REVIEW ARTICLE

Psoriasis-cell Mediated Autoimmune Disease: A Review

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ABSTRACT

Psoriasis is a widespread chronic inflammatory skin condition that affects about 2% of the population. It was recognized as a unique entity in the early 19th century by Robert Willan. The mechanism of infection is due to the exaggerated proliferation of keratinocytes secondary as a result of the activity of the immune system. Different factors cause psoriasis, which includes genetic factors, age, gender, stress, and Bacterial infection. There are several forms of psoriasis, the most prevalent of which is psoriasis Vulgaris (plaque-like psoriasis), which accounts for 90 percent of all cases. Biological therapy is an effective treatment for psoriasis and other autoimmune diseases comparing with chemotherapy and phototherapy.

Keywords: Biological Therapy, Keratinocytes, Psoriasis, T-Cells.

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INTRODUCTION

Psoriasis is a prevalent chronic inflammatory skin disease that affects around 2% of the population,[1] as well as psoriasis Vulgaris psoriasis is the most frequent kind, accounting for 90% of all cases.[2]

It is a distinct entity in the early nineteenth century recognized by Robert Willan and named by Ferdinand Hebra in 1841, and it influences the quality of life. A dynamic illness of morphological change occurs as a newly developed lesion develops into an advanced plaque that can steadily increase.[3]

The mechanism of the disease remained incomprehensible for decades until the studies and research carried out by the scientist Ferdinand Von Herbra (1841) through the data that he collected about the disease for a long time, that the disease affects 2–3% of the total population and the mechanism of infection due to exaggerated proliferation of keratinocytes secondary as a result of the activity of the immune system. The disease is more common in males aged 20–39 years and females aged 40–59 years, and the ratio is equal between males and females.[4]

A retrospective study was done in an outpatient clinic of Baquba Teaching Hospital in Diyala to study the incidence of psoriasis.It has been found that 10964 patients with skin disease were attended to the outpatient clinic department of dermatology. Out of this number 220 (2%) patients were diagnosed to have psoriasis and they were 102 (46%) female and 118 (54%) male.[5]

A study by A.Razzaq and his group (2015)[6] also confirmed that the IL-20RA gene hasa role in the genetic predisposition to psoriasis in the Iraqi population.

A study was done in outpatients' dermatological clinic in Al-Hussein teaching hospital and private clinic in Samawa city. On children patients, their ages range from 6 months to 14 years old. This study showed that plaque-type psoriasiswas the commest findings followed by scalp psoriasis and guttate psoriasis. Also this study showed that psoriasis occurred in females more than males.[7]

A study was designed to detect IL-23 and IL-17A levels in psoriatic patients at ImameinKadhimein medical city's Dermatology clinic in Baghdad, Iraq. This investigation revealed a significant difference in the levels of IL-23 and IL-17A in patients' sera compared to a healthy control group.[8]

Symptoms of Psoriasis

The most frequently reported symptoms connected to psoriasis are:

- Scaling of the skin
- Erythema
- Itching
- Fatigue
- Burning
- Bleeding
- Swelling.[9]

Causes of Psoriasis

Genetic Factors

The severity of the disease is thought to be influenced by genetic factors.[10] The MHC class I gene has been identified as the primary susceptibility factor for psoriasis. The psoriasis susceptibility region one gene locus has been identified as the gene locus at 6p21 that is significantly related to psoriasis

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development (PSORS1). Furthermore; The HLA-Cw6 gene was determined to be the PSORS1 locus's greatest susceptibility allele to early-onset chronic plaque-type and guttate psoriasis.[11]

Age

The disease can appear at any age, but a study revealed that this illness affects 75% of those under 70 years age. The mean age was 52,6 years; however, the study revealed that the age of onset of psoriasis patients was less than 46 years, with a mean age of 33,2 years.[12]

Gender

Psoriasis is a chronic multifaceted illness that affects both sexes equally, yet a recent study found that men had more severe conditions than women.[10]

Stress

Most clinicians and researchers agree on the role of stress in the course of psoriasis, where stress is one of the most important catalysts that have a role in the onset or exacerbation of the disease. Also, the reaction of stress in psoriasis patients is most likely mediated via the hypothalamic-pituitary-adrenal connection, which includes higher levels of neuroendocrine hormones and autonomic neurotransmitters.[13]

