香港風濕病基金會
Hong Kong Arthritis & Rheumatism Foundation Ltd.

CHARM issue 7

CARE, HEALTH, ARTHRITIC MANAGEMENT

JULY • 2012

Editorial Board

Editor's Message

Psoriatic arthropathy is the highlight of this issue of CHARM. It is a disease that brought the general public misconception as being contagious and the sufferers significant effort to overcome social stigma. Although water activities are good for their arthritic and spondylitic conditions, these patients are often turned away from public pools. Patients with psoriatic arthropathy are among the varoius rheumatic diseases supported by service provided by the Hong Kong Arthritis & Rheumatism Foundation.

In this issue, our rheumatologist is illustrating the clinical features, diagnosis and treatment of patients with psoriatic arthropathy in a case presentation. A dermatologist tells us how to recognize the various forms of skin lesions and the available therapies. Like other rheumatic diseases, psoriatic arthritis is also associated with systemic manifestations, most commonly ophthalmological complications. You can appreciate an article by an ophthalmologist on the various eye manifestations and treatment options. You will also learn the various biologic therapies available for treatment of psoriatic arthritis written by a pharmacist. We have also offered you information on the Hong Kong Psoriatic Arthropathy Association, a patient self help group that collaborates closely with the Foundation and aims to better social support and to provide updated information regarding quality care in the society offered to patients and carers.

Happy reading!

HKARF Patients Resources and Training Centre

The Hong Kong Arthritis and Rheumatism Foundation is proudly presenting the opening of its Resources and Training Centre on 1 June 2012 for patients, carers and the general public. The resource centre is located at Flat 103-106, Nam Wai House, Nam Shan Estate, Shum Shui Po, Kowloon. The Foundation's administrative office will be located in the centre with two full-time employed staff to handle administrative work including processing of patient and self help group support fund applications. The centre has a resource library with collection of educational materials regarding arthritis and rheumatism and a reading area that cater for patient education and is open to patients, carers and the general public. The centre also provides a venue for Foundation committee meeting, volunteer training, educational talks and programmes for physiotherapy and occupational therapy training and exercise classes.

Many of the charity activities organized by the Foundation is supported by dedicated patient volunteers. These volunteers are trained to assist the enquiry helpline at the centre. Programmes for physiotherapy and occupational therapy training and exercise classes are conducted to serve patients with rheumatic diseases and are offered for free or charged on a non-profit making basis. Besides, educational workshops and seminars will be organized in the Centre for patients and the general public.

Flat 103-106, Nam Wai House, Nam Shan Estate, Sham Shui Po, Kowloon

Case Presentation

Dr. YIM Cheuk Wan
Associate Consultant and Specialist in Rheumatology
Department of Medicine, Tseung Kwan O Hospital

Mr. Poon was a 45 year old gentleman with history of psoriasis since 1993. He had been receiving topical corticosteroid and emollients from dermatologist. He presented with arthritis for three months, affecting knees, ankles, right wrist and toes of the right foot. He also had back pain and stiffness which was worse in the morning for one year. On physical examination, there were plaque-psoriasis in the forehead, trunk and limbs, four swollen toes, arthritis in the knees and right ankle, restricted range of motions of lumbosacral and cervical region. X-ray of sacroiliac joints showed sacroiliitis with syndesmophytes in the lumbar and cervical spine.

Psoriatic arthritis affects 5-20% of patients with psoriasis. In the majority of cases, the arthritis occurs after the diagnosis of psoriasis although there are patients having arthritis before the skin manifestation. Nail dystrophy is present in around 80% of cases. The patterns of joint involvement are quite diverse. There are five classical types : 1) asymmetrical oligoarthritis in the lower limbs; 2) polyarthritis in the distal interphalangeal joints; 3) symmetrical polyarthritis mimicking rheumatoid arthritis; 4) spondylitis and 5) arthritis mutilans. However, it should be noted that more than one form of arthritis may be present at the same time. Rheumatologists rely on sets of classification criteria to help establish the diagnosis of psoriatic arthritis. The Classification criteria for Psoriatic Arthritis (CASPAR) are the latest set of criteria used worldwide. The presence of inflammatory arthritis in peripheral joints, spine or enthuses with at least 3 points from the following categories would be highly suggestive of psoriatic arthritis (sensitivity 98.7%, specificity 91.4%):

1. Evidence of current psoriasis, a personal history of psoriasis, or a family history of psoriasis (2 points)
    - Current psoriasis is defined as psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist
    - A personal history of psoriasis is defined as a history of psoriasis that may be obtained from a patient, family physician, dermatologist, rheumatologist, or other qualified health care provider.
    - A family history of psoriasis is defined as a history of psoriasis in a first- or second-degree relative according to patient report.
2. Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current physical examination (1 point)
3. A negative test result for serum rheumatoid factor (1 point)
4. Either current dactylitis, defined as swelling of an entire digit, or a history of dactylitis recorded by a rheumatologist (1 point)
5. Radiographic evidence of juxta-articular new bone formation appearing as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of the hand or foot (1 point)

At the moment, there is no cure for this illness. The goal of treatment is to reduce joint pain and swelling, preserve joint function, prevent joint damage and control skin lesions. There are non-pharmacological and pharmacological options to achieve good control.

Non-pharmacological treatments

The acute phase is characterized by joint pain and swelling suggesting active inflammation. Patients are advised to rest the joints as much as possible. Heat and cold treatments such as soaking in a warm tub or placing a cold pack on a painful joint can soothe pain and reduce joint swelling. Cold is best for warm and swollen joints whereas either may be used for joints that are painful with not much sign of inflammation. In some cases, splintage may be used to rest the joints and to deal with problems of joint malalignment or instability.

With gradual resolution of inflammation, patients may experience stiffness and weakness in the affected joints. Joint mobilization and exercise programs under the supervision of physiotherapists or occupational therapists form an essential modality of joint rehabilitation. Physical activity can also boost flexibility, strengthen muscles, improve sleep, strengthen the heart, reduce body weight and enhance physical appearance. However, high impact sports such as boxing, waterskiing and hockey are not recommended due to potential back and joint injury. Regular stretching exercise such as jogging, Tai Chi and swimming are beneficial to patients with peripheral arthritis and spondylitis.

Pharmacological treatments

Currently, there are three categories of medications to be considered in the treatment strategies for psoriatic arthritis:

- Nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids
- Disease-modifying antirheumatic drugs (DMARDs)
- Biological agents

Nonsteroidal anti-inflammatory drugs and Glucocorticoids

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are commonly used as initial therapy, prescribed for both axial and peripheral arthritis. Ibuprofen and naproxen may help control pain, swelling and morning stiffness, while indomethacin and diclofenac preparations are more potent. COX-2 inhibitors such as celecoxib and etoricoxib offer comparable symptomatic relief. All NSAIDs can irritate the stomach and intestine, and long-term use can lead to gastrointestinal bleeding. COX-2 inhibitors have lower incidence of gastrointestinal adverse effects. Other potential side effects include damage to the kidneys, fluid retention, high blood pressure and heart failure. In addition, NSAIDs may worsen skin problems associated with psoriatic arthritis.

Case Presentation

Glucocorticoids

Periodic intra-articular injection of glucocorticoid may be of value in patients with oligoarticular disease. Caution should be observed if there is active skin disease overlying the joints. Systemic glucocorticoid should be used judiciously because of possible risk of pustular flare in the skin disease upon drug withdrawal.

