An Overview about Clinical Findings of Psoriatic Arthritis and Its Ocular Manifestations

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Abstract

Psoriatic arthritis (PSA) is a psoriasis-related axial and/or peripheral inflammatory arthritis. Its symptoms include distal interphalangeal joint involvement, asymmetric arthritic distribution, dactylitis, enthesitis, spinal involvement, and frequent connection with HLA-B27. PSA can cause considerable disability, as well as a reduction in life quality and expectancy. Early diagnosis and treatment lead to improved outcomes, and this has become an apparent issue since the introduction of effective medicines. Many people have psoriasis for several years before to or concurrently with the onset of arthritis. The ocular manifestations of psoriasis can almost affect any part of the eye. There is a significant impact of disease severity on patient- reported psychosocial and physical quality of life, including loss of work productivity. However, eye affection in psoriatic patients are easily overlooked without a dedicated ocular examination. Also, surveys into the quality-of-life implications of psoriasis do not give much importance to ocular manifestations. Therefore, it is important to recognize the incidence and varied presentation of eye diseases in psoriasis patients, in order to make an early diagnosis and prevent ocular morbidity. Prevalence of ocular affection is variable among studies in the literature. It varies according to the population sampling, methods of studying, demographic data of patients, severity and duration of psoriasis The eye affection in psoriasis can lead to various complications including vision loss. These manifestations or complications may be seen more in psoriasis patients with arthritis **but** have also been occurred in psoriasis patients without arthritis. These affections are usually neglected by the physician who is not specifically looking for them.

Key Words: Psoriatic Arthritis, Ocular Manifestations

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Introduction

Psoriatic arthritis (PSA) is a psoriasis-related axial and/or peripheral inflammatory arthritis. Its symptoms include distal interphalangeal joint involvement, asymmetric arthritic distribution, dactylitis, enthesitis, spinal involvement, and frequent connection with HLA-B27 **(1).** Five patterns of joint inflammation were identified. They include distal interphalangeal predominant arthritis (DIP), arthritis mutilans, symmetrical polyarthritis, asymmetrical oligoarthritis and psoraitic spondylitis **(2)**.

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According to BPS (2020b) shallot production in PSA can cause considerable disability, as well as a reduction in life quality and expectancy **(3).** Early diagnosis and treatment lead to improved outcomes, and this has become an apparent issue since the introduction of effective medicines **(4).** Many people have psoriasis for several years before to or concurrently with the onset of arthritis. **(5).**

Epidemiology:

The epidemiology of psoriatic arthritis is complex and varies greatly among different population groups. Among the general population, it is projected to have a prevalence of 0.05 % to 0.25 %, while in psoriasis patients, it is estimated to have a frequency of 6 percent to 41 % **(6).**

Misdiagnosis contributes to the heterogeneity of psoriatic arthritis in psoriasis. According to a meta- analysis, the rate of untreated psoriatic arthritis could be as high as 15.5 %. Psoriatic arthritis commonly appears in the30s and 40s with equal distribution among males and females **(7)**.

Etiopathogenesis:

Environmental Factors:

Psoriasis was assumed to be triggered by a mix of genetic, epigenetic,and environmental variables which can alter genetic diversity and epigenetic modifications. Moreover, T lymphocytes represent a critical mediator in psoriasis. In addition, Environmental factors such as food, microbial infections, or ultraviolet (UV) radiation exposure, as well as unhealthy habits (smoking) could cause many changes in people who have a latent genetic vulnerability to inflammatory illnesses **(8).**

The combination of environmental and genetic factors is now widely accepted as contributing to the development and presence of clinical symptoms of psoriasis **(9)**

Infection:

Although the antigen required to activate T cells is unknown, there is a link between microorganisms and psoriatic lesions, such as streptococcal- hemolytic group A throat infections linked to guttate psoriasis **(10).**

A possibility of improving psoriosiform dermatitis, inhibiting differentiation of T cells, and the production of pro-inflammatory IL-17 and IL- 22 antibiotics aimed at Gram negative and Gram-positive bacteria were demonstrated. Also, T cells founded in psoriatic lesions would react to the streptococcal and staphylococcal peptidogly in an antigen-specular manner **(8).**

Trauma:

There is evidence that trauma contributes to the etiology of PSA. The emergence of psoriatic lesions following trauma to healthy skin areas of psoriasis patients, known as the Koebner phenomenon, occurs in 24 to 52 % of psoriasis patients. Subclinical trauma may also contribute to DIP joint arthritis, dactylitis, and enthesitis. A number of studies had found a link between traumatic injury and the onset of PSA at the site of injury. Moreover, psoriatic patients who were exposed to trauma had a higher risk of PSA than others **(11).** 6134

Clinical Features of Psoriatic Arthritis

PSA is characterized by a wide variety of articular, extra-articular features and comorbidities **(12).**

A) Articular Manifestations:

The patterns of joint involvement in PSA are heterogeneous. They include asymmetric oligoarticular affections. A rheumatoid arthritis-like distribution involving the symmetrical small joints of the hands, feet and wrists may occur in psoriatic arthritis. Moreover, the damaging effects of PSA are equally comparable to those seen in rheumatoid arthritis. DIP arthritis and arthritis mutilans, represent distinctive features of PSA. In the largest clinical series DIP arthritis has been reported in 34.5% of cases, with an increased frequency with disease duration. DIP arthritis is often associated with dactylitis and nail dystrophy. In more severe cases the erosive arthritis causes the complete resorption in entire phalanges, leading to arthritis mutilans **(13).**

Due to the loss of bone support; the finger soft tissues collapse leading to characteristic clinical features including 'falling joints'and digital telescoping with aspects of opera glass finger **(12).**

Axial PSA:

Spinal involvement in PSA includes inflammation in both the sacroiliac joints and the apophyseal joints of the spine. The distribution in PSA tends to be asymmetric. Sacroilitis may be absent or asymptomatic, and concomitant peripheral arthritis symptoms may overshadow those related to spinal inflammatory involvement. Radiologic features are variable and often useful to differentiate axial PSA from ankylosing spondylitis **(14).**

Clinically, axial inflammatory involvement causes pain and stiffness of the affected spinal tract or alternating buttock pain when the inflammatory involvement of the sacroiliac joint predominates. Axial PsA may only affect the cervical spine with sparing of other tracts of the axial skeleton **(12).**

Extra- Articular Manifestations:

1- Enthesitis, Tenosynovitis:

Enthesitis represents a hallmark of the clinical spectrum of PSA. It signifies inflammation at the insertion of tendons, ligaments, joint capsule fibers, or fascia insertion sites into bone (either in appendicular or axial skeleton). The Achilles tendon, plantar fascia, and lateral epicondyles are the most commonly detected sites. Over time, enthesitis can cause inflammatory and structural changes, causing cystic and erosive reactions. Prevalence of enthesitis in patients withspondyloarthropathies ranges between 10% and 60% of cases **(15).**

The clinical features of enthesopathy include pain and loss of function. Pain is usually more pronounced after a period ofrest, with improvement with movement. Peripheral enthesitis produces pain but may also be asymptomatic and only revealed by imaging techniques such as ultrasonography, especially if combined with power Doppler.Moreover, Achilles tendon enthesitis usually coexists with tenosynovitis and contributes to the 'bombe`- shaped' aspect of the tendon **(12).**

2- Dactylitis:

Dactylitis, or the 'sausage-shaped digit', has long been recognized as one of the cardinal features of PSA occurring in 5.6–53% of reported cases **(12).** It is a diffuse swelling of the entire digit. The swelling is believed to be due to a combination of flexor tenosynovitis andinterphalangeal joint synovitis **(16).**

Dactylitis is primarily diagnosed by clinical examination and is eventually supported by ultrasound and magnetic resonance imaging. It may occur in one or more digits concomitantly with presence of the typical signs of inflammation such as swelling, redness, pain, warmth and limited range of motion. Sometimes, after acute onset, a chronic phase with persistence of painless soft tissue swelling of the digit may be observed. In all cases the swelling of the digit is related to the inflammatory process affecting the underlying bone to the digit soft tissuewithout involving the tendon **(16).**

2- Skin Manifestations:

Skin psoriasis is a prerequisite for the diagnosis of psoriatic arthritis.