Obesity

Obesity is significantly linked to the incidence and worsening of psoriasis, and metabolic syndrome is frequent in psoriasis patients. The prevalence of obesity in patients with psoriasis is significantly high as well as a higher risk of obesity. A previous meta-analysis showed the association between obesity and severe psoriasis. Also a positive association between body mass index (BMI) and psoriasis. Obesity can be explained as the expansion of white adipose tissue. Different mediators secreted by adipose tissue lead to a low-grade inflammatory state that contributes to the pathogenesis of psoriasis.[14]

Bacterial Infection

Cutaneous microbiota was discovered 100 years ago, and subsequent research has proved the association between skin bacteria and psoriatic lesions, such as streptococcal-hemolytic group A throat infections connected to guttate psoriasis.[15]

Pathogenesis of Psoriasis

Psoriasis Vulgaris is an autoimmune skin condition caused by cells such as macrophages, dendritic cells, neutrophils, and others that produce chemokines and cytokines. T-helper cells (Th1, Th22, and Th17) and T cytotoxic.[16]

Immunologically,the immune circuits activated in psoriasis amplify the immune circuits that exist as foundational and stimulating pathways in normal human skin, including Keratinocytes, which are important participants in innate immunity and can stimulate subsets of T-lymphocytes recruited on the skin. Skin damage causes cell death and the creation of the AMP LL37 by keratinocytes.In plasmacytoid dendritic cells, DNA/LL37 complexes can bind to intracellular TLR9 (pDCs), activating them and causing them to produce IFN-and. TLR7 is triggered by LL37/RNA complexes, while TLR8 is activated by the same combination in plasmacytoid DCs. As a result, both the LL37/RNA complex and type 1 IFN can activate myeloid DCs.[17]

The interplay of adaptive and innate immunity is central to the molecular pathogenesis of psoriasis. T-cells and the release of cytokines appear to be the key reasons for lesion formation and persistence. Both IL-12 and IL-23 are produced by dendritic cells. IL-17 plays an important role in the genesis and maintenance of autoimmune inflammation. Endothelial cells and macrophages are the primary producers of pro-inflammatory cytokines in response to IL-17.[18]

Depending on the activation trigger or antigen, activation of skin-resident T lymphocytes may result in the IL-17, IFN-α, or IL-22 production. This can cause keratinocytes to produce chemokines, which subsequently enhances specific effector responses. Th1 activation results in increased IFN-production, which increases the manufacture of chemokines like CXCL9, CXCL10, and CXCL11 that can recruit more Th1 cells. Stimulation of Th17, increases the synthesis of CCL20, CXCL1, CXCL2, and CXCL8/IL-8, resulting in the recruitment of additional Th17 and neutrophils into the skin. When Th22 cells are activated, they produce more IL-22, which can cause keratinocyte hyperplasia.[17]

To restrict inflammation and avoid autoimmune and chronic inflammatory disorders, immunological homeostasis must be properly regulated. Treg-mediated inhibition of auto-reactive T cells is crucial for preventing spontaneous autoimmune illness. Psoriatic Treg cells have been revealed to exhibit a lack of regulatory competence, which leads to psoriasis pathogenesis. Several labs have separately identified functional abnormalities in Treg cells derived from patients with a variety of autoimmune disorders (Figure 1).[19]

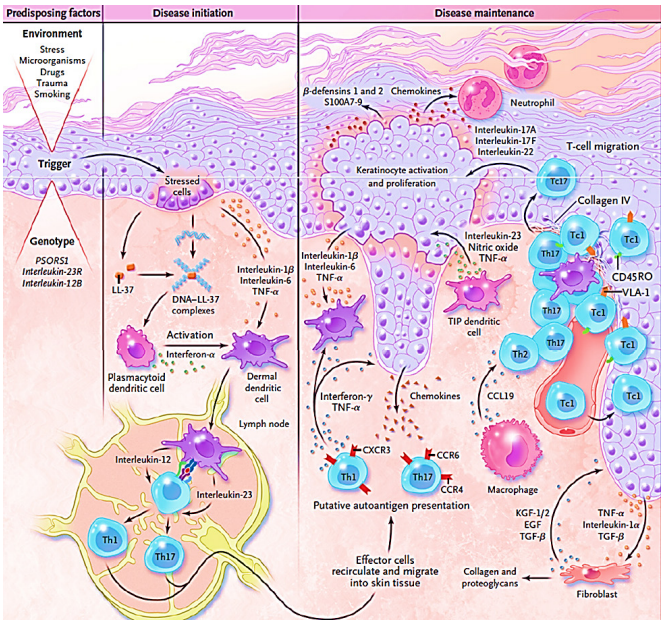

Figure 1: Proposed Diagram of the Evolution of a Psoriatic Lesion from Initiation to Disease Maintenance(20).

