Psoriatic arthritis is a chronic inflammatory arthropathy associated with skin psoriasis. It is considered a unique arthropathy with distinct clinical and radiologic features. Up to 40% of patients with psoriasis may develop psoriatic arthritis. Psoriasis usually precedes psoriatic arthritis, so dermatologists are in a critical position for screening patients of psoriatic arthritis early in the disease course. Psoriatic arthritis may be challenging to diagnose, especially for dermatologists, because it has an insidious disease course, non-specific symptoms, and no specific biomarkers. Psoriatic arthritis is a polygenic autoimmune disorder of unknown etiology, but immunologic roles have recently been validated. In recent years, treatment modalities have rapidly advanced in the fields of psoriasis and psoriatic arthritis. Biologic agents, including TNF-α inhibitors and anti-IL12/23 agents, have shown dramatic improvement.

Key Words: Dermatologist, Psoriasis, Psoriatic arthritis

INTRODUCTION

Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. Although PsA was once described as a variant of rheumatoid arthritis (RA), it has been included in the group of spondyloarthopathies. PsA was first defined by Moll and Wright in 1973 in patients who were seronegative for rheumatoid factor (RF) with positive history of psoriasis, current skin or nail psoriasis, and inflammatory joints of axial disease [1].

The exact estimation of PsA prevalence among psoriasis patients is difficult because several epidemiologic studies on PsA have not used validated criteria. In addition, PsA may present with considerable geographic variations in occurrence [2]. However, recent estimates of epidemiology might reflect an increasing recognition of the disease. PsA incidence has increased from 5% to 40% among patients with psoriasis [2-5]. Because PsA might be as common as psoriasis, it should not be overlooked.

Approximately 40% to 60% of PsA patients develop erosive arthropathy, and 17% have five or more deformed joints [6,7]. A delay in diagnosis and treatment may lead to erosive arthropathy, further progressing to physical disability and deformities [4]. Dermatologists who lack expertise in PsA might miss an opportunity for early treatment that could prevent functional joint disability. Unfortunately, many dermatologists are indifferent to psoriatic arthritis with any degree of severity and instead search for signs of hidden arthritis or skin disorders.

CLASSIFICATION AND DIAGNOSIS

The association between arthritis and psoriasis was first described by Alibert in 1818 and was designated psoriasis arthritique by Bazin in 1860 [8]. At that point, distinctive arthritis associated with psoriasis became widely accepted. However, in the 1950s, PsA was grouped with RA as a “rheumatoid
variant” or “rheumatoid spondylitis” [8]. Subsequently, the distinct nature of PsA was emphasized using clinical criteria. In 1973, Moll and Wright defined PsA and classified it into five subsets of distal interphalangeal arthritis, asymmetrical oligoarthritis, symmetrical polyarthritis, spondylitis, and arthritis mutilans [1]. Although several diagnostic and classification criteria have been developed, they have not been commonly accepted.

A diagnosis of PsA is based on clinical manifestations. Physicians usually make a diagnosis of PsA based on characteristic arthritis patterns together with the absence of rheumatoid factor and the presence of psoriasis skin and nail lesions. Since there are no specific serologic tests to confirm PsA diagnosis, radiographs can be helpful.

In 2006, simple and highly specific diagnostic criteria for PsA were introduced. These criteria, called the classification criteria for psoriatic arthritis (CASPAR) [9], provide better sensitivity (91.4%) than all previous criteria while maintaining high specificity (98.7%). To diagnose PsA according to CASPAR, patients should have inflammatory joint disease (peripheral, axial, or enthesitis) with at least three points from the five categories [9]. CASPAR criteria can be modified for dermatologists who screen for PsA among patients with skin psoriasis, as shown in Table 1. PsA classification is still an area of ongoing international discussion.

The detection of PsA requires detailed joint examination, which is not usually performed in a routine dermatologic clinic. Every psoriasis patient with musculoskeletal symptoms should ideally be referred to a rheumatologist, but this is impractical. A simple screening tool that identifies psoriasis patients who are more likely to have PsA would be tremendously valuable to dermatologists and other healthcare providers. A screening tool would also raise awareness in patients with psoriasis who are unaware of the relationship between psoriasis and musculoskeletal symptoms. Several appropriate PsA screening tools have been developed and are used worldwide, including PEST (Psoriasis Epidemiology Project), ToPAS (Toronto Psoriatic Arthritis Screening Tool), and PASE (Psoriatic Arthritis Screening and Evaluation Tool) [10-12].

