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PSORIASIS - A Mini Review

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Abstract

Psoriasis is a chronic inflammatory squamous cell disease of papules that is characterized by multiple remissions and relapses. This has long been considered a serious violation of keratinization. The successful use of traditional immune suppressants and new immune modulators in the treatment of psoriasis has led to the belief that psoriasis is, in fact, a disorder of Th1 cell immunodeficiency. Recent developments have led to several new discoveries such as the role of Th17 cells and evidence of skin barrier dysfunction in psoriasis similar to atopic dermatitis. Psoriasis is an atypical, systemic autoimmune disease of unknown cause, mainly affecting the skin, spreading further to the nails and joints and causing arthritis. The treatment protocol should be based on the patient's condition. People with mild psoriasis can be treated primarily with topical medications, while people with moderate to severe psoriasis can be treated with systemic medications.

Keywords: Chronic skin disease, Inflammation, Psoriasis

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Introduction

The term psoriasis comes from the Greek word "Psora" means itching and "lazis" means action condition.[1] Psoriasis is a chronic immune mediated inflammation disease associated with dysregulation of innate and adaptive immune response and includes the both genetic and environmental factor.[2] Psoriasis affects nearly 2–3% of general population.[3] It is a inflammatory disorder that effects the skin, nails, and joint.[4] Psoriasis is an inflammatory skin disease in which skin cell multiply very quickly. As a result, cell accumulation on the surface of the skin and thick plaques of erythematic are formed covered with silvery white scaly scalex.[5] It is characterized by certain erythematous plaques with loosely attached silvery white scale that often affect the elbows, knees, and scalp.[6-8]

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Further Explanation

Clinical Presentation of Psoriasis

1. Psoriasis vulgaris
2. Guttate Psoriasis
3. Generalized pustular psoriasis
4. Localized pustular psoriasis
5. Erythrodermic psoriasis
6. Psoriatic nail disease.

Psoriasis vulgaris

It is the most common form of the psoriasis and accounts for 70–80% of psoriasis patient also known as chronic plaque psoriasis. A clear round oval presented to the patient or hummular plaque (about the size of a coin) with loosely attached silver white scales, that is bordly affected elbows, knees, lumposacral area, inter gluteus cleft, and scope[10] Woronoff" s ring, a pale white ring, can be seen on the skin around of psoriatic plaques[11] gradual peripheral stretching of plaques leads to differences.

Configuration includes

a. Psoriasis loop: - Predominantly cured linear pattern
b. Annular psoriasis: - Annular lesions develop secondary to central clearance
c. Follicular psoriasis: - The presence of small scaly papules in the pyloric opening bag.

Guttate psoriasis

Guttate Psoriasis comes from the Greek word "gutta," which means droplet guttate psoriasis accounts for the 2% of all psoriasis.[12] This variety is characterized by the acute onset round erythematous exanthema (2–10 mm diameter) over the trunk and legs at a centripetal force. The number of lesion can vary from 5 to more than 100. Although the disease is self-limiting but a certain percentage of people recover on their own develop into chronic plaque psoriasis. It is often reported that about 10% of patient experience it chronic plaque psoriasis has a good attack of guttate lesions during their disease.[13] Guttate psoriasis often affects children's or adult with a family history of Psoriasis.[14] There is an estimated 40% increase risk of developing chronic Psoriasis after an attack, guttate variety.[15]

Generalized pustular psoriasis

Generalized pustular Psoriasis is rare and is an active unstable disease. The study reported that nearly 20% of patient at any point during the disease had pustular lesions covering the lesion with chronic plaque Psoriasis.[16] However only 2–5% Psoriasis patient has one predominant type of pustule with only the pustules predominating clinical features.[17] Acute generalized pustular Psoriasis usually developed after irritation topically treatment of

plaques Psoriasis or due to sudden withdrawal of corticosteroids.[18] Early acute generalized pustular Psoriasis is characterized by the systemic red and tender skin symptoms include fever, anorexia, and nausea. Countless pustules appeared within hours with erythematous background. Then the pustules join and form a pool of pus severe systemic symptoms. Hence, the pustule dry out and forms a glossy erythematous surface on which a new culture of pustules can appear. Can be geographic language polyarthritis and cholestasis associated with generalized pustular Psoriasis.[19]

Localized pustular psoriasis

There are two clinically different type of local pustular Psoriasis.

a. Acrodermatits continua of hollopeau.
b. Palmoplantar pustulosis.
    a. Acrodermatits continua rare rash of pustules on the fingers and toes following local trauma, beginning of the tip of one finger.[20] Then, the buds can coalesce and spread side by side, covering the back of arms, hands, and feet finally patients may develop osteolysis of the peripheral phalanges and associated nail dystrophy as well as anonymity of the affected image. Sometime pustules become common.
    b. Palmoplantar pustulosis is characteristic feature of this variety is a group of sterile yellow pustules with hyperkeratosis and erythema and scale affecting the central side of the palms or feet. The pustules are soft, dark brown in color with sticky scales or crusts are often associated with psoriatic nail lesions.[21]

Erytherodermic psoriasis

Psoriatic Erythropoietin is characterized by a high degree of skin damage in active psoriasis and manifests itself in one of two forms. It can form chronic plaques psoriasis gradually develops into large superficial area of the body.

