Chapter

1

Introduction

"Dear psoriasis,

Try as you might to slow me down,
I am living my life as fully as I can.

Yours sincerely-life"

"Psoriasis isn't contagious, but awareness is."

ETYMOLOGY

The word psoriasis is derived from Greek word *psora*, meaning "itch" and *-iasis*, meaning "action, condition". Galen (133–200 AD) was the first person to identify psoriasis as a health condition of the skin and penned the terminology. The Greeks used term *psora* to describe itchy skin conditions.[1]

Psoriasis is a polygenic skin disorder which is immune-mediated and involves mainly the skin and sometimes the nails with joints can be involved. It can present in any age group. Cases have been reported for its occurrence at birth and old age. Trauma, infections, medications, stress are various triggering factors that cause disease in genetically predisposed individuals.[2]

Sharply demarcated erythematous plaque with micaceous scale is the characteristic lesion. Sterile pustules are seen in some patients. Most common sites of involvement are scalp, elbow, knees, nails, and trunk. Extensor involvement is more common though flexors also get involved in extensive psoriasis.

Earlier it was believed to be a primary disease of keratinocytes. In the present scenario, increased levels of cAMP, TGF-alpha, epidermal growth factor receptor binding

protein kinase C point to abnormal T-cell function. Antigen-presenting cells, keratinocytes, Langerhans cells, macrophages, natural killer cells, Th-1, Th-17 and Th-22 helper cells, VEGF and keratinocyte growth factor are other factors in its pathogenesis. Recently, the role of NLR/CATERPILLAR family of genes has been postulated.[3]

Histologically, hyperkeratosis, parakeratosis, and acanthosis of the epidermis, tortuous and dilated vessels, and an inflammatory infiltrate composed primarily of lymphocytes are observed.

Psoriasis is a systemic disease process involving joints and up to 20–30% of the patients develop psoriatic arthritis. It is commonly asymmetric oligoarthritis involving small joints of hands and feet.

There is also an increased relative risk for metabolic syndrome and atherosclerotic cardiovascular disease in patients with moderate-to-severe psoriasis.

Treatment includes targeting key effector immune cells and cytokines using drugs like methotrexate, cyclosporine, phototherapy, biologics, etc. so as to break the vicious cycle.

PREVALENCE

Prevalence of psoriasis in different populations varies from 0% to 11.8%. For most of the data given, the range extends from around 0.5% to close to 2.5%. In USA, the prevalence of psoriasis was estimated to be around 4.6%, while in Canada it was 4.7%. In India it is found that the incidence of psoriasis among total skin patients ranged between 0.44% and 2.2%, with overall incidence of 1.02%. It is twice more common in males compared to females, and most of the patients are in their third or fourth decade at the time of presentation. About 30% of individuals with psoriasis will develop psoriatic arthritis and up to 15% patients may develop arthritis alone without skin involvement. Skin manifestations of psoriasis tend to occur before arthritic manifestations in about 75% of cases. Nail psoriasis occurs in 40–45% of people with psoriasis, affecting the skin and has a lifetime incidence of 80–90% in those with psoriatic arthritis.

AGE

Psoriasis can develop at any age, although it commonly appears between the ages of 15 and 22 years. A second peak appears during the 60–69 years age range. Females tend to develop psoriasis slightly earlier than males, and those with a family history also have an earlier age of onset. The disease may last for just a few weeks or for lifetime, with alternating periods of relapses and remissions. It is difficult to predict the course of the disease.

ETHNICITY

There are 44 known sequences of genes that influence psoriasis development. The scientists found that 10 of those gene sequences are only found in Caucasians and this explains why psoriasis is 10 times more common among Caucasians than ethnic Chinese persons.

PREDISPOSING FACTORS

Psoriasis is associated with risk factors like genetic susceptibility, physical trauma, infections, drugs, sunlight, stress, immunological alterations, etc.