Disease-modifying antirheumatic drugs (DMARDs)

In addition to reducing pain and inflammation, DMARDs help limit the amount of joint damage that occurs in psoriatic arthritis. As DMARDs act slowly, clinical effects may only be observed after weeks or even months.

Sulphasalazine

In several controlled studies, sulphasalazine has been shown to have a modest benefit in treating psoriatic arthritis. The action of sulphasalazine appears to be confined to peripheral arthritis and has no benefit in axial or skin disease. The therapeutic dosage range is 1.5-3 g per day in divided doses. Its potential toxicity is low. Some patients may experience rash, nausea and headache. Discoloration of urine is quite common and reassurance is all that needed. Reversible azoospermia, hepatic enzyme elevation, haemolytic anaemia in patients who are G6PD deficient and pulmonary infiltrate with eosinophilia require special alert and drug withdrawal is warranted. Complete blood count, renal and liver function at baseline with subsequent monitoring every one to three months is recommended.

Methotrexate

The efficacy of methotrexate in psoriatic arthritis was first demonstrated in a randomized controlled trial in 1964. Subsequent studies showed benefit at doses between 7.5 to 15mg per week. Methotrexate has effect on both arthritis and cutaneous component of psoriatic arthritis. However, the prescribing doctors must be aware of potential serious side effects and teratogenicity associated with methotrexate. Education and counseling, as well as baseline complete blood count, renal and liver function, hepatitis B and C serology are essential before initiation of treatment. Potential side effects include oral ulcers, gastrointestinal upsets, hepatotoxicity and haematologic toxicity (pancytopenia). Folic acid supplementation prevents or reduces the severity of these events. Pneumonitis is a severe complication which warrants immediate withdrawal of the drug. Liver biopsy is traditionally recommended when the cumulative dosage exceeds 2g. However, recent studies do not suggest increased liver toxicity in psoriatic patients comparing with those with rheumatoid arthritis. At present, there is no consensus on routine liver biopsy. However, the procedure may be considered if the levels of liver transaminases (AST and ALT) are persistently elevated (> 3 months) or if there is a decrease in the albumin level while on methotrexate.

Leflunomide

Leflunomide is a selective pyrimidine-synthesis inhibitor that targets activated T-cells lacking a salvage pathway. It has been shown to be effective in the cutaneous manifestation as well as peripheral arthritis. In a randomized study of which half of the patients had failed methotrexate, promising improvement was noted in terms of joint (Psoriatic Arthritis Response Criteria, PsARC0 and skin (Psoriasis Area and Severity Index, PASI) conditions. Potential adverse events include diarrhoea, weight loss, skin rash, neutropenia, hepatotoxicity and teratogenicity. The dosage ranges from 10-20mg daily. Monitoring schedule is similar to methotrexate. Leflunomide is regarded as an alternative if methotrexate is contra-indicated or not tolerated.

Cyclosporin A

Cyclosporin A at 3-5mg/kg/day demonstrated benefit in psoriasis as well as arthritis though the drug works better on skin than joint. It inhibits T-cell activation by blocking the interaction of calcineurin with calmodulin at the cellular level. The main concern is potential nephrotoxicity especially with concomitant use of NSAIDs. The drug level is increased by diltiazem while the risk of neuromyopathy would be higher with concomitant colchicine use. Further studies are required to determine the benefit and toxicity over a longer period. Other side effects include hypertension, gum hypertrophy and systemic infection.

Biological agents

In the past decade, we have witnessed remarkable advances in the treatment of inflammatory arthritis. The excellent efficacy of biological agents have demonstrated in clinical trials of psoriasis and psoriatic arthritis in various domains including pain, swelling, skin, radiographic changes, function and quality of life.

TNF inhibitors

Tumour necrosis factor (TNF)-α has been implicated as a key pro-inflammatory cytokine in psoriatic arthritis. The clinical impact of TNF inhibition on rheumatoid arthritis was first described in the late 1990s. Subsequent studies in the early 2000s confirmed the benefit of TNF inhibitors in the treatment of psoriatic arthritis. They are helpful for both the skin and joint disease. Currently there are many preparations:

- Adalimumab (Humira): 40mg subcutaneous injection every 2 weeks
- Etanercept (Enbrel): 50mg subcutaneous injection weekly
- Golimumab (Simponi): 50mg subcutaneous injection once monthly
- Infliximab (Remicade): 5mg/kg intravenous infusion once every 6-8 weeks after loading

TNF inhibitors carry potential risks including hypersensitivity reactions, infections (in particular reactivation of latent tuberculosis and hepatitis B), demyelinating syndromes and precipitation of cardiac failure. Thus, pre-biologic screening is essential to stratify risks. In addition to complete blood count with renal and liver function, the patient should be screened for hepatitis B and C status, evidence of latent tuberculosis infection (by tuberculin test or gamma-interferon assay, plus chest X-ray) and cardiac function.

Case Presentation

Other biologic agents

Alefacept is a fusion protein which acts by blocking the costimulatory molecule LFA-3/CD2 interaction in the T-cells.
Ustekinumab is a monoclonal antibody which blocks the interleukin-12 and interleukin-23 pathways.
Both agents are effective for skin disease only. They are not helpful for arthritis.

Conclusion

The goals of treatment in psoriatic arthritis are symptomatic improvement, restoration of function, prevention of joint damage and improvement in quality of life. A combination of physical therapy, NSAIDs, DMARDs and/or biological modifiers should be administered according to the needs of individual patient, at an optimal balance of efficacy and toxicity.

Reference

1. Gladman D D, Antoni C , Mease P, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64:ii14-ii17
2. Nash P, Clegg D O, Psoriatic arthritis therapy: NSAIDs and traditional DMARDs .Ann Rheum Dis 2005;64:ii74-ii77
3. Mease P J, Antoni C E, Psoriatic arthritis treatment: biological response modifiers. Ann Rheum Dis 2005;64:ii78-ii82
4. Gossec L, Smolen JS, Gaujoux-Viala C, et al. European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies. Ann Rheum Dis 2012;71:4-12
5. Wilkens RF, Williams HJ, Ward JR, et al. Randomized, double-blind, placebo-controlled trial of low dose methotrexate in psoriatic arthritis. Arthritis Rheum 1984;27:376-81
6. Clegg DO, Redas DJ, Mejias E, et al. Comparison of sulphasalazine and placebo in the treatment of psoriatic arthritis. Arthritis Rheum 1996;39:2013-20

PSORIASIS

Dr. Steven LOO
Specialist in Dermatology
MBChB(CUHK), MSc (CUHK), MRCP(UK), FHKCP, FHKAM(Medicine), PgDip Epi&Biostat (CUHK)

Introduction

Psoriasis is a chronic, immune-mediated inflammatory disease of the skin. Both genetic and environmental factors play a critical role in the pathogenesis. Clinically, psoriasis is one of the prototypic papulosquamous skin diseases characterized by erythematous papules or plaques with silvery scales. It is associated with various co-morbidities including psoriatic arthritis, inflammatory bowel disease, lymphoma, anxiety, depression and more recently, the cardiovascular complications. The disease leads to significant morbidity and impairment in quality of life.[1]

Epidemiology

Psoriasis is reported to affect 2-3% of the western population. According to a recent population based survey in mainland China, its prevalence in Chinese is estimated to be 0.47%, with regional variation of 0.31% in southern region and 0.78% in northern region of our country.[2] Psoriasis has a bimodal age distribution for disease onset. The first peak occurs around 20 years of age and the second peak around 60. Patients with young disease onset have stronger genetic predisposition compared with those with late onset disease and have higher prevalence of HLA-Cw6.[1]

