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Update Research in Psoriasis

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Abstract: ***Psoriasis is now considered a chronic inflammatory and proliferative skin disease mediated by lymphocytes. In European countries, the prevalence of psoriasis is 1%~3%, so the study of psoriasis is very important. Through research into immune pathogenesis and advances in genetic engineering techniques, it has progressively developed a wide range of biological agents with promising results in clinical trials or treatments. This paper discusses the typical clinical manifestations, genetic research and treatment of psoriasis.***

1. Introduction

1.1 Brief Description of Psoriasis

Psoriasis is a chronic inflammatory disease of the skin and joints, closely linked to areas of the major histocompatibility complex (MHC) [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]. Psoriasis can be divided into four types according to different clinical manifestations: vulgaris, pustular, articular and erythroderma, among which psoriasis vulgaris accounts for more than 90% of the total cases [3]. Although psoriasis is not a fatal disease, the condition is prolonged and recurrent, causing patients to experience severe suffering, and it has a significant impact on both the physical and psychological state of the patient. 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.

1.2 Types of Psoriasis

Psoriasis Vulgari (PV). 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 (PP). 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 (EP). Also known as psoriatic exfoliative dermatitis, it is considered a rare but severe form of psoriasis, which is usually caused by the deterioration of psoriasis due to clinical mismanagement [4]. Its main clinical manifestation is diffuse erythema involving almost all areas of the body surface (75-90%) [5]. There are also signs of swelling and flaking, enlarged superficial lymph nodes, and increased white blood cell counts.

Psoriatic Arthritis (PsA). Approximately 1/3 of patients with psoriasis progress to arthritic psoriasis, where they develop rheumatoid arthritis-like joint damage that can affect the entire body and joints, but is most characteristic of interphalangeal lesions. The presentation of PsA is heterogeneous and can affect both mesial and peripheral joints to varying degrees [6], with redness, swelling and pain in the affected joints. Joint symptoms often worsen or resolve in conjunction with cutaneous symptoms, and the blood is negative for rheumatoid factor.

1.3 Research Progress of Psoriasis Genetics

Psoriasis is a multifactorial hereditary disease, with genetic factors accounting for about 70% of the pathogenic factors [7]. Genetic studies of familial psoriasis by linkage analysis are known to have identified nine loci (PSORS1 to PSORS9) associated with psoriasis, and PSORS1, located in the MHC region, is a major determinant of psoriasis susceptibility, explaining approximately 35-50% of psoriasis heritability [8]. Research into the genetic factors of psoriasis is now key to updating psoriasis treatments. Since 2007, investigations using genome-wide association studies (GWASs) have identified more than 80 loci associated with psoriasis risk [9].

2. 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. Topical glucocorticoids are the mainstay of treatment for psoriasis. Topical agents and phototherapy are mainly used to treat mild plaque psoriasis, while moderate to severe psoriasis can be treated with systemic therapies such as biologics and small molecule drugs [10].

2.1 Phototherapy

Phototherapy is used as a treatment for psoriasis in patients with a high surface area of lesion involvement (>10% BSA)

and in patients who cannot be treated topically with topical agents. It plays an integral role in inducing cytokine phenotypic shift, induction of apoptosis of keratinocytes and T lymphocytes, and regulation of the immune system [11]. Although phototherapy is a traditional therapy, it has been shown to have synergistic effects with emerging biologic agents [12]. Also, the mechanism of combined use of phototherapy and biological agents may be related to the immunosuppressive effects of both.

2.2 Chinese Medicine Treatment

In recent years, Chinese medicine has conducted a lot of clinical and experimental research in the field of psoriasis treatment Traditional systemic treatment of psoriasis. Commonly used clinical treatment modalities, including internal and external Chinese medicine, combined internal and external Chinese medicine, combined Chinese and Western medicine and targeted treatment with Chinese herbal compounds or Chinese herbal monomers, all have significant regulatory effects on the development of psoriasis [13].

2.3 Traditional Treatment Methods

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. MTX was found to have an inhibitory effect on serum levels of IL6 and IL22 in patients with psoriasis [14] However, the frequent presentation of bone marrow toxicity, liver toxicity, and susceptibility to secondary infections greatly discouraged the use of MTX [15]. Acitretin, a systemic retinoid, exhibits antipsoriatic effects through its action on the nuclear retinoid receptors [16]. 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 thwarted by severe side effects, including renal failure and alterations in blood pressure [17]. 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.

3. TNF Inhibitor Studies

Numerous studies have confirmed that tumor necrosis factorαplays an important role in the pathogenesis of many chronic inflammatory diseases [18]. In patients with psoriasis, overexpression of tumor necrosis factorαin the body promotes keratinocyte production and affects cellular transport, thereby exacerbating disease progression [19]. The efficacy of Tumour necrosis factor α(TNFα) inhibitors is mainly due to their ability to block the activation of dendritic cells. The frequent adverse events seen with TNFα inhibitors include infections of the upper respiratory tract, rhinitis, and pharyngitis [20].

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.

3.1 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. Significant efficacy of anti-IL-17 and IL-23 agents in the treatment of psoriasis has raised the treatment target for psoriasis in clinical trials from PASI 75 to PASI 90 and PASI 100.

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.

3.2 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 kinase (JAK) plays a key role in the signal transduction of cytokines. Activation of cell membrane receptors by various cytokines leads to phosphorylation of signal transducer and activator of transcription (STAT) by members of the JAK family, which translocates to the nucleus and undergoes gene transcription, ultimately altering cell growth, maturation, differentiation and survival, as well as inflammatory and immune responses, among other functions [21]. In psoriasis, the cytokines IL-6, IL 23, and interferon (IFN)-γ, which are associated with the pathogenesis of psoriasis, have been linked to the JAK-STAT pathway [22]. First-generation JAK inhibitors and second-generation JAK inhibitors have been developed. First-generation JAK inhibitors target two or more different JAKs, such as Tofacitinib (JAK1/JAK3), Ruxolitinib (JAK1/JAK2) and Baricitinib (JAK1/JAK2), and have shown some clinical efficacy in IBD, but not in psoriasis. treatment has shown incomplete efficacy [23].

3.3 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 [24].

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 [25].

4. Conclusion

Psoriasis is a complex multifactorial disease, and despite various novel therapies that have become available in the past few years, psoriasis remains incurable. Decades ago, treatment was mostly applied by immunosuppressive methods to control the disease, however, with the advent of biological agents with high specificity for immune components, it provides better ways for patients to improve their condition. A better treatment would be to combine small molecule therapy with biologics, which would be more effective than using one therapy 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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