) is the most common immune-mediated hair loss disorder with a lifetime prevalence of 2% [17]. Early studies of the last decade showed that patients with psoriasis and psoriatic arthritis have a higher risk to develop other autoimmune disorders, particularly alopecia areata (AA) [1, 18]. Two large population studies demonstrated an odds ratio of 2.4 [1, 18].

The Renbeek phenomenon, the opposite of the Koebner phenomenon, was originally described in AA patients where hair growth was observed in psoriatic plaques. Generalizing, it is an interesting phenomenon where one skin condition inhibits other skin conditions and confirms once again the complex immunological overlap between these two skin diseases.

In the case of a patient with psoriasis and AA, the complexity of the common immunological paths that share these both skin disorders must be considered when selecting therapeutic regimens, to avoid worsening one of their inflammatory conditions while treating the other. For example, contrary to the initial hope that tumor necrosis factor α (TNF α) may have a role in the pathogenesis of AA, many reports have demonstrated the inefficiency of anti-TNF α drugs in the treatment of AA [19].

Moreover, careful selection of biological treatment regimens may offer therapeutic benefits for both their psoriasis and AA while giving us experience with the newer biologics in AA. The investigation of cytokine profile and the relation between different categories of cytokines is continuing in both psoriasis and AA. A recent example comes from a recent study where the authors conclude that psoriasis T helper type 17 (Th17) cytokines can inhibit some inflammatory processes involved in AA pathogenesis [20].

2.3 Psoriasis and bullous diseases

Autoimmune bullous diseases (AIBD) and more frequent pemphigoid group, often develop in patients with psoriasis. The rare nature of AIBD makes collecting epidemiologic data with a representative number of patients a laborious process. Among the pemphigoid diseases, bullous pemphigoid (BP), the most prevalent subcutaneous autoimmune bullous disease worldwide, is also the most prevalent blistering disease associated with psoriasis. This association has been studied and confirmed on large populations [21–24]. BP and psoriasis do not share any common HLA or otherwise genetic susceptibility. A consequence of epigenetic events related to the psoriatic inflammatory cascade and changes at the basal membrane zone in psoriasis is possible pathogenetic hypotheses, along with increased of certain Th1/Th17 cytokines and chemokines levels that may be another link for their association [25].

Antilaminin γ 1 pemphigoid is the second most prevalent AIBD associated with psoriasis, followed by the combination of BP with antilaminin γ 1 pemphigoid [26]. The explanation of the subepidermal blister formation in psoriatic patients is mainly provided by Mondello and Vaccaro studies [27, 28]. The cleavage and disruption of laminin 1 and laminin α 1 within basal membrane zone, either in apparent normal skin or psoriatic lesion [27, 28], might be the main trigger factor for several antibodies production, such as anti-laminin γ 1 and anti bullous pemphigoid antigen 180 (BP180). As a result, the development of BP rash is sometimes observed in psoriatic patients. In the same case series of Ohata et al. [26], three patients presented linear IgA bullous dermatosis and two epidermolysis bullosa acquisita.

The relation between psoriasis and BP seems to be bidirectional. The only published study that confirms that psoriasis occurs significantly more frequently in patients with BP than in the control group, comes from Taiwan [21]. Large population studies in each country are necessary to support this association.

Mucous membrane pemphigoid is also a rare chronic autoimmune disorder characterized by subepidermal blistering that has been observed in patients with psoriasis [29]. The laminin degradation stimulated by matrix metalloprotease 9 released from neutrophil infiltrate in the patients with psoriasis may contribute to decreasing the threshold of autoantibodies against laminin γ 1 production [30, 31].

A recent systematic review and meta-analysis evaluating the association between pemphigus and psoriasis confirm this association [32]. However, it is difficult to find common pathways between pemphigus and psoriasis pathophysiologic mechanisms.

3. When psoriasis coexists with other skin diseases

Often chronic skin inflammatory diseases coexist with psoriasis suggesting common pathogenic pathways.

Among them, hidradenitis suppurativa (HS) also exhibits a systemic inflammatory nature with systemic comorbidities similar to psoriasis. The systemic inflammation might explain the observation of a recent study, where it was found that in patients with both HS and psoriasis, the disease diagnosed first tended to take a more severe course than the later diagnosed (**Figure 2**) [33].