Types of Psoriasis

- *Plaque-like Psoriasis*

Involves 90 percent of all cases with papulosquamous plaques that are clearly differentiated from nearby normal skin. The plaques are red and have white or silvery scales on them. They can be thick, thin, large, or small. Plaques are most typically found on the elbows, knees, scalp, lumbosacral region, and umbilicus (Figure 2).[4]

- *Inverse Psoriasis*

It is a kind of psoriasis that appears in body skin folds such as the armpits, beneath the breasts, around the groin, and between the buttocks.[4]

- *Pustular Psoriasis*

Characterized by white blisters of non-infectious pus.[10] Localized pustular psoriasis contains two variants, Acrodermatitis continuous of Hallopeau and palmoplantar pustulosis.[21] Acrodermatitis and generalized pustular psoriasis are distinguished by diffused dark erythematous patches with visible sterile pustules that merge to produce huge pus lakes.[10]

- *Erythrodermic Psoriasis*

Active psoriasis can encompass the skin completely or partially, and it can take one of two forms. To begin, chronic plaque psoriasis may proceed gradually as plaques become confluent and widespread. Second, erythroderma may be a symptom of unstable psoriasis caused by infection, tar, medications, or the discontinuation of corticosteroids.[22]

- *Psoriatic Arthritis*

This type affects up to a quarter of psoriasis patients. It is an inflammatory joint condition that causes swelling, discomfort, and tenderness in the joints and surrounding ligaments. Psoriatic arthritis is distinguished clinically by the presence of psoriatic skin lesions as well as nail dystrophy, dactylitis, and enthesitis.[23]

Treatments for Psoriasis

Biological Therapy

Maini *et al*. performed one of the first attempts, targeting TNF-alpha as one of the key cytokines in the inflamed synovium, leading to one of the significant improvements in the treatment of inflammatory arthritis. TNF-blocking medications have been used to treat over one million patients since then. Infliximab (Remicade) was the first TNF-blocking agent to hit the market, followed by Etanercept (Enbrel) and Adalimumab (Humira).[24]

Also these biologics drugs are used after phototherapy, and conventional systemic treatments failed.[10]

Infliximab is a monoclonal antibody (mAb) that binds to the Fc region of IgG1 and includes the variable region (Fab) of a mouse anti-TNF antibody.Infliximab blocks the binding of TNF to related receptors and elicits an antibody and complement-dependent response against TNF-expressing cells.Etanercept (Enbrel) is another anti TNFmAb with a TNF receptor attached to the Fc part of human IgG1, giving it a longer half-life.[25]

Adalimumab (Humira) is amAb that binds toTNF-α, it is approved for psoriasis and psoriasis arthritis and other diseases such as ankylosing spondylitis, Crohn's disease, and ulcerative colitis.[26]

Chemotherapy

Methotrexate is a type of conventional synthetic DMARDs (csDMARDs),[27] it was the first drug used by Hoffmeister to treat patients with RA in early 1980,[28] is globally regarded as the first medical treatment option for RA,[29] and specified for use in the treatment of moderate to severe psoriasis who are unresponsive to topical and photo-therapy.[30] This medicine may alter the activity of many immune response