The second more serious form of erythropoiesis caused by triggers such as infection and far drug withdrawal. This unstable form of psoriasis is characterized by severe erythema and loss of clinical signs of psoriasis.[22] Erythroderma affects the skin ability to regulate body temperature and caused hypothermia, high-perform means heart failure, and metabolic changes that require immediate patient care.

Psoriatic nail disease

In psoriasis finger nails are affected more often than toe nails. A "cut in the nails" or a mall depression in the nail plate is the most common finding as a result of the formulation of false nail in the proximal part of the nail substrate. In addition, the nail may separate from the nail-bed which is called nail lysis and "oil" spots, that is, orange-yellow area is visible under the nail plate In addition, the nail plate can thicken degenerate, change color and turn yellow. Keratinous substances can form under the nails. Minor nail changes are seen in most people with psoriasis and large nail abnormalities are usually associated with psoriasis arthritis and scalp lesions.[23]

Diagnosis

The diagnosis of psoriasis is primarily clinical. There are different clinical types of psoriasis the most common of which is chronic plaque psoriasis, affecting 80–90% of patients with psoriasis. The hallmark of classic plaque psoriasis is well-demarcated, symmetric, and erythematous plaques with overlying silvery scale. Plaques are typically located on the scalp, trunk, buttocks, and extremities but can occur anywhere on the body. Patients might demonstrate nail involvement, which can present without concomitant plaques. Active lesions might be itchy or painful.[10] Evaluation and differential diagnosis less common variants of psoriasis include inverse psoriasis, pustular psoriasis, guttate psoriasis, erythrodermic psoriasis, and annular psoriasis. Often a dermatologist can only diagnose psoriasis with a skin test. However, a skin biopsy may be performed if more information is needed to confirm the diagnosis and rule out other causes of symptoms, such as eczema or cutaneous lupus.

Physical Exam

It is usually easy for your doctor to diagnose psoriasis, especially if you have plaques on areas such as you're:

- Scalp
- Ears
- Elbows
- Knees
- Belly button
- Nails.

Your doctor will give you a full physical exam and ask if people in your family have psoriasis.

Lab Tests

The doctor might do a biopsy remove a small piece of skin and test it to make sure you don't have a skin infection. There's no other test to confirm or rule out psoriasis.

Treatment

Many treatment methods are available for psoriasis, including topical therapy, physical therapy, and systemic therapy. Clinical physicians should weigh the reasonably choose a treatment regimen based on the individual condition, disease subtype, severity, and treatment requirements. If patients with moderate to severe psoriasis experience a poor effect of one treatment method, then combined, rotational, or sequential treatments should be performed.[10]

Principles of Treatment

1. The treatment should be standardized, and use of therapeutic drugs/methods recommended by the guidelines should be emphasized
2. The treatment should be safe, and adverse reactions should be avoided as much as possible
3. The treatment should be personalized. The patient's disease condition, willingness, tolerance, economic situation, treatment history, and adverse drug reactions should be comprehensively considered to develop a reasonable treatment regimen.

Treatment of Different Types of Psoriasis

Guttate Psoriasis

Guttate psoriasis is mainly treated with topical medications or phototherapy. Vitamin D3 derivatives (such as tacalcitol) are

suitable for the treatment of acute psoriasis. It can be used alone or in combination with mild to moderate glucocorticoids. It can also be combined with ultraviolet B (UVB). Mild to moderate glucocorticoids (e.g. hydrocortisone/mometasone furoate/fluticasone propionate ointment) can be combined with tacalcitol or UVB. The preferred phototherapy is NB-UVB. This treatment is even more effective when used in combination with moisturizers, glucocorticoids, or Vitamin D3 derivatives. Some people with previous psoriasis develop streptococcal sore throat. Tonsillectomy can improve the condition, prolong the time of remission, and make the treatment more effective. Systemic therapy includes antibiotics and bone marrow transplant. Retinoids and immunosuppressants are effective but should be used with caution.

Plaque Psoriasis

People with mild plaque psoriasis most often use topical therapy, and in most cases it can be effectively treated. Topical formulations include Vitamin D3 derivatives, retinoids, medium/high potency glucocorticoids, and calcineurin inhibitors. Topical phototherapy can also be used. An alternative use or a combination of two or more drugs may be chosen if the monotherapy causes obvious side effects or mild effects. Commonly used combination therapies include calcineurin inhibitors, Vitamin D3 derivatives, glucocorticoid derivatives, Vitamin D3, and glucocorticoid retinoids. People with moderate to severe plaque psoriasis require systemic therapy or phototherapy. Medications include retinoids, immunosuppressants (such as methotrexate [MTX], cyclosporine A [CsA], or tryptolides), and biologics.

Erythrodermic Psoriasis

People with erythrocytic psoriasis require systemic therapy. Medications include retinoids, methotrexate, CsA, and biologics. Acitretin and methotrexate have shown good long-term effects in the treatment of erythroderma psoriasis. However, the beginning is slow. A gradual dose reduction can effectively prevent relapse. CsA or biologics are recommended for patients with severe or unstable disease. Topical or systemic glucocorticosteroids are generally not recommended unless the patient has severe, life-threatening toxic symptoms. If the patient is seriously ill or has a medical emergency, systemic steroid therapy should be used to control acute inflammation. If the disease is under control, the dose can be gradually reduced until the drug is discontinued. If the patient has fever, hypoproteinemia, fluid and electrolyte imbalances, secondary infection, or liver dysfunction, the systemic condition should be monitored while nutritional support is provided.