### PATHOGENESIS

PsA is a polygenic autoimmune disorder of unknown etiology in which genetic susceptibility, environmental factors, and immune mechanisms play crucial roles [9]. Human leukocyte antigen (HLA)-C within the major histocompatibility complex (MHC) region is the strongest genetic association for PsA. Other class I HLA antigens associated with PsA include HLA-B13, B27, B38, B39, and B57. HLA-B27 is present in 20% to 60% of PsA patients, with increased incidence in the axial or spondylitic forms. HLA-B38 and B39 are most strongly associated with peripheral arthritis [8]. Regarding HLA class II molecules, DR4 is more commonly found in the erosive form, while DR7 is more commonly found in peripheral involvement [8]. HLA-B27 prevalence is much lower in axial PsA than in ankylosing spondylitis (AS), and it is strongly influenced by ethnicity [13,14].

Regarding immunopathogenesis, there is prominent lymphocytic infiltrate in both the skin and joints that is localized to dermal papillae in the skin and the sublining layer stroma in joint and inflammatory entheses. T lymphocytes, particularly CD4+ cells, are the most common inflammatory cells, with a CD4+/CD8+ ratio of 2:1 in the synovial fluid and peripheral blood. CD8+ T cells are more common at entheses. The inflammatory mechanism of PsA involves autoproliferation of T cells as well as production of cytokines from type 1 helper T cells (Th1) and type 17 helper T cells (Th17). These include tumor necrosis factor (TNF)-α, interferon (IFN)-γ, interleukin (IL)-1, IL-6, IL-8, IL-17, IL-22, IL-23, and intercellular adhesion molecule (ICAM)-1 [8,15]. High levels of TNF-α, IL-6, IL-8, IL-10, and matrix metalloproteinases (MMP) are present in the joint fluid, psoriatic plaque, and serum of patients with early PsA.

Table 1. CASPAR criteria (modified for dermatologists) for diagnosing psoriatic arthritis

| Psoriasis (skin and/or scalp) patients with inflammatory joint diseases, spine or tendons/entheses can be diagnosed with psoriatic arthritis if they fit at least one of the following categories: |
|---|
| Psoriatic nail dystrophy |
| Negative test result for rheumatoid factor |
| Dactylitis (now or in patient’s history) |
| Radiologic evidence of juxta-articular new bone formation |
CLINICAL ASPECTS AND DIFFERENTIATION OF PSORIATIC ARTHRITIS

PsA onset age is in the range of 30 to 50 years, and the condition affects men and women almost equally [4]. In approximately 70% of cases, psoriasis precedes the development of PsA by an average of 10 years. In approximately 15% of cases, PsA precedes the onset of psoriasis by more than 1 year, and in approximately 15% of cases the two conditions occur within 12 months of each other [6]. The pattern of joint involvement is variable and can change over time. There are two major patterns of arthritis with PsA: peripheral joint disease, which can be oligoarticular (≤4 involved joints) or polyarticular (≥5 involved joint), and skeletal or axial disease with or without peripheral arthritis [16]. Peripheral arthritis is generally more common. Approximately 95% of patients with PsA have involvement of the peripheral joints, predominantly the polyarticular form, while a minority has the oligoarticular form [17]. About 5% of patients have exclusively axial involvement, whereas 20% to 50% of patients have involvement of both the spine and peripheral joints, with peripheral joint involvement having predominance. Moll and Wright emphasized asymmetric arthritis as the most frequent pattern in PsA [1]. Several other recent studies confirm that asymmetric oligoarthritis is the most common pattern in early phase PsA [3,18]. Involved joints in PsA are usually less tender, less swollen, and less symmetric than in RA. As mentioned above, there might be ethnic differences in the pattern of joint involvement. In a Korean study, axial PsA was the major pattern [13]. Patients with oligoarticular peripheral PsA seem to have a shorter disease duration than patients with polyarthritis [6,19].

DIP arthritis and arthritis mutilans represent distinctive features of PsA. In the largest clinical series, DIP arthritis was reported in 1% to 59% of patients with PsA. In this series, disease duration increased with frequency. DIP arthritis is often associated with dactylitis and nail dystrophy [20,21]. Dystrophic nail changes, including pitting, subungual hyperkeratosis, and transverse grooves, are more frequent in PsA than psoriasis [8]. In roughly 5% of patients with longstanding disease, erosive arthritis causes complete resorption of the entire phalanges. This leads to characteristic clinical features of ‘falling joints’ or ‘opera glass fingers’, which is termed arthritis mutilans [22].

Clinical features are important in differentiating peripheral PsA from seronegative RA with coincidental psoriasis. Classical PsA affects the distal interphalangeal (DIP) joints, whereas RA affects the proximal interphalangeal (PIP) joint more frequently. Early phase PsA differs from RA by its asymmetric pattern.