Pityriasis rubra pilaris (PRP) is an inflammatory dermatologic disorder of unknown cause, which often is misdiagnosed as psoriasis. However, differentiating between erythrodermic PRP and pustular psoriasis is challenging even histologically. The same treatment is indicated in both diseases, despite the absence of standard

Figure 2.
A 65-year-old male patient. Hidradenitis suppurativa Hurley III coexists with psoriatic plaques. Photo from personal collection.

recommended treatment algorithms for PRP. According to recently published data, we must consider the coexistence of psoriasis and autoimmune diseases in patients with PRP [34]. From our personal experience, a patient can present with erythrodermic PRP and the improvement of the rash might be followed by the appearance of classical plaque psoriasis after treatment with an anti-TNF- α biological agent.

One of the most paradoxical relationships is between psoriasis and atopic dermatitis (AD). The Th17 immune response is dominant in psoriasis and causes neutrophil migration, induction of innate immunity, and increased epithelial metabolism, while Th2 immunity that characterizes AD is dominated by IL-4 and IL-13 cytokines leading to an impaired epidermal barrier, dampened innate immunity, and eosinophil migration. However, the association of AD with psoriasis is not so rare. Both diseases share many characteristics: high prevalence, chronicity, primary skin inflammation, associated comorbidities, important impact on the quality of patient's life due to itch and stigmatization. Some authors consider that the co-occurrence is an overlapping syndrome [35] and others found bidirectional association [36]. In Bozek's study [35] the patients with concomitant AD and psoriasis were frequently boys and overweight and had skin lesions equally distributed throughout the body. Despite the fact that the pathogenesis of psoriasis and AD is different, a family history of atopic disease is a more frequent finding in children with concomitant AD and psoriasis and in children with AD than in children with only AD or psoriasis [35]. Genetics and epigenetics studies with a focus on this topic might provide useful data regarding the particular management of patients with AD and psoriasis.

4. Conclusion

A new research field in many autoimmune skin diseases and the new therapeutic target molecule consequently developed constitutes the base for the addition of autoimmune skin comorbidities on the general list of psoriasis-associated diseases. Evidence increasingly suggests a relation between psoriasis and vitiligo, alopecia areata, and autoimmune subepidermal bullous diseases.

Recognizing all the comorbid disease burden of psoriasis is essential for ensuring comprehensive care of patients with psoriasis.

Conflict of interest

The authors declare no conflict of interest.

Author details

Florentina Silvia Delli* and Elena Sotiriou
First Dermatology Department, Aristotle University of Medical School Thessaloniki,
Greece

*Address all correspondence to: delliflorentina@ymail.com

IntechOpen

© 2022 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

- [1] Wu JJ, Nguyen TU, Poon KY, Herrinton LJ. The association of psoriasis with autoimmune diseases. *Journal of the American Academy of Dermatology*. 2012;**67**(5):924-930. DOI: 10.1016/j.jaad.2012.04.039. Epub 2012 Jun 2
- [2] Arunachalam M, Dragoni F, Colucci R, Berti S, Crocetti E, Galeone M, et al. Non-segmental vitiligo and psoriasis comorbidity—a case-control study in Italian patients. *Journal of the European Academy of Dermatology and Venereology*. 2014;**28**(4):433-437. DOI: 10.1111/jdv.12117. Epub 2013 Feb 26
- [3] Kridin K, Bergman R. Association between bullous pemphigoid and psoriasis: A case-control study. *Journal of the American Academy of Dermatology*. 2017;**77**(2):370-372. DOI: 10.1016/j.jaad.2017.02.057
- [4] Sharquie KE, Salman HA, Yaseen AK. Psoriasis and vitiligo are close relatives. *Clinical, Cosmetic and Investigational Dermatology*. 2017;**10**:341-345. DOI: 10.2147/CCID.S142819
- [5] Canu D, Shourick J, Andreu N, Gey A, Ballanger-Désolneux F, Barailler H, et al. Demographic and clinical characteristics of patients with both psoriasis and vitiligo in a cohort of vitiligo patients: A cross-sectional study. *Journal of the European Academy of Dermatology and Venereology*. 2021;**35**:e676-e679
- [6] Amico S, Barnette T, Dequidt L, Fauconneau A, Gérard E, Boursault L, et al. Characteristics of postinflammatory hyper- and hypopigmentation in patients with psoriasis: A survey study. *Journal of the American Academy of Dermatology*. 2020;**83**(4):1188-1191. DOI: 10.1016/j.jaad.2020.02.025. Epub 2020 Feb 14
- [7] Sheth VM, Guo Y, Qureshi AA. Comorbidities associated with vitiligo: A ten-year retrospective study. *Dermatology*. 2013;**227**(4):311-315. DOI: 10.1159/000354607. Epub 2013 Oct 4
- [8] Sandhu K, Kaur I, Kumar B. Psoriasis and vitiligo. *Journal of the American Academy of Dermatology*. 2004;**51**(1):149-150
- [9] Katz EL, Harris JE. Translational research in vitiligo. *Frontiers in Immunology*. 2021;**12**:624517. DOI: 10.3389/fimmu.2021.624517
- [10] Zhu KJ, Lv YM, Yin XY, et al. Psoriasis regression analysis of MHC loci identifies shared genetic variants with vitiligo. *PLoS One*. 2011;**6**(11):e23089
- [11] Yen H, Chi CC. Association between psoriasis and vitiligo: A systematic review and meta-analysis. *American Journal of Clinical Dermatology*. 2019;**20**(1):31-40. DOI: 10.1007/s40257-018-0394-1
- [12] Arakawa A, Siewert K, Stöhr J, Besgen P, Kim SM, Rühl G, et al. Melanocyte antigen triggers autoimmunity in human psoriasis. *The Journal of Experimental Medicine*. 2015;**212**(13):2203-2212. DOI: 10.1084/jem.20151093. Epub 2015 Nov 30
- [13] Chen L, Shen Z. Tissue-resident memory T cells and their biological characteristics in the recurrence of inflammatory skin disorders. *Cellular & Molecular Immunology*. 2020;**17**(1):64-75. DOI: 10.1038/s41423-019-0291-4. Epub 2019 Oct 8
- [14] Anthony N, Bourneau-Martin D, Ghamrawi S, Lagarce L, Babin M,