Pathogenesis

There is significant understanding in the pathophysiology of psoriasis in recent decades. Early studies revealed that the cell cycles of the epidermal cells are greatly accelerated in psoriasis. The epidermal transit time is shortened from the normal 28 days to as short as 3 days. Psoriasis is once considered as a primary disease of keratinization. The alteration in epidermal cell cycle is now believed to be triggered by a cascade of inflammatory cytokines released by activated dendritic cells, T cells and other immune cells. Psoriasis is classically considered to be a prototypic type I helper T cell (Th1) disease. Early research on therapeutics targeted T cells by cyclosporine A, providing proof-of-concept evidence to an immune basis of this disease. Indeed, biological treatment with anti-tumour necrosis factor (TNF) agents antagonising TNFα activity have been shown to be effective in psoriasis and is a popular therapy since the past decade. Recent studies have shown that Th17 cells and the "upstream" cytokines in the inflammatory cascade, IL-12 and IL-23, are involved in the disease process and administration of monoclonal antibody against IL-12/IL-23 results in significant improvement of psoriasis.[1,3]

CLINICAL FEATURES

Prototypic lesion

The typical lesion of psoriasis is a well-demarcated erythematous plaque with silvery scale on top of the plaque. The affected patient may experience itchiness to different extent. The plaques may affect anywhere of the skin surface over the body but mucosa is typically spared. The scales may only be loosely attached and easily fall off from the skin.[3]

1) **Chronic stable plaque psoriasis**
   This is the most common form of psoriasis and accounts for over 90% of the cases in daily clinical practice. Sites of predilection of the characteristic plaques include the extensor surfaces of the elbow, knee, lower back, and scalp. The genitalia and nails may also be affected. The plaques vary in size. New lesions may be induced at traumatised skin such as surgical scar, or even scratch marks (known as Köbner phenomenon).

2) **Guttate psoriasis**
This is a variant characterised by small coin or even punctate lesions with less amount of scale and affects mostly young people. The disease may be precipitated by upper respiratory tract infection. Over half of these patients have some evidence of preceding streptococcal infection. A few may have prolonged disease remission after the acute episode. However, disease may persist and many patients will develop chronic plaque psoriasis.

3) **Unstable psoriasis**
Such lesions are angry looking with more intense inflammation. These may be beefy red in colour with less scaling. Lesions may be less well-demarcated and exudation and crust are occasionally found. Patients may experience more itchiness, irritation and even pain. Further progression to erythrodermic or pustular psoriasis can occur. Inappropriate use of corticosteroids, excessive irritation and sunburn may be associated with unstable psoriasis.

4) **Erythrodermic psoriasis**
When more than 90% of the body is involved by psoriasis, it is defined as erythrodermic psoriasis. The affected patient is characterised by generalised redness of skin and scaling. The face may occasionally be relatively spared. Individual plaque may not be obvious and pustules may sometimes be found. Affected patients may have systemic features such as fever, malaise, chills, rigors and high output cardiac failure.

5) **Pustular psoriasis**
Tiny superficial pustules with a background of erythema may occur. The roof of these pustules is easily broken. These pustules can be distributed throughout the whole skin surface or more localized especially in and around unstable lesions. Some patients may have lesions with matted scales and yellowish hue, though very discrete pustules may not be seen readily. Steroid withdrawal is the commonest precipitating factor for pustular psoriasis. Localised pustular psoriasis on the palm and sole is reported to be associated with smoking.

DISEASE ASSESSMENT

A comprehensive and holistic approach should be adopted for assessment of each psoriasis patient.[4]

1. **Psoriasis Disease Characteristics**
   i. Disease Severity:
   Rules of ten: Body Surface Area>10%, *Psoriasis Area Severity Index (PASI) >10, Dermatology Life Quality Index (DLQI) >10
   ii. Regional involvement:
   iii. Plaque Features: Stable or unstable (intense inflammation), small or large plaque, thin or thick plaque, whether pustule is present

2. **Joint Involvement**
Screening of arthropathy is important as up to 70% of skin psoriasis precedes arthropathy by 5-10 years. It is important to look for clinical features of early morning stiffness, enthesitis, joint swelling, tenderness and dactylitis.

3. **Psychosocial Impact**
To explore and address the major concern of patients about their disease and their expectation is important. Up to 40% of patients may have various extent of anxiety or depression.

4. **Cardiovascular Risk Assessment**
Recent epidemiological studies have shown that patients with psoriasis and psoriatic arthropathy have increased risk of cardiovascular comorbidities. Some authorities suggest that baseline screening of body mass index, waist circumference, blood pressure, fasting glucose and lipid levels are clinically useful in the management of psoriasis patients.[5]

*** PASI is calculated as follows:**
Σ [area score of the region x extent indicator of the region x sum of severity indicator of the region]
= 0.1 ÅHead (E + S+ T) + 0.2 ÅUpper limbs (E + S+ T) + 0.3 ÅTrunk (E + S+ T) + 0.4 ÅLower limbs (E + S+ T) wherein Å refers to area of the suffix region according to a 7-point scale (0-6); E, S, T refers to the degree of erythema, scaling and thickness respectively according to a 5-point scale (0-4). The maximum score is 72.

GENERAL TREATMENT PRINCIPLES

Appropriate skin care, avoidance of aggravating factors, keeping a good treatment history, cessation of smoking, avoidance of excessive alcohol, reinforcement of the non-contagious nature and chronicity of the disease condition and that psoriasis is amenable to very good control are important messages to be conveyed to patients especially in the first few clinical encounters.[4,6]

Treatment options
Treatment for psoriasis can be classified as:

1. **Topical drugs:** topical steroids, vitamin D analogues, tar, dithranol (which was withdrawn from the local market due to potential carcinogenicity), keratolytics e.g salicylic acid, calcineurin inhibitors, tazarotene (vitamin A analogues which is not available in the local market)

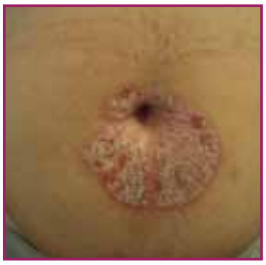
PSORIASIS

2. **Ultraviolet(UV) light therapy:** UVB including narrow band UVB (NBUVB), Psoralen- UVA(PUVA), targeted phototherapy such as UVB delivered with the laser system (Excimer ® 308)
3. **Traditional systemic therapy:** methotrexate, systemic retinoid and cyclosporine A (FDA approved); hydroxyurea, 6-thioguanine, azathioprine, mycophenolate mofetil and fumaric acid esters (off-label use). Fumaric acid esters are commonly used in Germany but are not available in the local market.
4. **Biologic therapy:** etanercept, infliximab, adalimumab which targets TNFα; ustekinumab which targets IL-12 & IL-23 (they are available in the local market but not in government dermatology clinics)

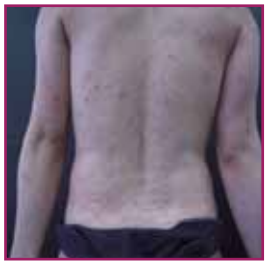
Detailed illustration of various treatment modalities is beyond the scope of this article. In general, they can be used as monotherapy, but more commonly in combination or rotational therapy to minimize side effects of individual treatments. Topical treatment remains the mainstay of treatment in psoriasis, with compliance being the key factor for treatment success. Systemic medications are generally considered for severe disease, as defined by rules of ten as mentioned above, and are considered for patients with unstable or erythrodermic lesions. However, treatment decision in psoriasis is a complex issue and is highly individualized. Factors such as patient compliance, tolerability, treatment expectation, acceptance of side effects, cost and availability of treatment modalities should all be considered before commencing systemic treatments. Education on the concept of disease chronicity and maintenance therapy for long-term disease control, like other chronic diseases such as diabetes and hypertension, is important after achieving satisfactory disease control.