Pustular Psoriasis

Retinoids, MTX, CsA, and biological agents can be chosen for patients with generalized pustular psoriasis. Acitretin is the standard therapeutic drug; after the acute disease process has been controlled, the dose is gradually reduced for maintenance. In severe cases, biological agents or CsA can be applied for initial treatment. After the disease is controlled, retinoids or MTX can be used for maintenance.

Glucocorticoids can rapidly control pustule dissemination and relieve systemic symptoms; however, they should be used carefully. Glucocorticoids are recommended only when the disease is severe or life-threatening, the efficacy of other measures is poor, or other treatments are contraindicated. These treatments should be combined with acitretin or immunosuppressive agents; after satisfactory efficacy is obtained, the dose should be gradually reduced until drug withdrawal.

Topical medication is primarily applied for protection. When pustules are not broken, calamine lotion can be used to relieve swelling; after the pustules are broken, the skin is primarily treated with cleaning.

In addition to local therapy, systemic therapy can also be used to treat patients with localized pustular psoriasis.

Arthropathic Psoriasis

The goals of arthropathic psoriasis treatment are to control inflammation and prevent injury and damage to the joints. The nature and severity of joint damage should be fully evaluated. Patients should get adequate rest and avoid overwork to avoid sprains. Patients should also be advised to perform moderate functional joint exercises. Systemic therapies include non-steroidal anti-inflammatory drugs, methotrexate, and biologics. Triptolide and total peony glucoside supplements can reduce joint discomfort.

Future Prospects

Home Based Photo Therapy

Future prospect of psoriasis, home-based phototherapy is as effective and safe as phototherapy in an outpatient setting. Patients were more satisfied with home-based phototherapy. Factors that negatively influence the prescription of or choice for home-based phototherapy can be summarized in terms of lack of control, lack of knowledge, and lack of a good reimbursement system.

Phototherapy is a widely used and effective treatment for moderate to severe psoriasis. Numerous studies have demonstrated the therapeutic efficacy of various phototherapy treatments for psoriasis. (Treatment according to Göckermann) It is used on an outpatient basis. Patients can stay at home during treatment and do most of their daily activities. Patients come to the hospital for treatment 2–3 times a week. A big step forward is the fixed environment, but it has other disadvantages as well. Patients must go to the hospital 2–3 times a week, especially during working hours, which is expensive and difficult to implement in everyday life.

In 1979, Larkö and Swanbeck reported the first home use of BB-UVB phototherapy.[24] Home care has the benefits of less travel discomfort for patients and more control over their schedule. Instead of going to the hospital 2 or 3 times a week, you can be treated at home. This is a big step forward for people with psoriasis in a society where individualization and planning and patient autonomy are increasingly important. There have been several studies on low-dose UV treatments, especially NB-UVB treatments.[25] However, this treatment is not the best choice for healthcare professionals. Outpatient UV treatment appears to be the standard of care.

Effectiveness of home based phototherapy

As early as 1985, Able had difficulty obtaining comparative data due to different treatment regimens, radiation units, and different

treatment response criteria. There is also a problem with this operation. The first phototherapy for psoriasis was performed in 1979 by Larkio and Swanbeck at the patient's home and at the BB-UVB home for psoriasis patients. When the skin lesions disappeared, the patient received maintenance therapy on the same apparatus twice a week. Of the 28 patients in the study cohort, 20 achieved complete disappearance, but 25 showed moderate phototoxicity. Patients underwent biopsies before and after irradiation, and there were no changes in the epidermis or increased photoelasticity.[26]

Jordan *et al*. investigated a modified treatment for Heckermann with a BB-UVB home light source. All 55 psoriasis patients who completed the treatment program were completely excluded after 42–60 UV-B treatments. No serious side effects or phototoxicity were reported.[27]

Paul *et al*. investigated the use of low-intensity phototherapy machines at home. The device emits 300–320 nm, including some UVA. In the home phototherapy group, only 8 of 20 patients who had psoriatic lesions completely eradicated psoriatic lesions compared with 18 of 20 who used standard outpatient UV-B phototherapy. However, the home care group used a different protocol compared to the standard UV-B treatment group. This resulted in lower doses for the previous treatment group.[28]

Feldman *et al*. investigated the use of BB phototherapy equipment at home. A study of 31 psoriasis patients found that 22 patients who responded to treatment in the past 2 years received approximately 6.2 min of treatment per week. This was due to the guidelines existing at the time. The average frequency of follow-up visits was 4.5 months. In general, respondents reported that U-VB phototherapy at home helps with psoriasis.[29]

Cameron *et al*. studied the clearance rate in patients with psoriasis and other photoreactive diseases when treated with NB-UVB at home. 18 out of 30 psoriasis patients achieved clearance or minimal residual activity (MRA) with home phototherapy after an average of 22.5 treatments. The rate of self-reported erythema was higher in the home phototherapy group than the rate of erythema found in the outpatient setting.[30]

Haykal and DesGroseilliers do the survey below25 patients with psoriasis. Twenty of them got homework based phototherapy. They came to the conclusion that all patients receiving phototherapy at home happy with them. Treatment is planned to continue and will recommend another patient.[31]