The most common form of manifestation is plaque psoriasis with predominant affection of the extensor sides of the extremities and the scalp. Also face and large body folds including the genitoanal region are often affected **(17).**

3- Nail changes:

Nail involvement is a common feature of both skin psoriasis and psoriatic arthritis. It has been estimated to occur in up to 50% of patients with uncomplicated skin psoriasis and is even more prevalent (63% - 83%) among patients with PSA **(18).**

The main clinical findings of nail psoriasis include pitting of the nails, an increased thickness of the horny layer of the nail, separation of the nail from the nail bed, inflammation of the folds of skin surrounding the nail, and abnormal whitening of the nails. Other patterns include subungual distal hematoma, multiple transverse grooves, and trachyonychia, a condition where the nails are rough, like sandpaper. Also, brownish-yellow spots (oily spots) may be present. It reprents collection of skin debris and fluid in the space left by nail separation **(17).**

The ocular manifestations of psoriasis can almost affect any part of the eye. There is a significant impact of disease severity on patient- reported psychosocial and physical quality of life, including loss of work productivity **(19)**. However, eye affection in psoriatic patients is easily overlooked without a dedicated ocular examination. Also, surveys into the quality-of-life implications of psoriasis do not give much importance to ocular manifestations. Therefore, it is important to recognize the incidence and varied presentation of eye diseases in psoriasis patients, in order to make an early diagnosis and prevent ocular morbidity **(20)**.

Prevalence of ocular affection is variable among studies in the literature. It varies according to the population sampling, methods of studying, demographic data of patients, severity and duration of psoriasis.

Anyhow, psoriasis affects 1–3 % of the adult population with higher occurrence of ocular lesions in males and during psoriasis exacerbations **(21).**

Psoriatic arthritis (PSA) related inflammatory ocular manifestations may affect multiple ocular structures and can occur in up to 32.63% of patients (Peluso et al, 2015). Ocular symptoms, which are observed in PSA patients and may be directly associated with the diseaseor secondary to treatment. Alongside this, ophthalmic manifestations have also been described in patients having psoriasis sin arthritis (PSO) **(22).**

The eye affection in psoriasis can lead to various complications including vision loss. These manifestations or complications may be seen more in psoriasis patients with arthritis but have also been occurred in psoriasis patients without arthritis. These affections are usually neglected by the physician who is not specifically looking for them. Psoriatic eye manifestations may precede articular changes. Therefore, regular eye examinations are

recommended in psoriasis patients by the expert dermatologist and ophthalmologist who should remain mindful of a known history of psoriasis when evaluating ocular symptoms **(23).**

Campanati et al (24) reported that the ocular involvement in psoriasis is poorly understood. However, many etio-pathogenetic mechanisms had been contributed to the development of ocular manifestations. They included direct eye involvement with psoriatic plaques, psoriasis-related immune-mediated inflammatory processes, and complications of psoriasis treatments; especially oral retinoids and phototherapy . Ocular problems of psoriasis are many and occur much later, after the skin involvement. Additionally, they can affect any part of the eye with a variable incidence among literature **(25).**

Cantini et al (12) reported that anterior uveitis is the most common ocular manifestation associated with PSA (estimated prevalence 2–25%). In contrary, **Lima et al (26)** and **Aragona et al (22)** reported that dryeye (keratoconjunctivitis sicca) is the commonest ocular manifestations related to psoriatic arthritis (PsA).

Lima et al (26) reviewed many studies that investigated prevalence of eye affection in psoriatic patients. They found that the most frequently observed ophthalmic complications were conjunctivitis (19.6%), uveitis (5%), blepharitis (12.5%), cataracts (10%), glaucoma (10%), superficial punctate keratitis (22.5%), pinguecula (20%), and keratoconjunctivitis sicca (15%).

On the other hand, **Ramos et al (27)** reported that the most common ophthalmic disorders were dry eye (60.9%), cataracts (56.5%), blepharitis (47.8%), keratitis (43.5%), meibomitis (30.4%), pterygium (26, 1%), and pinguecula (13%). Also,more than half of all patients demonstrated recent onset (>5 years) and severe symptoms according to Clinical Disease Activity Index for Psoriatic Arthritis (DAPSA).