CONCLUSION

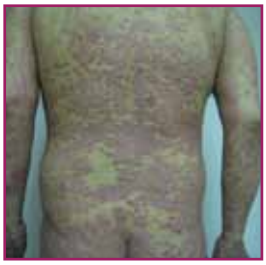
Psoriasis is a chronic immune mediated inflammatory skin disease which causes significant functional impairment to those affected. Multidisciplinary and holistic approach is the key in the management of psoriasis. A constellation of treatments are now available which can achieve satisfactory disease control in majority of our patients.



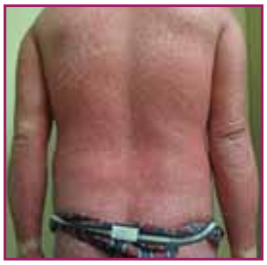
Chronic Plaque Psoriasis



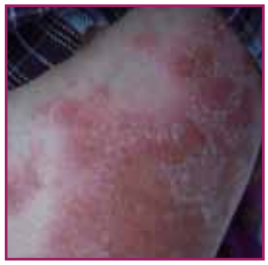
Guttate Psoriasis



Extensive Chronic Plaque psoriasis



Erythrodermic Psoriasis



Pustular Psoriasis

Reference

1. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med. 2009;361:496-509.
2. Ding XL, Wang TL, Shen YW, et al. Prevalence of psoriasis in China: An epidemiological survey in six provinces. Chin J Derm Venerol. 2010;24:598-601
3. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet. 2007;370:263-71.
4. Menter A, Griffiths CE. Current and future management of psoriasis. Lancet. 2007;370:272-84.
5. Kimball AB, Gladman D, Gelfand JM, et al. National Psoriasis Foundation clinical consensus on psoriasis comorbidities and recommendations for screening. J Am Acad Dermatol. 2008 ;58:1031-42.
6. American Academy of Dermatology Work Group, Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions.J Am Acad Dermatol. 2011;65:137-74.

OPHTHALMOLOGICAL COMPLICATIONS OF PSORIATIC ARTHROPATHY

Dr. LEUNG Yu-lung, Dexter
Honorary Consultant and Specialist in Ophthalmology
Hong Kong Sanatorium & Hospital

Ophthalmic manifestations of psoriasis are diverse and virtually all structures of the eyeball can be affected. Eye manifestations can arise as part of the presentation of the psoriatic disease or as complications from treatment. The exact incidence and prevalence of ocular manifestations remains uncertain as there is a lack of population-based published data. In a small Singaporean cross-sectional survey, as many as 67% of their patients with psoriasis had at least one ophthalmic manifestations.[1] Eye doctors in Hong Kong do not generally have an impression that these manifestations are commonly seen. More studies are needed to examine if the discrepancy may be related to under-referral, under-diagnosis, or genuine ethnic differences in disease prevalence.

Uveitis is one of the main ocular manifestations of psoriasis. Uveitis refers to inflammation of part or all of the pigmented structures within the eye. Anterior uveitis or iridocyclitis occurs as a result of inflammation of the iris and ciliary body, both pigmented structures and is a potentially serious eye manifestation. Uveitis has been reported to occur in 7.1% of psoriatic patients with arthropathy.[2] Preliminary data in the literature also suggested that the arthropathic form of psoriasis might be more associated with development of anterior uveitis. It has also been suggested that uveitis may be more severe in those with presence of HLA-B27[3] or with more severe skin disease based on the Lattice System Physician Global Assessment (LS-PGA).[1]

Ophthalmological complications of Psoriatic Arthropathy

Uveitis typically presents as red eye with dull pain and moderate level of blurring of vision. There is classically perilimbal redness with maximum injection around the corneal-conjunctival junction as a result of inflammation at the ciliary body (Figure 1). The pain is usually dull and deep but can become sharp and intense if complicated by acute and grossly raised intraocular pressure. Vision is impaired due to cells and protein floating inside the anterior chamber during acute inflammation, and due to development of cataract, small pupil from posterior synechiae (adhesions of pupil to anterior lens capsule resulting in small, irregular and fixed pupil), glaucoma, and macular edema in chronic lesions.

Treatment of uveitis and its associated complications is a broad subject. Newer generation of topical steroids such as loteprednol etabonate and rimexolone may offer less ocular hypertensive side effects with excellent efficacy. Newer topical non-steroidal anti-inflammatory drugs (NSAIDs) such as nepafenac, and intravitreal injections of triamcinolone, may offer superior resolution of macular edema. Investigational therapeutic options include intravitreal dexamethasone implants for more sustained effect. There are also significant therapeutic advances in cataract surgery as well as glaucoma eyedrops and surgery. Newer glaucoma surgical interventions such as tube implants and non-penetrating deep sclerectomy with collagen implants reduce intraocular pressure offering promising efficacy and safety.

Inflammatory keratitis and corneal melting have been reported in patients with psoriasis.[4] This, together with uveitis, should need more urgent ophthalmic referral for management since keratitis and uveitis are both potentially vision-threatening. Episcleritis, scleritis and conjunctivitis have also been reported. Dry eyes and sicca are associated with psoriasis, like other rheumatic diseases. Artificial tears (preservative-free ones if frequent application needed), collagen punctal plugs, and newer agents such as topical cyclosporine-A in reducing ocular surface inflammation offers better clinical outcomes compared to traditional methylcellulose eyedrops.

As psoriasis is an epithelial disease, eyelid and conjunctiva are targets of skin manifestations. Blepharitis with meibomian gland disease are reported to be more common in psoriasis patients.[5] Psoriatic plaques may appear on the eyelids but are uncommon as are skin lesions on the face. Facial sparing may be the result of chronic ultraviolet irradiation exposure such that facial and eyelid psoriasis has been suggested to be a marker of severe psoriasis disease.[6]

Systemic and topical steroid for treatment of psoriasis may lead to eye complications. Ocular hypertension, glaucoma and cataract are well-known adverse effect from high dose or prolonged use of corticosteroid. Patients with ocular hypertension may remain asymptomatic, only when the optic nerve has been damaged by elevated intraocular pressure in glaucoma would visual field constriction occur. Corticosteroids may increase the chance of infection in all layers of the eyeball, particularly infective keratitis, and endogenous endophthalmitis. These patients present with painful loss of vision and a red eye. Central serous choroidoretinopathy (CSCR) is a known complication of systemic corticosteroid and present with central scotoma, metamorphopsia (perceiving straight lines to be wavy), micropsia (perceiving objects to be smaller than usual) or macropsia. CSCR have also been reported in psoriasis patient.[7]

Cataract in patients with psoriatic arthropathy may be age related, or can occur due to the effect of chronic uveitis, chronic use of systemic or topical corticosteroid. PUVA therapy for psoriasis may potentially contribute to cataract formation by causing photochemical changes in lens proteins.[8] There are reports of some rare clinical ophthalmic complications in patients with psoriasis. One example is Brown syndrome which is associated with inflammation of the trochlea/ tendon complex and presents with binocular double vision and limited elevation of eye in adduction.[9]

In conclusion, rheumatologists should be alerted to eye symptoms of psoriasis patients. Early ophthalmic consultation is recommended for patients who develop ocular symptoms, or those who required long term systemic steroid for routine ophthalmological screening for complications.