In 2009 Koek *et al*. carried out in a randomized controlled Home study of NB-UVB phototherapy compared with outpatient setting. They examine effectiveness, quality of life, Treatment severity and patient satisfaction. Results the efficiency measures are the proportion of Patients who achieve at least 50%, 75%, or 90% reduction of SA output (self-applied) -PASI/PASI results are called Results of PASI/SA-PASI 50/75/90. No statistics significant difference in these results between the two groups, but only a small difference in the results of SA-PASI 50/75/90 support phototherapy at home and small differences in PASI 50/75/90 supports phototherapy in outpatients frame. Quality of life improved equally in both groups. That However, the severity of treatment was significantly lower in origin group; these patients rate their satisfaction more often than "very satisfied." Most of the participants in both the group said they preferred phototherapy at home. KK continues to increase wherever phototherapy is given, but patients who are treated at home rate their therapy as significantly more common than outpatients (42% vs. 23%). In on the other hand, patients treated with phototherapy at home assess waiting time as an outpatient more often (26% vs. 21%).[32]

Cameron *et al*. conducted a study and a cohort study for the period 1998–2011. Clearance values or MRA were studied in patients treated with NB-UVB home phototherapy. The results of outpatient U-VB phototherapy in 2011 were used as a comparison. Two hundred of 249 examined courses of therapy associated with patients with psoriasis. Nearly 75% of these patients achieved complete clearance or MRA with an average of 31 treatments compared with 68% achieving MRA at a median of 29 exposures in the outpatient U-VB phototherapy group.

In general, patients reported that they were very satisfied with home phototherapy. The results in terms of effectiveness in improving disease severity and quality of life were variable but generally positive.[33]

Pharmacogenetics and Pharmacogenomics in Psoriasis Treatment

Pharmacogenetics

Pharmacogenetics is the study of how people respond differently to drug therapy based upon their genetic makeup or genes. The most commonly used pharmacogenetic approach to assess variability in the efficacy and toxicity of psoriasis and PsA treatment is to assess single nucleotide polymorphisms (SNPs) present in genes encoding drug-metabolizing enzymes, drug transporters, and receptors. Genetic variant associated with response to disease-specific active substance, followed by genetic variants associated with responses to traditional systemic agents and responses to biologic agents used to treat psoriasis and PsA.

Disease-specific agents

Calcipotriol

Calcipotriol is a topical steroid analogue of Vitamin D used to treat plaque psoriasis. There are several polymorphic sites in the Vitamin D receptor (VDR) gene, in particular, one site, Taq1, is associated with response variability. The presence of one or two Taq1 alleles was more common in patients who did not fail with calcipotriol treatment compared with the control group (p. 0.01 and p. 0.025, respectively).[34] In contrast, Halsall *et al*. we have demonstrated that the VDR polymorphisms A-1012G, Fok1, and Taq1 are associated with responses to calcipotriol. Due to the lack of pharmacogenetic studies on calcipotriol, further research is needed.[35]

U-VB phototherapy

UV light is a well-established and widely used treatment for psoriasis.[36] UV light can be thought of as UVB radiation (290–320 nm), a narrow band of U-VB. Applied (311 nm) or photochemotherapy (320–400 nm). While different psoriasis responses to ultraviolet light treatments genetic factors have not been systematically investigated, several studies have been conducted. Two genes encoding antioxidant enzymes (namely, GSTM1 and GSTT1) and one gene involved in melanin production (namely MC1R) were tested for Response to U-VB phototherapy in psoriasis patients. Deletions in the highly polymorphic GSTM1 and GSTT1 lead to loss of functional enzymes, which are found in approximately 50% and 20% of whites, respectively. MC1R is also highly polymorphic and has been associated with increased skin cancer and changing the ultraviolet-R sensitivity.[37]

NSAID-PSA

NSAIDs are the first line of treatment for patients with PsA. However, there are individual differences in treatment efficacy and side effects such as gastrointestinal bleeding. Nonsteroidal anti-inflammatory drugs are mainly metabolized by the cytochrome P450 enzyme (CYP), but it is still difficult to establish the prognostic profile of the NSAID genotype.[38] Likewise, CYP2C9 * 2 and CYP2C9 * 3 correlated with reduced metabolic clearance of NSAIDs compared to subjects with the CYP2C9 * 1 (wild-type) allele.[39]

Traditional systematic agents

Methotrexate

Methotrexate is the main systemic drug used to treat moderate to severe psoriasis and PsA. This is because it is effective in controlling the symptoms of skin and joint diseases. In addition, current clinical efficacy is unpredictable and it is impossible to predict which patients will experience side effects. Genetic polymorphisms associated with the response to methotrexate fall into two categories: Those that affect cell membrane transport (e.g. ABCC1, ABCG2, and SLC19A1) and those that affect the metabolic/signaling pathway enzymes of methotrexate (e.g. ADORA2A). Three strains ABCC1, rs35592 (P = 0.008), rs2238476 (P = 0.02) and rs28364006 (P = 0.02) and two ABCG2 variants, rs13120400 (P = 0.03) and RS17731538 (P = 0.007) were found. This was associated with improved response in psoriasis patients treated with methotrexate. Six ABCC1 variants (i.e. rs2238476, rs3784864, rs246240, rs3784862, rs1967120, and rs11075291) were associated with side effects. As in the case of psoriasis, polymorphisms associated with the response of methotrexate to PsA are subdivided into polymorphisms that affect the transport of methotrexate across cell membranes and polymorphisms that affect enzymes in the methotrexate pathway. We investigated the relationship between the polymorphism of the folate pathway gene and the efficacy, toxicity and survival of methotrexate. The rs1232027 allele in DHFR was associated with a statistically significant increase in response to methotrexate. There is also evidence that the TT genotype (rs1801133) MTHFR, which encodes an amino acid substitution (Ala140Val), is associated with an increased risk of hepatotoxicity (p-04). Although many pharmacogenetic studies have been performed with methotrexate, the genetic variables identified so far are not applicable in the clinical setting.[40]