CLINICAL FEATURES

Plaque psoriasis is the most common form of the condition (90% of people with psoriasis) and is characterised by well delineated red, scaly papules and plaques.[4] The plaques merge to involve large areas. The extent of involvement is variable, ranging from a few localised patches at extensor sites, to generalised involvement involving any site. Rarely, psoriasis may involve the whole body to cause erythroderma, in which case it becomes difficult to diagnose. In patients recovering from psoriatic erythroderma, the localised psoriatic plaques eventually may start appearing.

Flexural (also known as inverse or intertriginous) psoriasis refers to plaque psoriasis at submammary, groin, axillary, genital and natal cleft sites, and is typically less scaly.

Seborrheic psoriasis ("sebopsoriasis") is similar in appearance and distribution to seborrheic dermatitis (hence the

name) and may occur in isolation or associated with plaque psoriasis elsewhere.

Guttate psoriasis is an acute eruption of small (<1 cm) papules of psoriasis which appear over a period of a month or so and is preceded by a streptococcal infection in majority of patients.

Pustular psoriasis includes generalised pustular psoriasis (GPP) and localised forms (i.e. palmoplantar pustulosis and acrodermatitis continua of Halopeau).

Nail involvement occurs in around 50% of all those affected and are more common in those with psoriatic arthritis. Nail involvement is also common in patients with a long history of psoriasis.

Occasionally, combinations of the different types develop simultaneously or sequentially over time in the same person.

The term "difficult-to-treat sites" encompasses the face, flexures, genitalia, scalp, palms and soles and are so called because psoriasis at these sites may have an especially high impact, may result in functional impairment, require particular care when prescribing topical therapy and can be resistant to treatment.

COMORBIDITIES

Aside from the burden of psoriatic arthritis, and psychological morbidity, a number of studies have suggested that people with psoriasis are also at risk of cardiovascular disease. Risk factors include obesity, type 2 diabetes mellitus,[5] metabolic syndrome, excess alcohol intake or alcoholism, smoking and hyperlipidaemia (which may be partly iatrogenic due to agents such as ciclosporin and acitretin). Some studies suggest that people with psoriasis, particularly those with severe disease, may also be at increased risk of lymphoma and nonmelanoma skin cancer. The relative influence of known confounders such as concomitant therapy with immunosuppressants, phototherapy, smoking, and alcohol is unclear.

TREATMENT

Before treating the patient, various tools used to assess the disease activity and severity so as to evaluate the treatment includes:

- Body surface area (BSA)
- Psoriasis area and severity index (PASI)
- Physician global assessment (PGA)
- National Psoriasis Foundation-psoriasis score (NPF-PS) index
- Nail psoriasis severity scoring index (NAPSI)

Treatment of psoriasis has undergone much evolution since last many years. It was recognized even in ancient times that sunlight seemed to have an effect on the severity of symptoms of psoriasis and, to an extent, this was utilized in the treatment of the condition. Hippocrates (460–377 BC) was the first physician to use coal tar in the treatment of psoriasis to increase sensitivity to sunlight, but he also supported the use of topical arsenic for the treatment of psoriasis. However, with recent advances, stepwise approach to novel and new drugs is needed in most patients. Based on these, first-line therapy describes the traditional topical therapies such as corticosteroids, vitamin D and analogues, dithranol and tar preparations. Second-line therapy includes phototherapy, broad or narrow band ultraviolet (UV) B light, psoralen plus UVA light (PUVA), and nonbiological systemic agents such as ciclosporin, methotrexate and acitretin. Third-line therapy refers to systemic biological therapies that use molecules designed to block specific molecular steps important in the development of psoriasis such as TNF antagonists adalimumab, etanercept and infliximab, and ustekinumab (anti-IL12-23 monoclonal antibody).[6]

PSYCHOLOGICAL IMPACT

Skin condition like psoriasis has a visible psychological and social impact on patient with complaint of one of the following:[7]

- Feelings of guilt, shame, embarrassment or helplessness

- Poor self-esteem and low self-worth, sometimes leading to social isolation
- Sexual dysfunction, due to self-consciousness or painful lesions
- Suicidal ideation, which occurs in up to 10% of patients with psoriasis
- Decreased vocational opportunities for people with psoriasis, due to discrimination or perceived restrictions on career choices, which can lead to employment and economic difficulties
- Interference with activities of daily living, including dressing, bathing and sleeping
- A negative impact on the patient's family functioning, including financial hardship, caregiver burnout and degeneration of patient-family relationships
- Stress, which can trigger flares of psoriasis in 43–68% of patients
- Depression, due to a decreased quality of life.