- Briet M. Drug-induced vitiligo: A case/ non-case study in Vigibase®, the WHO pharmacovigilance database. *Fundamental & Clinical Pharmacology*. 2020;**34**(6):736-742. DOI: 10.1111/fcp.12558. Epub 2020 Apr 27
- [15] Méry-Bossard L, Bagny K, Chaby G, Khemis A, Maccari F, Marotte H, et al. New-onset vitiligo and progression of pre-existing vitiligo during treatment with biological agents in chronic inflammatory diseases. *Journal of the European Academy of Dermatology and Venereology*. 2017;**31**(1):181-186. DOI: 10.1111/jdv.13759. Epub 2016 Jun 13
- [16] Marasca C, Fornaro L, Martora F, Picone V, Fabbrocini G, Megna M. Onset of vitiligo in a psoriasis patient on ixekizumab. *Dermatologic Therapy*. 2021;**34**(5):e15102. DOI: 10.1111/dth.15102. Epub 2021 Sep 2
- [17] Gilhar A, Etzioni A, Paus R. Alopecia areata. *The New England Journal of Medicine*. 2012;**366**(16):1515-1525. DOI: 10.1056/NEJMr1103442
- [18] Sy C, Chen YJ, Tsteng WC, Lin MW, Chen TJ, Hwang CY, et al. Comorbidities profiles among patients with alopecia areata: The importance of onset age, a nationwide population-based study. *JAAD*. 2011;**65**(5):949-956. DOI: 10.1016/j.jaad.2010.08.032. Epub 2011 May 25
- [19] Strober BE, Siu K, Alexis AF, Kim G, Washenik K, Sinha A, et al. Etanercept does not effectively treat moderate to severe alopecia areata: An open-label study. *Journal of the American Academy of Dermatology*. 2005;**52**(6):1082-1084. DOI: 10.1016/j.jaad.2005.03.039
- [20] Guttman-Yassky E, Nia JK, Hashim PW, Mansouri Y, Alia E, Taliencio M, et al. Efficacy and safety of secukinumab treatment in adults with extensive alopecia areata. *Archives of Dermatological Research*. 2018;**310**(8):607-614. DOI: 10.1007/s00403-018-1853-5. Epub 2018 Aug 18
- [21] Chen YJ, Wu CY, Lin MW, Chen TJ, Liao KK, Chen YC, et al. Comorbidity profiles among patients with bullous pemphigoid: A nationwide population-based study. *The British Journal of Dermatology*. 2011;**165**(3):593-599. DOI: 10.1111/j.1365-2133.2011.10386.x. Epub 2011 Jul 28
- [22] Tsai TF, Wang TS, Hung ST, Tsai PI, Schenkel B, Zhang M, et al. Epidemiology and comorbidities of psoriasis patients in a national database in Taiwan. *Journal of Dermatological Science*. 2011;**63**(1):40-46. DOI: 10.1016/j.jdermsci.2011.03.002. Epub 2011 Mar 16
- [23] Phan K, Goyal S, Murrell DF. Association between bullous pemphigoid and psoriasis: Systematic review and meta-analysis of case-control studies. *The Australasian Journal of Dermatology*. 2019;**60**(1):23-28. DOI: 10.1111/ajd.12899. Epub 2018 Aug 23
- [24] Kridin K, Ludwig RJ, Schonmann Y, Damiani G, Cohen AD. The bidirectional association between bullous pemphigoid and psoriasis: A population-based cohort study. *Frontiers in Medicine (Lausanne)*. 2020;**7**:511. DOI: 10.3389/fmed.2020.00511
- [25] Dainichi T, Kabashima K. Interaction of psoriasis and bullous diseases. *Frontiers in Medicine (Lausanne)*. 2018;**5**:222. DOI: 10.3389/fmed.2018.00222
- [26] Ohata C, Ishii N, Koga H, Fukuda S, Tateishi C, Tsuruta D, et al. Coexistence of autoimmune bullous diseases (AIBDs) and psoriasis: A series of 145 cases. *Journal of the American Academy of Dermatology*. 2015;**73**(1):50-55