The following are examples of the reported ocular affections in psoraitic arthritic patients (PSA):

a. Eyelids:

Blepharitis is found to be the most common ocular finding in psoriatic patients. When the skin around the eye is involved, it appears in the form of erythema, edema, and plaque formation which can lead to complications like trichiasis, madarosis, cicatricial ectropion. Furthermore, in severe cases, desquamation of eye lid skin can compromise with the person's vision. Although, the mechanism of this dysfunction is not known, it was supposed to be due to increased epithelial turnover leading to high volumes of cell production and subsequent shedding that may ultimately lead to a mechanical block through the meibomian ducts **(28).**

Other manfestations of psoraitic lid affection include appearance of psoriatic plaques on the lid and lid margin. Patients usually complaint of burning and itching which cause considerable discomfort. In addition, the eyelids may be red, swollen, crusted and flaky with scales covering the lashes **(29).**

Moreover, eyelid dermatitis, a nonspecific irritation of the eyelids, is another common entity with a frequency of 2.3% to 7% in patients with psoriasis **(30,31)**. Also, pustules may develop on the lid margins with focal peripheral sterile corneal infiltratesand punctuate epithelial keratopathy **(31).**

b. Conjunctivitis:

Th e prevalence of conjunctivitis in psoriasis patients was reported to be as high as 64.5%. A chronic nonspecific conjunctivitis is the most common form of conjunctivitis in psoriasis and can occur with or without eyelid margin lesions. This high incidence was attributed to the fact that conjunctivitis is a commonly occurring eye condition that can be caused by psoriasis, but itis more commonly due to allergies, bacterial or viral infection **(23).**

Symptoms of conjunctivitis can include redness, tearing, or thick yellow discharge. Conjunctival lesions have been described as demarcated, yellowish- red plaques on the palpebral conjunctiva or as areas of dry hornyfied appearance on the bulbar conjunctiva. It is more common for conjunctival plaques of psoriasis to occur separately than to extend from the eyelid. Conjunctivitis can lead to xerosis, symblepharon, and trichiasis with further complications involving the cornea **(32).**

c. Dry eye (Xerosis or Keratoconjunctivitis sicca):

Keratoconjunctivitis sicca may be either a complication of blepharitis and conjunctivitis or an independent finding (Joshi, 2004). It had been reported at a prevalence rate of 2.7% - 18.75% of psoriatic arthritis patients. Dry eye syndrome, where the lacrimal gland produces a decreased amount of the aqueous component, can be the presenting finding of a systemic autoimmune disease, such as psoriasis. The association between psoriasis and dry eye has been documented andis accompanied by L-arginine deficiency and increased b-defens in production **(33).**

This causal link has been hypothesized to involve the L-arginine human cationic amino acid transporter that transports 80% of L-arginine in mammalian cells and whose concentration has been shown to be significantly reduced in the stratum granulosum of psoriatic plaques **(33).**

d. Episcleritis:

It is an inflammation of the connective tissue overlying the sclersa underneath the conjunctiva. It may occur in conjunction with psoriasis and presents with pink or even blue hyperemia pink or even blue, tenderness and watering **(34).**

e. Uveitis:

Uveitis is a loose term that refers to a large group of diverse diseases. It is characterized by inflammation involving the uveal tract and associated ocular structures. The International Uveitis Study Group classified intraocular inflammation into anterior (iritis or iridocyclitis)), intermediate (pars planitis), posterior (choroididitis), or panuveitis **(34).**

Fraga et al (35) noted that uveitis is more frequent and severe in the presence of HLA- B27. In contrary, **Chandran et al (36),** reported that there is no correlation between uveitis and severity or extent of joint findings. Moreover, people with concurrent severe psoriasis and psoriatic arthritis have the highest risk of incident uveitis while those with mild psoriasis and psoriatic arthritis and those with severe psoriasis but without psoriatic arthritis have a moderately increased risk of incident uveitis. They stressed that clinicians might use this finding as a guide for uveitis risk stratification among patients with different inflammatory presentations on the spectrum of psoriatic disease. Also, patients with psoriasis should be educated about the increased risk and manifestations of uveitis **(37).**

Some studies reported that inflammatory joint manifestations preceded uveitis **(22).** On the other hand, **Kolli et al (38)** showed that uveitis can occur even before psoriatic skin disease. Moreover, uveitis had been reported as the first presenting sign of psoriatic arthritis in 0% to 11.4% of cases. Also, severity of ocular inflammation may correlate with symptoms of the skin disease **(34).**