For treating physician, it is utmost important to discuss expected outcomes before treatment is initiated, in order to ensure that realistic expectations are in place. It is also beneficial to discuss whether total symptom relief is a necessary component to living a better life or not. In addition, addressing patients to find the right words to explain their visible symptoms to others can help them feel less self-conscious and more confident in a public setting and help them build the skills required to reduce the psychosocial impact of their condition.

DISEASE COURSE AND PROGNOSIS

Psoriasis is chronic dermatoses affecting the skin with long term remission or relapses depending upon individual and its treatment. Most people with psoriasis experience nothing more than mild skin lesions that can be treated effectively with topical therapies, however psoriasis is known to have a negative impact on the quality of life of both the affected person and the individual's family members. Depending on the severity and location of outbreaks, individuals may experience significant physical discomfort and some disability.

REFERENCES

1. Gruber F, Kastelan M, Brajac I (2004). "Psoriasis treatment-yesterday, today, and tomorrow". Acta Dermatovenereol Croat.
2. Farber EM, Nall L. Epidemiology: natural history and genetics. In: Roenigk Jr HH, Maibach HI, editors. Psoriasis. New York: Dekker; 1998. p. 107–57.
3. Roberson, E. a. (2010). Psoriasis genetics : breaking the barrier. Trends in Genetics, vol. 26(9),415–23.
4. Parisi R, Griffiths CEM, Ashcroft DM. Systematic review of the incidence and prevalence of psoriasis. British Journal of Dermatology 2011;165(6):e5.
5. Qureshi AA, Choi HK, Setty AR, Curhan GC. Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses. Archives of Dermatology 2009;145(4): 379–82.
6. National Institute for Health and Clinical Excellence. Adalimumab for the treatment of adults with psoriasis, NICE technology appraisal 146. London: National Institute for Health and Clinical Excellence; 2008.
7. Fletcher T; Psoriasis And Psoriatic Arthritis Alliance (PAPAA). The psychosocial burden of psoriasis. 17 June 2013.

Chapter
2

Etiopathogenesis

1. GENETIC FACTORS

A positive family history is seen in 35% to 90% of patients with psoriasis. A study showed that the risk of their child developing psoriasis was 41% if both parents had psoriasis, whereas if only one parent were affected, the risk was 14% and the risk was 6% if just one sibling had psoriasis.[1] The inheritance is polygenic. The responsible genes are "jumping genes or retrotransposons" as their locations vary among populations (Table 2.1).

Classical genome wide analysis has identified at least nine chromosomal loci with statistically significant evidence for linkage that is PSORS1-PSORS9 (psoriasis susceptibility) (Table 2.2). However, the most important genetic region is PSORS1. It is located in HLA class I region on chromosome 6p and it accounts for up to 50% of psoriasis risk. HLA-Cw-6 is the most common gene associated and it is important in antigenic stimulation. The corneodesmosin (CDSN gene) is also contained in PSORS1 locus and encodes for a protein in differentiated keratinocytes.

HLA-Cw-6 is strongly associated with age of onset of psoriasis. HLA-Cw6 is expressed in 90% of the patients with early-onset psoriasis and in 50% of those with late-onset psoriasis. Early-onset psoriasis, a positive family history of psoriasis and expression of HLA-Cw-6 is type 1 psoriasis and late-onset disease, no family history, and a lack of expression of HLA-Cw-6 is type 2 psoriasis.[2–3]