Cyclosporine

Absorption of CSA, which predominantly takes place in the intestines, is often low and highly variable between patients.[41] This interindividual variability can be explained in part by the expression and function of the metabolizing CYP-3A isozymes in the liver (i.e. CYP3A4 and CYP3A5) and the multidrug efflux transporter P-glycoprotein (MDR1-ABCB1). Although the CYP3 enzyme can influence the oral bioavailability and systemic excretion of CSA, no psoriasis-specific studies have successfully investigated the impact of CYP3A variants. In a study where 84 psoriasis patients were monitored over a 3-month period during CSA treatment, the 3435T genotype in ABCB1 (rs1045642) occurred more frequently in nonresponders compared with responders (P = 0.0075). Given the paucity of pharmacogenetic studies of CSA, additional studies are warranted.[42]

Sulfasalazine

Sulfasalazine is effective on Improvement of peripheral synovitis symptoms on PsA even if the effect is small. It consists of 5 aminosalicylic acid and sulfapyridine to metabolism in large intestine. There is a positive correlation between sulfapyridine serum concentration and effectiveness and toxicity Colon.[43] The acetate group is bound to sulfasalazine via fa via N-acetyltransferase 2 (NAT2) for the formation of N-acetylsulfasalazine, which subsequently undergo renal excretion. People who are fast acetylators tend to have lower acetylators Sulfasalazine plasma concentrations, causing this patient to less prone to side effects and possibly higher demands dosage to maintain effectiveness.[32] NAT2 has seven variants (e.g. RS1801279, RS1041983, RS1801280, RS1799929, RS1799930, rs1208, and rs1799931) which are believed acetylation rate. In addition, homozygosity or Pound heterozygosity in this variant affects whether individuals are fast, medium, or slow acetylators. In addition, homozygosity additional pharmacogenetic studies in PsA are needed to confirm that the NAT2 variant is indeed a contributing factor side effects in patients treated with sulfasalazine.[44]

Biological agents

Tumor necrosis factor(TNF)-α inhibitor

Clinically available TNΦα inhibitors in psoriasis includes etanercept (TNF. recombinant human receptor protein), infliximab (chimeric anti-TNF antibody) assessment of the mouse variable region and human immunoglobulin Region G1) and adalimumab (a fully human monoclonal anti-TNF) antibodies) which can be prescribed as monotherapy, or in combination with traditional system agents. For PPE, Tolizumab and golimumab have also been approved. TNFα TNFα is an important effector of the innate immune response. In important for psoriasis, TNFα induces inflammation production motor chemokines and pro-inflammatory leukocytes, including neutrophils, monocytes, and activated T cells.[45] In important for PsA, TNFα stimulates bone loss and decreases Bone formation through inhibition of osteoblast differentiation and Functions.Elevated levels of TNFα are correlated with dysfunction. Weight relief for skin and serum in patients with psoriasis and that TNFα levels were normalized with TNFα inhibitors treatment. Considering the various anti-TNFα agents used and their relationship smaller cohorts for each biology, most studies perform a "group" or "class" analysis (i.e. etanercept, inflix Imab, and Adalimumab) to increase statistical significance. These first class studies are reviewed and identified first genetic variants in TNFα and T-helper-17 (Th-17) cell signaling transmission The pathways are also important for disease pathogenesis. A study in 80 psoriasis patients treated with TNFα inhibitors analyzed five variants in TNFα (i.e. rs361525, rs1800629, and rs1800629) rs1799724), TNFRSF1A (i.e. rs4149584), and TNFRSF1B (i.e. Rs 4149584 and Rs 1061622).[11] There is a relationship between the two CC genotypes in TNFα (i.e. rs1799724; P = 0.027) and TT Genotypes in TNFRSF1B (i.e. rs1061622; P = 0.019) and improved response to etanercept treatment.[11] TNFAIP3 is encodes the protein gene that interacts with the interacting product TNIP1 to limit NF--mediated immune responses. Variants identified in TNFAIP3 (i.e. rs2230926 and rs610604) positively associated with response to TNFα inhibitors. Gallo *et al.* reported that TNFα-238GG, TNFα-857CT/The TT, and TNFα -1031TT genotypes have been associated with improved therapeutic response after 6 months. Together, this study strongly demonstrates the important role for genetics variants involved in TNFα signaling with TNFα response inhibitors.[46]

