Update research in psoriasis

Abstract: Psoriasis is now more recognized as a chronic-lymphocyte mediated inflammatory and proliferous skin disease.In European countries, the prevalence of psoriasis is 1%~3%, so the study of psoriasis is very important.With the study of immune pathogenesis and the progress of genetic engineering technology, it has been gradually developed a wide range of biological agents, And achieved good results in clinical trials or clinical treatment.This paper discusses the typical clinical manifestations, genetic research and treatment of psoriasis.

Introduction

Brief description of psoriasis

Psoriasis is a chronic inflammatory disease of the skin and joints that is strongly associated with the major histocompatibility complex (MHC) region.[1]Its typical bedside manifestation is squamous erythema or plaque, which is localized or widely distributed, without transmission, difficult to treat and often suffers lifelong.[2] Approximately 6 % – 42 % of psoriasis patients are also affected by chronic arthritis (psoriatic arthritis: PsA) in their lifetime.[3] Worldwide, the prevalence of psoriasis is about 2 %; however, prevalence varies by population.[4] For example, the prevalence of psoriasis in Europe is 1.3 %−11.4 %.[5] The majority of epidemiological differences for psoriasis apparently originate from the genetic background of those affected. Large-scale genome studies have been conducted, and the genetic basis of psoriasis in Europeans has been summarized in previous reviews.[6] Current treatment is not able to avoid recurrence, but aggressive treatment can significantly reduce skin lesions and improve or quality of life.In European countries, the prevalence of psoriasis is 1% ~ 3%, so the study of psoriasis is very important.

Types of psoriasis

Psoriasis Vulgaris.For the most common type, more acute onset. It is typically characterized by erythema of various shapes and sizes with a clear boundary, surrounded by inflammatory halo. Slightly infiltrated and thickened. The surface is covered with many layers of silvery scales. Scales are easy to scrape off. After scraping, the translucent film is bright red, and small bleeding points can be seen when the film is broken (Auspitz sign). Skin lesions are usually found on the head, sacral region and extensor sides of the extremities. Some patients feel different degrees of itching.

Pustular psoriasis.Less common, divided into general hairstyle and palm plantar type. The whole body can be affected. More periodic attacks, often in remission of psoriasis vulgaris lesions.Palmar plantar pustular disease skin lesion is limited at hand and foot, symmetrical occurrence, general condition is good, illness is stubborn, break out repeatedly.

Erythrodermic psoriasis.Also known as psoriatic exfoliative dermatitis, is a serious form of psoriasis. It is characterized by diffuse flushing, swelling and desquamation of the skin, accompanied by systemic symptoms such as fever, chills and discomfort, superficial lymph node

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enlargement and increased white blood cell count.

Arthropathic psoriasis.Also known as psoriatic arthritis. Rheumatoid arthritis-like joint damage occurs simultaneously in patients with psoriasis, which can affect the whole body and joints, but is most characteristic of terminal finger (toe) interarticular joint lesions. The affected joint is red, swollen and painful, and the skin around the joint is often red and swollen. Joint symptoms are often aggravated or relieved at the same time as skin symptoms. Blood rheumatoid factor negative.

Research progress of psoriasis genetics

Psoriasis is a multifactorial genetic disease for which the genetic factors explain about 70 % of disease susceptibility.[7] From linkage analysis, nine loci (PSORS1 to PSORS9) were associated with psoriasis. Of these loci, PSORS1 is known to be the major determinant of psoriasis susceptibility; it is in the MHC region, it explains about 35 %−50 % of the heritability of psoriasis.[8] and it is associated with early-onset psoriasis. With recent research, HLA-Cw6 has been identified as the susceptibility allele of PSORS1, and the general importance of identifying human leukocyte antigen (HLA) alleles associated with psoriasis has been recognized.[9].

Innovation in the treatment of psoriasis

At present, there are many methods to treat psoriasis in clinic, including various local drug therapy, systematic therapy, light therapy and traditional Chinese medicine treatment, etc. At present, new biological agents and the continuous research of photodynamic also bring a lot of good news to patients with psoriasis. There are 15 kinds of marketed chemical drugs for the treatment of psoriasis, mainly glucocorticoid receptor (GR), Vitamin D receptor (VDR) and Retinonic Acid receptors (Retinonic Acid receptors). RARs/Retinoid X re ceptors RXRs) drugs. Glucocorticoids are the main treatment for psoriasis. Topical preparations and phototherapy are predominantly useful in treating mild plaque psoriasis , Agents such as Vitamin-D (Vit-D) analogues,topical corticosteroids, dithranol, tacrolimus, tazaro tene, Babchi oil, and 8-methoxypsoralen come under this category. Most of these are marketed as lotions, ointments, and gels.The potential side effects of systemic exposure are mitigated significantly with these agents.[10]Moderate to severe forms of psoriasis can be treated with systemic therapies like biologics and small molecules.

Traditional systemic treatment of psoriasis

In fact, even with the rapid development of biologics today, traditional systemic therapy is still recommended by various guidelines as first-line treatment for psoriasis.