- [27] Mondello MR, Magaudo L, Pergolizzi S, Santoro A, Vaccaro M, Califano L, et al. Behavior of laminin 1 and type IV collagen in uninvolved psoriatic skin. Immunohistochemical study using confocal laser scanning microscopy. *Archives of Dermatological Research*. 1996;**288**(9):527-531. DOI: 10.1007/BF02505249
- [28] Vaccaro M, Magaudo L, Cutroneo G, Trimarchi F, Barbuzza O, Guarneri F, et al. Changes in the distribution of laminin alpha1 chain in psoriatic skin: Immunohistochemical study using confocal laser scanning microscopy. *The British Journal of Dermatology*. 2002;**146**(3):392-398. DOI: 10.1046/j.1365-2133.2002.04637.x
- [29] Lee J, Seiffert-Sinha K, Attwood K, Sinha AA. A retrospective study of patient-reported data of bullous pemphigoid and mucous membrane pemphigoid from a US-based registry. *Frontiers in Immunology*. 2019;**10**:2219. DOI: 10.3389/fimmu.2019.02219
- [30] Mezentssev A, Nikolaev A, Bruskin S. Matrix metalloproteinases and their role in psoriasis. *Gene*. 2014;**540**(1):1-10. DOI: 10.1016/j.gene.2014.01.068. Epub 2014 Feb 8
- [31] Dainichi T, Kurono S, Ohyama B, Ishii N, Sanzen N, Hayashi M, et al. Anti-laminin gamma-1 pemphigoid. *Proceedings of the National Academy of Sciences of the United States of America*. 2009;**106**(8):2800-2805. DOI: 10.1073/pnas.0809230106. Epub 2009 Feb 5
- [32] Phan K, Ramachandran V, Smith SD. Association between pemphigus and psoriasis: A systematic review and meta-analysis. *Dermatology Online Journal*. 2020;**26**(8):13030/qt5g78q4f4
- [33] Pinter A, Sarlak M, Zeiner KN, et al. Coprevalence of hidradenitis suppurativa and psoriasis: Detailed demographic, disease severity and comorbidity pattern. *Dermatology*. 2021;**237**(5):759-768. DOI: 10.1159/000511868
- [34] García-Briz MI, García-Ruiz R, Zayas-Gávila AI, et al. Pityriasis rubra pilaris. Something more than a disorder of queratinization? *Medicina Cutánea Ibero-Latino-Americana*. 2018;**46**(1):7-12
- [35] Bozek A, Zajac M, Krupka M. Atopic dermatitis and psoriasis as overlapping syndromes. *Mediators of Inflammation*. 2020;**2020**:7527859. DOI: 10.1155/2020/7527859
- [36] Dai YX, Tai YH, Chang YT, Chen TJ, Chen MH. Bidirectional association between psoriasis and atopic dermatitis: A nationwide population-based cohort study. *Dermatology*. 2021;**237**(4):521-527. DOI: 10.1159/000514581. Epub 2021 Mar 18