Figure 1. Anterior uveitis is an important ophthalmic manifestation of patients with psoriatic arthropathy.

Note the injection at perilimbus is more intense (ciliary flush). This patient also has cataract, irregular pupil with posterior synechiae.

Reference

1. Chandran NS, Greaves M, Gao F, et al. Psoriasis and the eye: prevalence of eye disease in Singaporean Asian patients with psoriasis. J Dermatol 2007;34:805-10.
2. Lambert JR, Wright V. Eye inflammation in psoriatic arthritis. Ann Rheum Dis 1976;35:354-6.
3. Durrani K, Foster CS. Psoriatic uveitis: a distinct clinical entity? Am J Ophthalmol 2005;139:106-11.
4. Boss JM, Peachey RD, Easty DL, et al. Peripheral corneal melting syndrome in association with psoriasis: a report of two cases. Br Med J (Clin Res Ed) 1981;282:609-10.
5. Zengin N, Tol H, Balevi S, et al. Tear film and meibomian gland functions in psoriasis. Acta Ophthalmol Scand 1996;74:358-60.
6. Bernhard JD. Is eyelid involvement a sign of severe psoriasis? Dermatologica 1987;174:151.
7. Ezra N, Taban M, Behroozan D. Central serous chorioretinopathy associated with topical corticosteroids in a patient with psoriasis. J Drugs Dermatol. 2011 Aug;10:918-21.
8. Crylin M, Pedvis-Leftick A, Sugar J. Cataract formation in association with ultraviolet photosensitivity. Ann Ophthalmol 1980;12:786-9.
9. Thorne JE, Volpe NJ, Liu GT. Magnetic resonance imaging of acquired Brown syndrome in a patient with psoriasis. Am J Ophthalmol. 1999 Feb;127:233-5.

Updates on biologic agents used in the treatment of Psoriatic Arthritis

Mr. LAW Kwok-ming, Kenneth
Pharmacy Department Manager, QEH, Kowloon Central Cluster, Hospital Authority, Hong Kong

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy of the peripheral joints, spine, and enthuses, associated with psoriasis. PsA is regarded as a member of the spondylarthritis (SpA) family. The disease is characterized by (1) infrequent seropositivity for rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP); (2) association with HLA-B27 alleles and (3) clinical features that are distinguishable from rheumatoid arthritis (RA) e.g. involvement of distal interphalangeal (DIP) joints, dactylitis, enthesitis, sacroiliitis, spinal involvement and psoriasis. PsA has a uniquely diverse pathophysiologic and clinical features and can progress into destructive arthritides. Preferential improvements in either the skin or joints are sometimes seen with newer therapies which suggest that many more factors are at play in the pathophysiology of PsA. Thus, agents used in RA cannot simply be empirically applied to PsA.

Conventional therapies for PsA

Therapeutic agents used in PsA are similar to those used in RA. NSAIDs are mainstay first line for pain relief but are of no value on joint disease or psoriasis. Traditional DMARDs (disease modifying anti-rheumatic drugs) affect the immune systems with various mode of actions. Common agents include sulfasalazine, methotrexate (MTX), leflunomide and cyclsporin A. They usually take 2 to 3 months for effects to be evident.

New targeted therapeutic agents for inflammatory arthritides

Much progress in treatment of RA, ankylosing spondylitis (AS) and PsA has been seen in recent years, partly attributed to better understanding of the pathogenesis of these diseases at cellular and molecular levels in addition to development of biological agents with specific targets. Biologics used in inflammatory arthritides are usually TNF-targeting or Non-TNF targeting (TNF = Tumor Necrosis Factor).

TNF-targeting agents licensed in Hong Kong for at least one of the three conditions include (1) etanercept (Enbrel®); (2) infliximab (Remicade®); (3) adalimumab (Humira®) and (4) golimumab (Simponi®).

Etanercept (Enbrel®) is indicated for treatment of PsA, RA, JRA (juvenile rheumatoid arthritis), AS and plaque psoriasis. The drug is a soluble TNF receptor – IgG1 fusion protein that can inhibit the actions of TNF. Administration route is by subcutaneous injection at 25mg twice a week or 50mg weekly. Significant improvements in skin lesions, QOL and function can be expected. Inhibition of PsA disease progression measured radiographically was first demonstrated in phase III trial of etanercept[1]. Skin responses were often observed after improvements seen in the joints.

Infliximab (Remicade®) is indicated for treatment of psoriasis, Crohn's disease, AS, PsA, RA as well as ulcerative colitis. The drug is a chimeric (murine-human origin) monoclonal antibody specific for soluble and membrane-bound. Randomized, placebo-controlled trials have illustrated its efficacy[2]. Decreased disease activities, improvement in dactylitis and enthesitis with inhibition of radiological disease progression were observed at 24 weeks of treatment.

Adalimumab (Humira®) is indicated for RA, PsA, AS, Crohn's disease, psoriasis and juvenile idiopathic arthritis. It is a monoclonal antibody of human origin targeting TNF. Adalimumab is for subcutaneous injection at 40mg every other week for RA, PsA and AS. RA patients not receiving MTX, may have frequency increased to 40mg weekly. In the ADEPT study, significant improvements in skin lesions, inhibition of radiographic progression, QOL and functional indices observed at 24 week[3].

Golimumab (Simponi®) is another human monoclonal antibody that forms high affinity, stable complexes with both the soluble and transmembrane bioactive forms of TNF-α, preventing the binding of TNF-α to its receptors. Golimumab is approved to treat RA, PsA and AS. It is the first patient-administered, once a month injectable anti-TNFα drug on the market. Efficacy of golimumab in PsA was observed in the GO-REVEAL study[4]. Disease activity markers such as serum levels of C-reactive protein (CRP), interleukins IL-6 and IL-8 were lower at 4 weeks after initial treatment which were generally maintained through to week 24.

Non-TNF biologic agents

Three biologic agents targeting different immune mediators are also available in Hong Kong for treatment of RA but currently not for PsA. Abatacept (Orencia®) is a T-cell co-stimulation modulator. Rituximab (MabThera®) is a chimeric anti-CD20 monoclonal antibody. Tocilizumab (Actemra®) is a humanized anti-IL6 receptor monoclonal antibody.

Impact of biologic treatments in RA, AS and PsA.

Use of biological response modifiers (BRM) for RA began in the late 90's. Therapeutic position of these drugs has changed from the last resort to now an early treatment. Agents effective in RA may not necessarily be useful in PsA, for example those non-TNF targeting biologics. Etanercept, infliximab and adalimumab demonstrate excellent clinical efficacy in PsA. Joint symptoms responded well and disease progression slowed with radiological evidence. In PsA, benefits of TNF blockers extended to skin lesions, enthesitis as well as dactylitis.