At present, traditional systemic anti-psoriasis drugs such as cyclosporine, methotrexate, avitamin and fumaric acid are suitable for different situations. Methotrexate is recommended for arthropathic psoriasis.Studies from a few groups have reported the suppressive effect of MTX on the levels of IL6 & IL22 in the serum of psoriasis patients.[11] However, the frequent presentation of bone marrow toxicity, liver toxicity, and susceptibility to secondary infections greatly discouraged the use of MTX.[12] Acitretin, a systemic retinoid, exhibits antipsoriatic effects through its action on the nuclear retinoid receptors.[13]Cyclosporine, an immunosuppressive agent, popularly used in organ transplant patients to prevent immune rejection, surfaced as a very effective treatment for plaque psoriasis. Nevertheless, the long-term use of cyclosporine is

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thwarted by severe side effects, including renal failure and alterations in blood pressure.[14]It is only suitable for short-term use. Fumaric acid is safe but should not be used in pregnant women. The use of cyclosporine, methotrexate, avitamin, fumaric acid requires clinicians to carefully evaluate and weigh the risks and benefits.

Nowadays, biologics are constantly being developed and have remarkable efficacy. However, traditional systematic treatment drugs still have their own unique advantages as they are affordable, only need to be administered orally and their safety is known.

TNF inhibitor studies

Tumour necrosis factor α (TNFα) is the major cytokine of the Th1 innate immunity pathway.[14] The efficacy of TNF α inhibitors is primarily due to their role in preventing the activation of dendritic cells, which produce IL23 and activation of Th17 lineage and its effector molecules (IL17 & IL22). These actions further prevent the interactions between T cells, dendritic cells, and keratinocytes.[15]

The FDA approved Infliximab, adalimumab, etanercept, and certolizumab to treat plaque psoriasis. Infliximab is a monoclonal antibody (chimeric) that directly neutralizes TNF-α [16].Certolizumab comprises a single Fab' unit of the human anti-TNF antibody, lacks the Fc' unit, and is conjugated with a polyethylene glycol (PEG) molecule. The frequent adverse events seen with TNF α inhibitors include infections of the upper respiratory tract, rhinitis, and pharyngitis.[17]

However, the original TNF inhibitors are still relatively expensive, and their bioanalogues give patients more options. Biosimilars are cheaper and have the same efficacy as the original drugs. In the use of TNF inhibitors, regular hospital monitoring is time-consuming and labor-intensive. For monitoring in the process of use, experts are also working on the development of home sampling, rapid detection methods, in order to bring good news for patients.

Targeting IL-17 and IL-23 in psoriasis

"Until a cure is found, the best treatment is to strike the right balance between improvement of skin lesions and side effects and inconvenience." IL-17, IL-23 and TNF are important factors in the pathogenesis of psoriasis, and various biological agents targeting IL-17, IL-23 and TNF have been developed.

In the treatment of psoriasis, patients often face more than one choice, clinicians need to choose drugs according to the efficacy and safety of drugs, the type and degree of activity of the disease, as well as the patient's age, gender and treatment expectations.

Advances in pathophysiology-based new therapeutic targets

Psoriasis is a skin disease characterized by excessive proliferation, inflammatory infiltration of lymphocytes and dendritic cells, and abnormal epithelial differentiation of psoriasis similar to wound healing -- sometimes referred to as "regenerative maturation." The pathophysiological mechanism of psoriasis is very complex, and different types of psoriasis are related to different cytokines.

Janus kinases, together with signal transducer & activator of transcription (JAK-STAT), are complex pathways involved in many disease pathologies,in psoriasis, many early-phase cytokines such as IL6, INF γ , IL12 & IL23 activate JAK-STAT communication for their immune responses. The most extensively studied JAK inhibitor, Tofacitinib, targets JAK 1,2 &3 proteins and was developed by Pfizer. To date, tofacitinib was approved only to treat psoriatic arthritis but not plaque

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psoriasis. Tofacitinib has shown safety concerns during its testing, including neoplasms, neutropenia, thrombosis, and severe cardiovascular complaints.[18] While inhibition of multiple proteins in the JAK-STAT pathway improves therapeutic potential, it raises safety issues that arise due to systemic inhibition, especially the development of neoplasms due to prolonged suppression of immune surveillance.

Research progress of small molecule drugs

With the deepening of the pathogenesis of psoriasis research, small molecule targeted drugs for the treatment of psoriasis are constantly developed, compared with biological agents, small molecule drugs have the advantages of safety, good efficacy, good stability, simple preparation and low cost. Benvitimod is an Aryl hydrocarbon receptor agonist with anti-inflammatory properties. In preclinical and Ex vivo studies, benvitimod has shown to prevent T-cell activation and inhibit key inflammatory markers like IL17A, IL17F, IL2 & IL23.[19]

Although the efficacy of small molecule drugs is not as fast as that of biological agents, small molecule drugs only need oral or external coating, without injection, easy to use and high safety. In view of the advantages of high efficiency, safety, low cost and stability of organic small molecule compounds, the establishment of efficient and specific screening model for organic small molecule compounds has become an important topic in the field of new drug development. Therefore, small molecule anti-psoriasis drugs are still the guidance of market demand.[20]

Conclusion

Psoriasis is a complex multifactorial disease, and despite various novel therapies that have become available in the past few years, psoriasis remains incurable.A couple of decades back, the treatment strategy focused more on managing the disease with general immune suppression.However, with the arrival of biologics with high specificity for immune components,it provides better ways for patients to improve their condition.A better treatment approach is to combine small molecule therapies with biologics to reap the beneficial outcomes of both classes of drugs than using either agent alone. It is believed that with the continuous progress of new drug development, it will provide more effective treatment for patients with psoriasis.

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