IL-12/IL-23 inhibitors

Its recommended genes involved in the IL-12/IL-23 signaling pathway play a role important role in chronic inflammation of the epithelium as well patient response to treatment.[47] Ustekinumab has demons high efficiency and acceptable maintenance safety profile plaque psoriasis by inhibiting IL-12/IL-23. Inflammation Way no statistical significance found between SNPs in IL-12B, IL-23R, and IL-6 and the response to Ustekinumab. Multiparametric logistic regression analysis found that HLA-Cw6 was a better positive predictor Ustekinumab response in the absence of IL12B AA Genotype (i.e. rs3212227), genotype IL-6 GG (i.e. rs3212227) rs1800795) or the presence of IL-12B GG (i.e. rs6887695) Genotype. The response to Ustekinumab was significant increased and occurred more rapidly in HLA-Cw6 positive patients. From week 12, PASI 75 response was found in 96.4% HLA-Cw6 positive people compared with 65.2% for HLA-Cw6-negtive persons ($P < 0.008$). A similar trend is observed, though measuring the response of patients who achieved PASI 90.[18] be accepted Perez *et al*. studying anti-IL-17 drugs to treat moderate to severe psoriasis. An association has been identified between IL-17F (i.e. rs763780) and does not fit Kinumab after 3 and 6 months relationship between IL-17. Gene and the IL-12/IL-23 pathway is established Observation that IL-23 can induce differentiation and activation specific populations of T cells, including Th-17 cells, in turn, produce cytokines such as IL-17 and IL-22, with IL-17 Stimulates an inflammatory response that causes Problems such as bone erosion in addition to clinical features such as inflammation of the synovium and skin, whereas IL-22 may cause osteoporosis in addition to other inflammatory activities Ferration as seen in PsA. In a study at the HLA-Cw6 locus in Chinese patients with psoriasis, differences in susceptibility to Reaction to Ustekinumab.[48] HLA-Cw6-position - Patients are more likely to reach PASI 75 after 4 weeks treatment (38%) versus those who were HLA-Cw6 negative (9%); ($P = 0.019$), with the same results after 28 weeks ($P = 0.035$).

Pharmacogenomics

Compared with pharmacogenetics, significantly less general genomic studies to study the effects of genetic variation Lectures on psoriasis or PsA treatment. This is mainly due to the high cost of genome research. In recent years, the costs associated with aiming for the next generation have gone up sequence, order of whole eczema and number of copies Analysis of variance continues to decline, so pharmaceutical macogenomic studies are feasible.

Traditional systematic agents

Methotrexate

Methotrexate is a synthesized analog folate, which selectively inhibits dihydrofolate reductase.[49] In analysis of microchip transcripts of patients with psoriasis, patients who responded to 16 weeks of methotrexate treatment had significant reduction in the regulation of helper T cells (i.e. Th-1, Th-17, and Th-22 mRNA expression was compared with non- Sponsors. Tests that look at monoperipheral blood Nuclear cells (PBMCs) from psoriasis patients found that miR- 223 and miR-143 are significantly associated with this disease Severity and in patients with psoriasis treated with methotrexate there is significant regulation of miR-223 and miR-143 in 3–5 weeks. There is only one study of the overall transcriptome response to methotrexate in PsA. Using a microchip approach, it was found that methotrexate responders had overexpression of 12 genes and reduced expression of 33 genes compared with untreated PsA controls. More genome-wide studies are clearly needed to identify additional genetic variants associated with methotrexate responses.[50]

Biological agents

TNFα inhibitor

Etanercept is a recombinant human TNF receptor fusion protein consisting of two identical chains of p75 extracellular ligand binding moiety. TNFα TNFα receptors bind to free and membrane-bound TNFα and thereby inhibit TNFα activity.[51] A number of studies have investigated gene expression in impaired skin and lesions in psoriasis patients treated with etanercept. Suarez-Farinas *et al*.[54] who examined 15 initial psoriasis patients on 12 weeks of etanercept therapy found that most of the biomarkers returned to near non-lesional values. However, approximately 248 genes did not show a >75% increase, including IL-12p35, MX1, IL-22, and IL-17. IFN-γ previous work by the same group demonstrated that the expression of IL-1β and IL-8 in psoriasis patients does not show a response rate to treatment and suppression of Th-17 is important for response to etanercept. Another study used a candidate gene approach to examine gene expression responses in psoriasis patients treated with etanercept. These studies demonstrated that mRNA expression levels in crowd-like receptors (TLRs) 2 and 9 ($P < 0.001$) and in key pathway genes (i.e. NOTCH1, NOTCH2, and JAGGED1) were significantly reduced compared with untreated psoriasis patients. A recent study found that survivin and caspase 3 gene expression was increased in both damaged and undamaged skin after etanercept. Treatment has shown that the mechanism of action of etanercept is related to increased apoptosis of psoriatic keratinocytes and their physiological inhibitory system. MiRNAs, miR106b, miR142-3p, miR-223, and miR-126 were found to be significant it was not significantly regulated in etanercept responders compared to non-responders. There are no studies on PsA; however, one study used an expression microchip with 12,000 genes and observed downregulation of 161 genes and upregulation of 27 genes in PsA patients treated with etanercept with untreated controls.[52]