Advances in biologic therapies for RA, AS and PsA have revolutionized these diseases' treatment. Improvement in symptoms has also led to better QOL and function for patients at different levels, including work, family and social interactions. Nevertheless, several important questions remain to be answered. Reportedly, between 1/4 to 1/3 of patients had their first biologic treatment e.g TNF inhibitor, discontinued within 1 year of therapy due to primary inefficacy or adverse events[5]. Alternative strategies are required for those non-responders. In unresponsive patients, change to a different TNF blocker or an agent with a different mechanism of action might prove useful. Long term efficacy, tolerability and side effects require continuing study as wide clinical use of these agents onlybegan around 10 years ago. Risk for cancer is a subject of concern. FDA issued a warning in April 2011 about potential risks of Heptatosplenic T-Cell Lymphoma, a rare form of blood cancer, in adolescents and young adults associated with use of TNF blockers. Increased infection risks including sepsis, pneumonia, invasive fungal infection and opportunistic infections have been reported. In September 2011, FDA further imposed a boxed warning about infection by Legionella and Listeria bacteria for the entire class of Tumor

Updates on biologic agents used in the treatment of Psoriatic Arthritis

Necrosis Factor-alpha (TNF-α) blockers. Reactivation of latent tuberculosis has been observed which has led to the introduction of pre-initiation screening. Formation of neutralizing antibodies against etanercept, infliximab and adalimumab have been reported which is another significant factor that could reduce treatment effectiveness of TNF blockers.

Conclusions

TNF inhibitors gradually become standard therapy in management of inflammatory arthritides. Use in combination with DMARDs in early disease appears more beneficial. NSAIDs remain valuable for pain control. Only four TNF blockers in Hong Kong are licensed for PsA. Their efficacy did not confine to joint symptoms but also in skin lesions, dactylitis and enthesitis which are key symptoms of PsA. Despite highly effective in RA, AS and PsA, new biologic therapies have several challenges to meet for instance, identifying predictors for responders or non-responders, risk factors for ADR or early discontinuation as well as long term knowledge in safety and side effects. Treatment strategies for patients unresponsive to biologics need to be developed. Without doubt, the arrival of biologic therapy has transformed the management of PsA and changed the lives of many patients previously tormented by this progressive disease. However, it is already known that TNF inhibition does not provide the magical cure that are longed for in PsA. Therefore, continual search for new treatment targets and modality would still be essential.

Reference

1. Mease PJ et al. Etanercept treatment of psoriatic arthritis: safety, efficacy and effect on disease progression. Arthritis Rheum 2004;40:2264-72
2. Antoni CE et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis 2005;64:1150-7.
3. Mease PJ et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. Arthritis Rheum 2005;52:3279-89.
4. Kavanaugh A et al. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. Arthritis Rheum 2009;60(4):976-86.
5. Simard JF et al. Ten years with biologics: to whom do data on effectiveness and safety apply? Rheumatology 2011;50:204-213

The Hong Kong Psoriatic Arthritis Association

Ms. Christine LEUNG
Senior Manager, Hong Kong Society for Rehabilitation

The Hong Kong Psoriatic Arthritis Association is a patient self help group founded at the end of 2007. It was registered in the Police Department and is now a charity organization under the registration of the Inland Revenue Department. With the support of medical professionals, social workers of the Hong Kong Society for Rehabilitation, pharmaceuticals and a group of very committed patients, the Association's service has been growing over four years. The Association welcomes sufferers of psoriatic arthritis to join as foundation members and patients with psoriasis as affiliated members. There are now over 200 registered members and another 200 close relations and patient carers. The association aims to promote mutual aid and support amongst members and their care givers. Besides, patient education and encouragement of developing positive attitudes towards the disease advocating for a better quality of care and therapy are major mission of the Association.

During the years, the Association has launched various educational talks and seminars to patients, carers and the public. The Association joins local commemoration activities of International Psoriatic Day and the International Arthritic Day in Hong Kong every year and is proactive in the design of a series of educational posters, flyers, web-based educational programs. A number of school sharing sessions have been held in 2010 with the support of the "Love Hong Kong Love Ideas" Fund. Furthermore, with subsidy from the Social Welfare Department for the fiscal year of 2012, the Association can afford a dedicated part-time staff who will assist the Association to offer more sustainable and better services for its members and the public.

East meets West Educational Series "Traditional Chinese Medicine in Arthritis"

The scientific committee of the Hong Kong Arthritis and Rheumatism Foundation has organized an "East meets West" educational series since 2009. This educational series aim to promote interflow of knowledge and experience on patient management between health care professionals practicing western medicine and traditional Chinese Medicine in the field of rheumatology.

Last year, the symposium on "Traditional Chinese Medicine in Arthritis" was held on 17 September 2011 at The Boys' and Girls' Clubs Association. Prof Feng Yi Bin from School of Chinese Medicine, the University of Hong Kong, was invited to deliver a talk on "Pharmacology of traditional Chinese Medicine in Internal Medicine". Besides, Prof Tong Yao from School of Chinese Medicine, the University of Hong Kong, gave a lecture named "The role of traditional Chinese Medicine in the management of arthritis". Ms Tung Shong from HKU School of Professional and Continuing Education also shared with us knowledge and experience on "Diet and nutritious supplement in arthritis". The symposium was well received.




The role of traditional Chinese Medicine in the management of arthritis

Prof. Y TONG, Chair Professor, Director, School of Chinese Medicine, the University of Hong Kong

Introduction

Arthritis is a pathological disorder that involves inflammation of joints. In addition to western medicine, Traditional Chinese Medicine (TCM) also plays a significant role in the management of arthritis with good efficacy and few adverse effects. TCM mainly involves application of Chinese Herbal Medicine, acupuncture and Tui-Na (推拿).

Etiology and Pathology in the Theory of TCM

Under the theory of TCM, arthritis is classified under Bi syndrome (痹症) due to factors attacking the body when the body resistance is weak (正虛邪入) . The underlying pathology is believed to involve wind, cold and dampness that invade the body and stay in muscles and meridian that cause stagnate Qi and circulation leading to pain, numbness and dysfunction in extension and flexion of joints. Thus, therapeutic principle of TCM is to improve the movement of Qi and circulation by reinforcing Qi, nourishing dispelling wind and cold and to eliminate dampness.

Chinese Herbal Medicine for Arthritis

The treatment strategy of Chinese herbal medicine is based on the classification of Chinese medicine syndrome (中醫証型) and uses different Chinese medicinal formula. Generally speaking, the disease is excessive (邪實) at early stage and prolonged condition may induce deficiency of vital energy (正虛). The typical syndromes and formula are listed as below:

1. Wind-Rheumatism “typical symptom :ambulant pain”: Fangfeng Tang (防風湯).
2. Cold-Rheumatism “typical symptom: severe pain”: Wutou Tang (烏頭湯).
3. Dampness-Rheumatism “typical symptom :numbness”: Yiyiren Tang (薏苡仁湯).
4. Heat-Rheumatism “typical symptoms: tumefaction and heated”: Bai Hu Jia Guizhi Tang (白虎加桂枝湯).
5. Chronic-Rheumatism “typical symptoms: some weak symptoms due to prolonged condition”: Du Huo Ji Sheng Tang (獨活寄生湯).

Caution must be paid to the use of some toxic herbal medicine in the treatment of arthritis such as Radix Aconiti (川烏), Sabia japonica Maxim (清風藤) and Buthus martensii Karsch (全蠍).

Acupuncture for Arthritis

Acupuncture is performed using thin needles inserted in specific points on the body that represent concentration of body energies. Both acupuncture and moxibustion are used in the management of rheumatism related to wind, cold or dampness. Acupuncture without moxibustion and bloodletting are considered for rheumatism related to heat. The selection of acupoints also depends on the location of pathological changes.