Another important differential diagnosis to consider in patients with PsA is osteoarthritis (OA). DIP involvement is possible in both PsA and OA. However, the classic Heberden’s nodules in OA are bony spurs whereas the DIP involvement in PsA is merely joint inflammation. Morning stiffness and stiffness after prolonged inactivity are common in PsA whereas stiffness tends to occur with joint activity in OA. Although PsA occurs equally in males and females, OA of the hands and feet is more frequent in females. Dactylitis, enthesitis, and sacroiliitis are common in PsA but are generally not present in RA and OA.

There are a wide variety of clinical manifestations and peripheral arthritic symptoms in axial PsA that may overshadow those related to spinal inflammatory involvement. Patients with axial PsA may have similar clinical features to patients with AS. However, asymptomatic involvement of the spine and sacroiliac joints may occur more often in PsA than AS. Furthermore, patients with axial PsA have asymmetric disease that tends to be less severe. While the radiologic features vary, they can be helpful in detecting asymptomatic disease and differentiating axial PsA from AS. However, bilateral fusion of the sacroiliac joint may occur with disease progression. In axial PsA, spondylitis may affect any spinal level in a skip fashion or it may affect only the cervical spine while sparing other tracts of the axial skeleton [23]. Axial PsA is characterized by a better prognosis than AS, and patients with PsA seldom progress to ankylosis.

Enthesitis is usually defined by the presence of tenderness and swelling on palpation or pressure in the insertion sites of tendons, ligaments, or capsules. Clinical features of enthesopathy include pain and loss of function. The pain intensity depends on disease location and severity. Pain is usually more pronounced after a period of rest and improves with movement. Entheses of the lower limbs are more frequent.
than those of upper limbs. Enthesitis represents a hallmark of the clinical features of PsA and is now regarded as the primary lesion [9]. Achilles tendon enthesitis usually coexists with tenosynovitis and contributes to the ‘bomb-shaped’ tendon [18].

Dactylitis is defined as diffuse swelling of a digit, or ‘sausage-shaped digit’ (Fig. 1). It may occur in one or more digits concomitantly with the typical signs of inflammation, such as swelling, redness, pain, warmth, and limited range of motion. Dactylitis has long been recognized as one of the cardinal features of PsA [1]. It is an expression of active PsA and will respond well to anti-TNF-β therapy [24]. Table 2 compares PsA with other rheumatologic conditions.

Table 2. Comparison of psoriatic arthritis with rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis [25]

|                  | PsA                | RA             | OA        | AS             |
|------------------|--------------------|----------------|-----------|----------------|
| Peripheral disease | Asymmetric         | Symmetric      | Asymmetric| No             |
| Sacroilitis      | Asymmetric         | No             | Symmetric | Symmetric      |
| Stiffness        | In morning and/or with immobility | In morning and/or with immobility | With activity | Yes           |
| Female: male ratio | 1:1               | 3:1            | Hand/foot more common in female patients | 1:3           |
| Enthesitis       | Yes                | No             | No        | No             |
| High titer rheumatoid factor | No               | Yes            | No        | No             |
| HLA association  | CW6, B27          | DR4            | No        | No             |
| Nail lesions     | Yes                | No             | No        | No             |
| Psoriasis        | Yes                | Uncommon       | Uncommon  | Uncommon       |

AS: ankylosing spondylitis, OA: osteoarthritis, PsA: psoriatic arthritis, RA: rheumatoid arthritis.

Skin lesions such as psoriasis can be localized, diffuse, guttate, or pustular (Fig 2). There is no specific skin involvement associated with a certain pattern of joint involvement. Thus, patients with any pattern and degree of arthritis can develop psoriasis vulgaris, severe generalized pustular psoriasis, or erythrodermic psoriasis [8]. Iridocyclitis represents the most frequent extra-articular feature, with an estimated prevalence of 2% to 25% of cases [6,7,9,19]. Iridocyclitis is characterized by an acute onset over 1-2 days, eye pain, redness, miosis, photophobia, and vision blurring.

CONCLUSION

What is the role of dermatologists in the field of PsA–screening, diagnosis, or management? Some assert that if the primary problem is skin psoriasis, PsA can be managed by a dermatologist. If the chief complaint is a joint symptom,
Dermatologists can conduct a full screening and confirm PsA in psoriasis patients who are visiting a dermatologic department. When managing PsA, oligo- and DIP arthritis can be managed by dermatologists, whereas polyarthritis, spondylitis, and arthritis multilans should be referred to rheumatologists (Fig. 3).

Recently, more physicians have become aware of the relationship between PsA, atherosclerosis, and increased cardiovascular risk in patients with PsA. Psoriasis and PsA should no longer be regarded as diseases limited to joint or skin. They should be accepted as systemic disorders. Clinical dermatologists should be thoroughly aware of the nature of PsA, and an interdisciplinary approach is needed.

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