IL-12/IL-23 inhibitors

Ustekinumab is human a monoclonal antibody that binds to the p40 subunits of IL-12 and IL-23, which prevents IL-12 and IL-23 from binding to cellular receptors, respectively, thereby inhibiting Th-1 and Th inflammatory activity and formation. Inhibited -17 Cells currently there are four studies that investigated gene expression profiles after Ustekinumab Treatment. Different types of psoriasis are depicted in the Figures 1-6. To date, however, no published studies have examined Ustekinumab in profiling PsA expression. Several pathophysiological psoriasis genes were significantly reduced in respondents after 2 weeks of Ustekinumab treatment. Then another study found that after 4 weeks of a single injection of Ustekinumab NGF was significantly reduced, whereas expression of GATA3 and IL-22RA1 increased, which supports a reduced response to epidermal activation. For non-respondents compared to respondents, expression of IL-20, IL-21, and p40 mRNA in lesions skin at study entry was significantly adjusted.[52] The key to genes on the NOTCH signaling pathway and reduced NOTCH1 and NOTCH2 mRNA expression in skin biopsies from psoriasis patients treated with Ustekinumab.Additional genomic studies are needed.[53]

IL-17 inhibitor

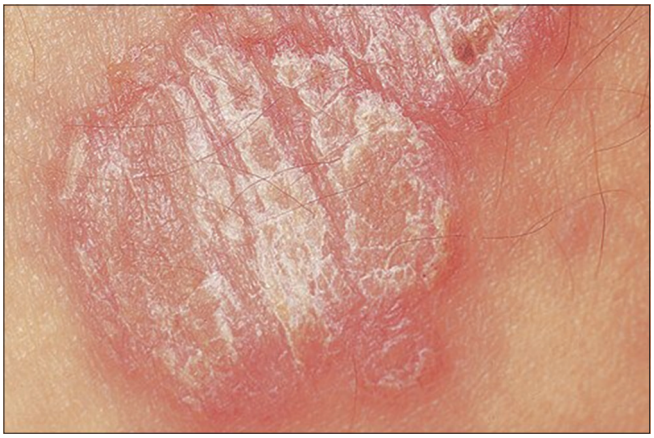

Figure 1: Psoriasis vulgaris

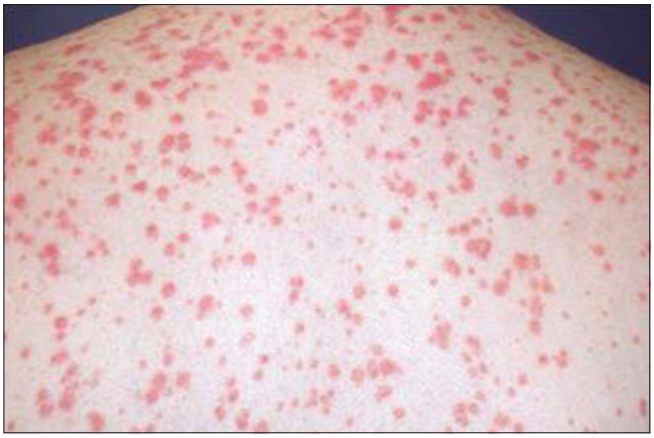

Figure 2: Guttate psoriasis

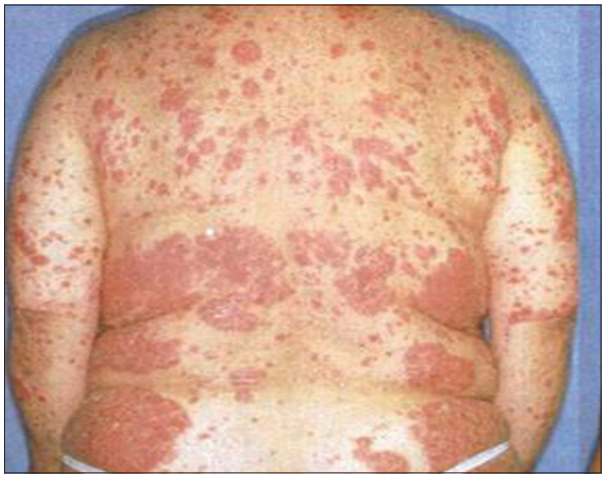

Figure 3: Generalized pustular psoriasis

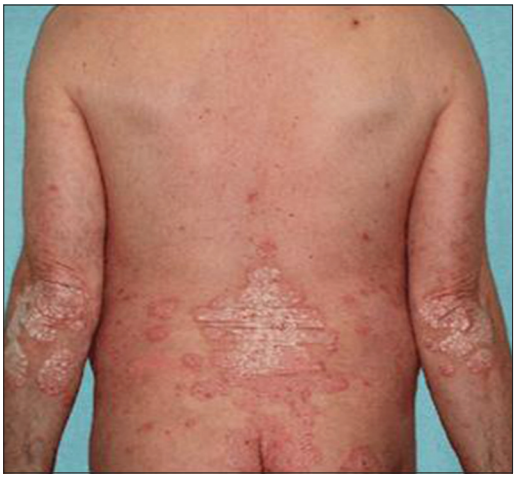

Figure 4: Localized pustular psoriasis

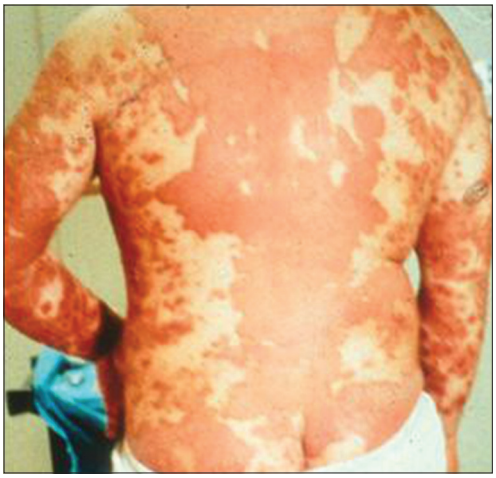

Figure 5: Erythrodermic psoriasis

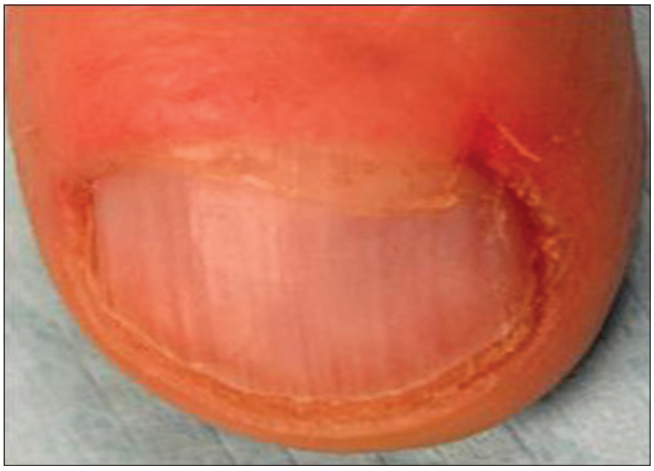

Figure 6: Psoriatic nail disease

Secukinumab is an anti-IL-17A monoclonal antibody that inhibits the effector function of IL-17A.and was recently approved for psoriasis worldwide. And is being examined for PsA treatment Patients with psoriasis treated with secukinumab show distinct effects on suppression of gene expression in chemokines and cytokines, which are associated with pathophysiology.[54] There was a significant reduction of Th-17-related genes (i.e. IL-17A, IL-17F, IL-21, Il-22, IL-8, and DEFB4), Th-1-related genes (i.e. IFN-γ and IL-12B), proliferation markers (e.g. Kertain 16), genes associated with innate immune pathways (e.g. TNFα and IL-6) and downstream CCL20 cytokines. Ixekizumab is a humanized

monoclonal antibody that inhibits IL-17A] and is in clinical trials for the treatment of skin psoriasis[54] Kruger *et al*. Examined skin biopsies of lesions from patients with phase1 psoriasis in the ixekizumab study. Past observed that RNA expression of IL-19, IL-8, CXCL1, CCL20, Granzym B and Lipocalin was suppressed by more than 6 times baseline values after 6 weeks of treatment. This oppression the response was greater than in patients treated with etanercept, suggesting that ixekizumab had a greater effect on the baseline psoriasis protocol. In addition, it was found that 1200 genes in psoriasis Skin baseline values - after 2 weeks of treatment with ixekizumab, 643 genes were normalized. Wang *et al.