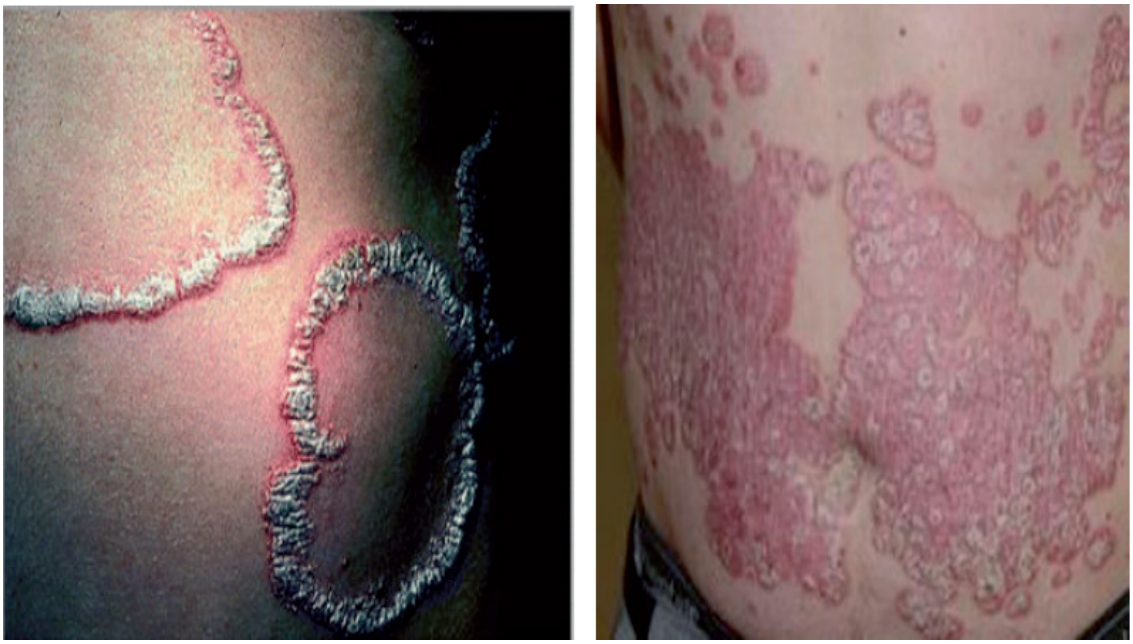

Figure 2: Plaque-like psoriasis[4]

by reducing proliferation and immunoglobulin production of peripheral lymphocytes by lowering polyamine synthesis. By inhibiting AICAR, MTX raises adenosine levels, causing anti-inflammatory effects:

- Preventing leukocyte accumulation and neutrophil-mediated endothelium damage in inflammatory sites.
- Proliferation inhibition and apoptosis induction in peripheral blood lymphocytes.
- Natural killer and monocyte/macrophage inhibition.

MTX may decrease inflammatory cytokines such as TNF- and IL-17 in the rheumatoid synovium.[31]Also, there are other treatments for psoriasis, topical therapy, and phototherapy

- **Topical therapy** is the first form of treatment for psoriasis; it is used to treat mild and localized psoriasis,in which this treatment can lower the number and thickness of plaque lesions, as well as the proportion of body surface affected.[4]
- **Phototherapy** is still an essential treatment option for psoriasis and other dermatologic illnesses,[32] because a vast variety of chromophores in the skin's various layers interact with and absorb UV. The most beneficial effects of UV rays from sunshine drive epidermal cells to make vitamin D, while the bad effects cause other skin illnesses.[33]

CONCLUSION

Psoriasis is a form of autoimmune skin disease that affects 2–3% of the population and is a prevalent chronic inflammatory skin condition. Mediated by the cells like macrophages, dendritic cells, Neutrophils that produced chemokines and cytokines. And adaptive immune systems T-helper cells such as (Th1, Th22, and Th17) and T cytotoxic. Many therapies are used for psoriasis treatment, such as biological therapy, chemotherapy, topical therapy, and phototherapy.