Tui-Na for Arthritis

Different from other types of massage, Tui-Na has therapeutic effect based on accurate diagnosis of the clinical symptoms and theory of TCM. Some research showed that Tui-Na increased activity of the circulation and nervous system so as to relieve muscle tension and pain.

Reference

1. MacPherson H, Blackwell R. Rheumatoid arthritis and Chinese medicine. The European Journal of Oriental Medicine 1994; 1(3):17–29.
2. World Health Organization. A proposed standard international acupuncture nomenclature: report of a WHO scientific group. WHO. Geneva: World Health Organization, 1991.
3. Chrubasik JE, Roufogalis BD, Chrubasik S. Evidence of effectiveness of herbal anti-inflammatory drugs in the treatment of painful osteoarthritis including chronic low back pain. Phytotherapy Research 2007; 21:675–683.
4. Berman BM, Lao L, Langenberg P, et al. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Annals of internal medicine 2004; 141(12): 901–10.
5. Zijlstra FJ, van den Berg-de Lange I, Huygen FJ. Anti-inflammatory actions of acupuncture. Mediat Inflamm 2003; 12(2):59–69.

Pharmacology of Traditional Chinese Medicine and Internal Medicine

Dr. Yibin FENG, PhD, Associate Professor, School of Chinese Medicine, The University of Hong Kong

Traditional Chinese Medicine (TCM) is a unique system of medical therapeutics in contrast to western medicine. Chinese medicinal herbs, animal parts, minerals and their combination are commonly used in TCM. Chinese materia medica refers to study of theory and application of TCM, whereas pharmacology is a recent subject in Chinese materia medica that studies TCMs using modern scientific methodology and technology. There are a total of 12807 kinds of TCM, among which 500 are commonly used in clinical practice. Clinical use of TCM is based on theories such as Yin-Yang, Zangfu, Meridians and some other therapeutic principles that form essential basis for the properties and action of TCM. The properties are mainly covered in four natures (cold, cool, warm and hot), five flavors (pungent, sweet, sour, bitter and salty), lifting, lowering, floating and sinking, meridian tropism and toxicity. TCM practitioners prescribe remedies to treat diseases according to these theories and the properties of different TCM. TCM can be divided into 18 categories in clinical practice. These classifications are different from that of Western medicine, but the traditional classification and clinical use often provide important clues for modern scientific research. A combination of TCM is referred to as composite formulae (Fufang in Chinese). Composite formulae is often preferred over single TCM to treat diseases in order to enhance therapeutic efficacy and to reduce adverse effects. The rationale of TCM use is guided by compatible methodology of “Principal”, “Minister”, “Assistant” and “Servant”.

Many clinical studies have been done with TCM used singly and as composite formulae. The major differences between the practice of TCM and western medicine are the medicinal agents used and the underlying theories. There have been extensive studies on the pharmacokinetics and pharmacodynamics of TCM and TCM are comprised of multiple components with pleiotropic targets. As TCMs is a resource of drug discovery and alternative therapy for hard-to-cure diseases, more and more biomedical scientists make efforts to explore the therapeutic principles and active chemical components. TCMs commonly used for treatment of rheumatoid diseases includes Tripterygium hypoglaucum (Kunming Shanhaitang Pian) and Tripterygium wilfordii Hook. f. (Leigongtengduogan Pian).

Medicated diet for Arthritis patients

Ms. TUNG SH Jenny, Assistant Lecturer, HKU SPACE

According to the theories of Traditional Chinese Medicine (TCM), arthritis patients suffer from Qi deficiency. It is believed that these patients are infected by external pathogens like wind, coldness, dampness or heat, resulting in dysharmony of Qi, blood and nutrient-defense, with blockade of some meridians causing arthritis. Accordingly, nutritional treatment is guided by individual and seasonal factors as well as locations.

Clinical studies in TCM showed that arthritis patients of the wind-pattern type commonly present with multiple joint pain. Symptomatic relief may be achieved by taking congee with added herbal medicine like seed of Coix, sclerotia of Poria cocos wolf that fortify the spleen and drain dampness and root of Saposhnikovia divaricate Schischk that dispels wind and stops pain. Bark of the root of Acanthopanax gracilistylus can dispel wind and drain dampness, wine can dispel wind to free the collateral vessels and stop pain, and snakes are most effective for relieving pain by dispelling wind to free the collateral vessels. Snake wine is the mostly used nutritional supplement in Chinese society.

Patients of cold-dampness-pattern type will experience more pain than other types, that may be worsened by coldness. Processed root of Aconitum carmichaeli combined with lamb or wine are good at dissipating cold and stopping pain. Patients of dampness-pattern type commonly feel heavy pain and numbness. Treatment using black soybean, seed of Coix and the fruit of Chaenomeles speciosa are preferred. Patients of dampness-heat-pattern type commonly present with red joints with scorching pain, treatment for which involves food with added seed of Coix, leaves of Mentha haplocalyx, seeds of Phaseolus radiates and root of Pueraria lobata.

Patients with long medical history commonly show characteristics of liver-kidney deficiency, their deformed joints are restricted in extension and flexion, and the functions of body organs are generally deficient. They need food supplements rich in nutrition combined with herbs which can supplement Qi and blood of the liver and kidney, for example root of Panax Ginseng, root of Astragalus membranaceus, bark of Eucommia ulmoides, root of Dipsacus aspercides, bark of Cinnamomum cassia, combined with lamb, pork, snake meat and eel etc.

Disclaimer

Donation

Cash Donation via 7-ELEVEN®

You can make cash donation with minimum amount of HK$100 to "Hong Kong Arthritis & Rheumatism Foundation" via any 7-ELEVEN® in Hong Kong. The cashier will issue a transaction record for you when the transaction is completed. Please keep the transaction record and send to "Hong Kong Arthritis & Rheumatism Foundation, Flat 103-106, Nam Wai House, Nam Shan Estate, Sham Shui Po, Kowloon" to request for an official donation receipt.

7-11(HSBC)

3739 9987 6541 0360 3

Please present promotional materials with barcode for donation at any 7-ELEVEN® in Hong Kong.

CHARM is an official publication of the Hong Kong Arthritis and Rheumatism Foundation (HKARF), which is a charity entirely supported by voluntary contributions and public donations. If you wish to have further information about our work, or to make a donation or a monthly contribution, please contact us:

Hong Kong Arthritis & Rheumatism Foundation Ltd.

Flat 103-106, Nam Wai House,
Nam Shan Estate, Sham Shui Po, Kowloon

Tel : (852) 2346 6336
Fax : (852) 2346 6136

Email : mail@hkarf.org
Website : www.hkarf.org

Enbrel® etanercept 恩利®

ENBREL works differently[1]

- The only fully human soluble tumor necrosis factor (TNF) receptor[1-3]
- No neutralizing antibodies[1]
- Short half-life[1]
- Lower risk of tuberculosis[4]

With 17 years of collective clinical experience[5]

ENBREL is indicated for:

- Rheumatoid Arthritis (RA)
- Ankylosing Spondylitis (AS)
- Psoriatic Arthritis (PsA)
- Juvenile Idiopathic Arthritis (JIA)
- Adult and Children Plaque Psoriasis (PsO)

Pfizer Corporation Hong Kong Limited
16/F., Standope House, 738 King's Road, North Point, Hong Kong
Tel: (852) 2811 9711 Fax: (852) 2579 0399
Website: www.pfizer.com.hk

ENB10042P

References: 1. Enbrel® (etanercept) Hong Kong Prescribing Information (25mg Lyo powder - Nov 2009/25mg and 50mg PFS - Oct -2007). 2. Humira® (Adalimumab) Full Prescribing Information, Annual MIMS 20th Edition: 463-471. 3. Remicade® (Infliximab) Full Prescribing Information, Annual MIMS 20th Edition: 814-822. 4. Tubach F, Salmon D, Ravaud P, et al. Risk of tuberculosis is higher with anti-tumor necrosis factor monoclonal antibody therapy than with soluble tumor necrosis factor receptor therapy. Arthritis Rheum. 2009;60:1884-1894. 5. Data on file, Wyeth Pharmaceuticals. Further information is available upon request.