* the assay used to enrich the gene set combined with the expression of Microchip analysis in peripheral blood of psoriasis patients treated with ixekizumab.Most of the genes amplified in psoriasis reference transcripts were significantly suppressed by ixekizumab in the treated transcripts. Interestingly, there was significant suppression of genes associated with cardiovascular disease and atherosclerosis ($P < 0.005$) – the most suppressed gene was ALOX5AP ($P < 0.001$). Cardiovascular events are associated with psoriasis as a comorbidity. Overall, these results are promising as suppression of the IL-17 signaling pathway can be reduced this occurrence in patients with psoriasis; however, additional genomic studies are needed.[55]

Conclusion

Psoriasis is an atypical, systemic autoimmune disease of unknown cause, mainly affecting the skin, spreading further to the nails and joints and causing arthritis. Despite advances in treatment, a complete cure for this disease has not yet been determined. Thus, once a disease is identified, quality of life is certainly seriously impaired, and conscious efforts and protocols are required since disease management is an important tool for disease control. Psoriasis is an incurable disease and the goal of treatment is to control the progression of the disease and maintain its effectiveness over the long term. The treatment protocol should be based on the patient's condition. People with mild psoriasis can be treated primarily with topical medications, while people with moderate to severe psoriasis can be treated with systemic medications. The target biological agent can be appropriately selected in the case of psoriasis resistant to conventional systemic treatments. In the treatment for psoriasis, home-based phototherapy is as effective and safe as phototherapy in an outpatient setting. Patients were more satisfied with home-based phototherapy. Pharmacogenetic studies performed to date have been limited to genetic variants with biological treatment response using a candidate gene approach. These studies serve to highlight genetic variants located in pathways either directly or indirectly associated with the pharmacokinetics or pharmacodynamics of therapies for psoriasis and/or PsA. The most intriguing genetic variants have been identified in key signaling pathways associated with biologic agents, in particular, TNFα and IL-12/IL-23 inhibitors. The vast majority of the reported associations have rarely been replicated in larger cohorts, and combined with contradictory studies; strongly suggest the vulnerability of these genetic associations. With respect to pharmacogenomics, all of the available data on treatment in psoriasis and PsA are considered preliminary, with studies focusing strictly on mRNA and miRNA expression profiling. Similarly, pharmacogenomic studies have also identified some interesting genetic variants in pathways, contributing to disease pathogenesis and signaling of biologic agents. Although it is clearly evident that additional investigations are required to advance this field, with accelerated advancements in genetic and genomic technologies expected to continue in the future, an enhancement in study design correcting for key weaknesses of the previous investigations (as described in detail below), and emerging targeted anti-cytokine therapies that are expensive, a real potential exists for translating genetic and/or epigenetic markers from bench to beside.

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