REFERENCES

1. Christophers E. Psoriasis−epidemiology and clinical spectrum. Clinical and Experimental Dermatology. 2001;26(4):314-320.
2. Griffiths CEM, Barker JNWN. Pathogenesis and clinical features of psoriasis. The Lancet. 2007;370(9583):263-271.
3. Villanova F, Flutter B, Tosi I, Grys K, Sreeneebus H, Perera GK, Chapman A, Smith CH, Di Meglio P, Nestle FO. Characterization of innate lymphoid cells in human skin and blood demonstrates increase of NKp44+ ILC3 in psoriasis. Journal of Investigative Dermatology. 2014 Apr 1;134(4):984-991.
4. Zangeneh FZ, Shooshtary FS. Psoriasis—types, causes and medication. InPsoriasis-Types, Causes and Medication 2013 Apr 17. IntechOpen.
5. Murad AA, Hussien WM. Incidance of Psoriasis in Patients with Different Skin Diseases in Baquba City. Diyala Journal of Medicine. 2017;12(1):25-28.
6. Razzaq MSA, Al-Saadi MAK, Ahmed MM, Naji AT. Assessment of genetic variations associated with susceptibility to psoriasis among Iraqi population. Karbala Journal of Medicine. 2015; 8(1):2049-2055.
7. Abdul-Hussein AA, Hussain FE. Childhood psoriasis a clinical and epidemiological study in Samawa city. Muthanna Medical Journal. 2019;6(2):29-34.
8. Hassoon HJ, Risan FA, Abdul-Muhaimen N. Estimation The concentration of IL-23, and IL-17A in the sera of patients with psoriasis in Baghdad city. Iraqi Journal of Biotechnology. 2014; 13(2): 75–85.
9. WHO. Global report on psoriasis. 2016.
10. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015;386(9997):983-994.
11. Chandra A, Ray A, Senapati S, Chatterjee R. Genetic and epigenetic basis of psoriasis pathogenesis. Molecular Immunology. 2015;64(2):313-323.
12. Nevitt GJ, Hutchinson PE. Psoriasis in The community: prevalence severity and patients' beliefs and attitudes towards the disease. British Journal of Dermatology. 1996;135(4):533-537.
13. Basavaraj KH, Navya MA, & Rashmi R. Stress and quality of life in psoriasis: an update. International Journal of Dermatology. 2011;50(7):783-792.
14. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk factors for the development of psoriasis. International Journal of Molecular Sciences. 2019;2020(18):4347.
15. Zeng J, Luo S, Huang Y, Lu Q. Critical role of environmental factors in The pathogenesis of psoriasis. The Journal of Dermatology. 2017;44(8):863-872.
16. Kim J, Krueger JG. The immunopathogenesis of psoriasis. Dermatologic Clinics. 2015;33(1):13-23
17. Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of psoriasis. Annual Review of Immunology. 2014;32:227-255.
18. El-Darouti M, Hay RB. Psoriasis: highlights on pathogenesis, adjuvant therapy and treatment of resistant and problematic cases (part I). J. Egypt. Women. Dermatol. Soc. 2010;7:64-67.
19. Goodman WA, Cooper KD, McCormick TS. Regulation generation: The suppressive functions of human regulatory T cells. Critical ReviewsTM in Immunology. 2012;32(1):65-79.
20. Nestle FO, Kaplan DH, Barker J. Psoriasis. The New England Journal of Medicine. 2009;361(5):496-509.
21. Raychaudhuri SK, Maverakis E, Raychaudhuri SP. Diagnosis and classification of psoriasis. Autoimmunity Reviews. 2014; 13(4-5):490-495.
22. Langley RGB, Krueger GG, GriffiThs CEM. Psoriasis: epidemiology, clinical features, and quality of life. Annals of The Rheumatic Diseases. 2005;64(2): ii18–ii23.
23. Lønnberg AS, Skov L. Co-morbidity in psoriasis: mechanisms and implications for treatment. Expert Review of Clinical Immunology. 2017;13(1):27-34.

Caporali R, Pallavicini FB, Filippini M, Gorla R, Marchesoni, A, Favalli EG, Sarzi-Puttini P, Atzeni F, & Montecucco C. Treatment of rheumatoid arthritis with anti-TNF-alpha agents: a reappraisal. Autoimmunity Reviews. 2009;8(3):274-280.

24. Abbasi M, Mousavi MJ, Jamalzehi S, Alimohammadi R, Bezvan MH, Mohammadi H, Aslani S. Strategies toward rheumatoid arthritis therapy; The old and the new.Journal of Cellular Physiology. 2019;234(7):10018-10031.
25. Azevedo VF, Della CL. Adalimumab: A review of the reference product and biosimilars. Biosimilars. 2016;6:44-29.

Smolen JS, van der Heijde D, Machold KP, Aletaha D, Landewé R. Proposal for a new nomenclature of disease-modifying antirheumatic drugs. Annals of The Rheumatic Diseases. 2014; 73(1):3-5.

26. Doan T, Massarotti E. Rheumatoid arthritis: an overview of new and emerging therapies. The Journal of Clinical Pharmacology. 2005;45(7): 751–762.

27. Kaltsonoudis E, Papagoras C, Drosos AA. Current and future role of methotrexate in the therapeutic armamentarium for rheumatoid arthritis. International Journal of Clinical Rheumatology. 2012; 7(2):179.
28. Peters BP, Weissman FG, Gill MA. PaThophysiology and treatment of psoriasis. American Journal of Health-System Pharmacy. 2000;57(7):645-659.
29. Cipriani P, Ruscitti P, Carubbi F, Liakouli V, Giacomelli R. MeThotrexate: an old new drug in autoimmune disease. Expert Review of Clinical Immunology. 2014;10(11):1519-1530.
30. Walker D, Jacobe H. Phototherapy in the age of biologics. 2011;30(4): 190-198.
31. Juzeniene A, Moan J. Beneficial effects of UV radiation other than via vitamin D production. Dermato-Endocrinology. 2012;4(2):109-117.