Important Safety Information: Serious infections, including sepsis and tuberculosis, have been reported with the use of ENBREL. Some of these infections have been fatal. These infections were due to bacteria, mycobacteria, fungi, and viruses. Opportunistic infections have also been reported. Patients who develop a new infection while undergoing treatment with ENBREL should be monitored closely. Administration of ENBREL should be discontinued if a patient develops a serious infection. Caution should be exercised when considering the use of ENBREL in patients with a history of recurring or chronic infections or underlying conditions which may predispose patients to infections. Treatment with ENBREL should not be initiated in patients with sepsis or risk of sepsis, or in patients with serious active infections. Before initiation of therapy with ENBREL, any patient at increased risk for tuberculosis (TB) should be evaluated for active or latent infection. Prophylaxis of latent TB infection should be initiated prior to therapy with ENBREL. Physicians should monitor patients receiving ENBREL for signs and symptoms of active TB, including patients who tested negative for latent tuberculosis infection. Applicable local guidelines should be consulted. Reports of malignancies affecting various sites have been received in the postmarketing period. In clinical trials of TNF antagonists, more cases of lymphoma were seen among patients receiving a TNF antagonist compared to control patients. However, there is an increased background lymphoma risk in RA patients with long-standing, highly active, inflammatory disease. Combining the results of controlled portions of clinical trials of ENBREL, more cases of non-melanoma skin cancer were seen in patients receiving ENBREL compared with control patients, particularly in patients with psoriasis. A possible risk for the development of lymphomas or other malignancies in patients treated with an anti-TNF agent cannot be excluded. Do not start ENBREL in patients with hypersensitivity to ENBREL or its components. Allergic reactions associated with ENBREL administration have been reported. If any serious allergic or anaphylactic reaction occurs, discontinue administration of ENBREL immediately. There have been rare reports of CNS demyelinating disorders in patients treated with ENBREL. Rare cases of pancytopenia, and very rare cases of aplastic anemia, some fatal, have been reported in patients treated with ENBREL. Exercise caution in patients who have a previous history of blood dyscrasias. Advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. If blood dyscrasias are confirmed, discontinue ENBREL. Reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus who are receiving anti-TNF agents, including ENBREL, has been reported. Patients at risk for HBV infection should be evaluated for prior evidence of the virus before initiating anti-TNF therapy. Although a causal relationship has not been established for ENBREL, caution should be exercised when administering ENBREL for patients identified as carriers for HBV. There have been reports of worsening of hepatitis C in patients receiving ENBREL, although a causal relationship with ENBREL has not been established. Physicians should use caution when using ENBREL in patients who also have moderate to severe alcoholic hepatitis.

ENBREL™ ABBREVIATED PACKAGE INSERT: 1. TRADE NAME: ENBREL™. **2. PRESENTATION:** Lyophilized powder (each vial contains 25 mg of etanercept in powder form, and supplied along with a clear colorless solvent for constitution. Reconstitute 25mg Enbrel in 1mL of solvent); Pre-Filled Syringe- PFS (each syringe contains 25mg or 50mg etanercept in solution for injection, solution is clear and colorless or pale yellow). **3. INDICATIONS:** Rheumatoid Arthritis (RA); Polyarticular juvenile idiopathic arthritis; Psoriatic arthritis (PsA); Ankylosing spondylitis (AS); Plaque psoriasis; Pediatric plaque psoriasis - lyophilized powder only. **4. DOSAGE: Adult: 1. RA, PA & AS:** 25mg twice/week or 50mg once/week; **2. Plaque psoriasis:** 25mg twice/week or 50mg once/week; alternatively 50mg twice/week up to 12 weeks followed, if necessary by a dose of 25mg twice/week or 50mg once/week. Continue with treatment until remission is achieved, for up to 24 weeks. Discontinue treatment if patient show no response after 12 weeks. If re-treatment is indicated, dose should be 25mg twice/week or 50mg once/week. **Children & adolescents: a. Juvenile idiopathic arthritis - age 4 years and above:** 0.4 mg/kg (up to a maximum of 25 mg/dose) twice/week as a subcutaneous injection with an interval of 3-4 days between doses. (50mg PFS for patients weighing 62.5 kg or more; 25 mg PFS is available from which doses less than 25 mg can be administered.) **b. Pediatric plaque psoriasis - Lyophilized powder only - age 8 years and above:** 0.8 mg/kg (up to a max. of 50 mg/dose) once/week, for up to 24 weeks. Treatment should be discontinued in patients who show no response after 12 weeks. If re-treatment is indicated, the dose should be 0.8 mg/kg (up to a maximum of 50 mg/dose) once week. **1. CONTRAINDICATIONS:** Hypersensitivity to the active substance, any of the excipients; Sepsis or risk of sepsis; Not to be initiated in patients with active infections incl. chronic or localized infections. **2. WARNINGS & PRECAUTIONS:** Infections; Tuberculosis; Hep. B virus reactivation; Worsening of Hep. C; Hypoglycemia in patients treated for diabetes; Concurrent treatment with anakinra/ abatacept; Alcoholic hepatitis; Allergic reactions; Immunosuppression; Malignancies and lymphoproliferative disorders; Live Vaccinations; Autoantibody formation; Hematologic reactions; CNS disorders; Combination therapy with DMARD; Renal and hepatic impairment; Congestive heart failure; Wegener's granulomatosis. **3. INTERACTIONS:** Concurrent treatment with anakinra/ abatacept/ sulfasalazine treatment. **4. PREGNANCY AND LACTATION:** Not recommended in pregnant women, and women of child-bearing potential should be advised not to get pregnant during Enbrel therapy. Can be excreted in human milk, a decision should be made whether to discontinue breast-feeding or to discontinue Enbrel while breast-feeding. **5. SIDE EFFECTS: Very common (≥1/10):** Infections (incl. upper respiratory tract infections, bronchitis, cystitis, skin infections); injection site reactions (incl. bleeding, bruising, erythema, itching, pain, swelling). **Common (≥1/100, <1/10):** Allergic reactions (see Skin and subcutaneous tissue disorders in full prescribing information); Autoantibody formation; Pruritus; Fever. **Uncommon (≥1/1000, <1/100):** Serious infections (inc. pneumonia, cellulitis, septic arthritis, sepsis); Thrombocytopenia; Uveitis; Angioedema; Urticaria; Rash; Psoriasiform rash; Psoriasis (new onset or exacerbation including all sub-types) and non-melanoma skin cancers; interstitial lung disease (incl. Pneumonitis and pulmonary fibrosis). **Reference:** HK PI Version Oct/2007 (PFS) Nov/2009 (Lyo powder). **Date of preparation:** May2010. **Identifier number:** ENBR5510. **FULL PRESCRIBING INFORMATION IS AVAILABLE UPON REQUEST.**