Acute psoriatic uveitis tends to be bilateral, prolonged, and more severe than non-psoriatic cases. Although uveitis has also been reported in psoriatic patients without arthritis, presence of human leukocyte antigen (HLA)-B27 is seen in these cases **(39).**

Although anterior uveitis has been reported to occur in 2%–25% of psoriatic patients, it is the most common ocular manifestation associated with PSA **(12).** On the other hand, posterior uveitis may be difficult to appreciate on examination. Meanwhile, it is more commonly responsible for the loss of vision, increasing the urgency for inflammation treatment **(34).**

Wu et al (40) suggested that there is a link between chronic plaque psoriasis and uveal involvement, particularly anterior uveitis. They added that uveitis is usually associated with the arthropathic form of psoriasis. In addition the recurrent uveitis may be an indicator of disease activity prior to other inflammatory markers.

f. Cornea:

Corneal involvement in psoriasis is rare and usually secondary to eyelid or conjunctival complications such as xerosis and trichiasis. The most common presentation is punctuate epithelial keratitis. Corneal lesions can induce superficial or deep opacities, stromal infiltrates, neo-vascularization, erosions, scarring, and even stromal melts. Histologically, opacities with thickened and vascularized epithelium were seen in some corneas of PSA patients. They revealed parakeratosis of the corneal epithelium similar to changes seen in psoriatic skin lesions. The lesions are usually bilateral and located more toward the limbus **(41).**

Omar and Helaly (42) reported that corneal involvement in psoriasis appeared to comprise 3 components: a thickening of the epithelium with erosions, an infiltrated zone under Bowman layer with superficial vascularization, and a homogenous deep stromal opacity. They added the clinician should remain mindful of the fact that intravenous methotrexate, a treatment for psoriasis, may cause its own ocular complications including keratitis, conjunctival injection, and dry eye symptoms. In addition, eye pain after UV therapy sessions, frequently several hours later, may be the result of UV keratitis and is often the result of poor-fitting eye protection.

Although peripheral corneal melting syndrome is most often described in association with systemic diseases such as rheumatoid arthritis, Sjogren syndrome, polyarteritisnodosa, Wegener granulomatosis, and systemic vasculitis, **Cao et al, (43)** reported that it can occur in psoriasis.

g. Cataract:

Lens abnormalities in patients with psoriasis are generally thought to be incidental findings. 63% of patients had bilateral cataracts. PUVA therapy in humans had been suggested to be responsible for the increased risk of ocular lens abnormalities. An increased risk for anterior cataract formation was seen in early guinea pig studies which used high doses of UV radiation. However, subsequent studies using psoralen doses comparable with standard therapeutic human doses failed to showsimilar risk. However, a large and long prospective study, which followed up patients treated withPUVA for psoriasis at 5 and 10 years, has not shown any causal relationship between level of PUVA exposure and the risk of developing

a lens abnormality. Moreover, the results are equivocal for those patients who did not protect their eyes from UV rays **(36).**

On the other hand, **Au et al (44)** attributed this high incidence as an association of cataract with corticosteroid or other ocular manifestations:

h. Other Rare Ocular Affections:

•Bilateral pigment dispersion syndrome was reported by **Chandran et al (36).** It is an uncommon condition characterized by the disruption of iris pigment epithelium with deposition of melanin pigment in the anterior segment of the eye.

• Abdulaal et al (2016) reported that vascular endothelium changes are strictly involved in PSA pathogenesis developing retinal damage. They attributed theses retinal changes to the disturbances in the balance of pro- angiogenesis and anti-angiogenesis factors which can lead to the progression of vascular damage in several chronic inflammatory conditions with the occurrence of retinal involvement at multiple levels. Although the presence of subclinical retinal involvement can be studied using modern techniques, such as the spectral-domain optical coherence tomography (SD-OCT) and fundus perimetry (FP); the early detection of subclinical abnormalities in retinal morphology and function in PSA patients and sine-PSO has not been illustrated (Krajewska–Włodarczyk et al, 2018).

• Another ocular affection in PSA is birdshot chorioretinopathy. It is a rare chorioretinitis entity that is strongly associated with HLA-A29 butwithout an established systemic disease association **(25).**

Conigliaro et al, (2018) suggested that the assessment of disease activity in PSA patients may be “apparently” adequate when evaluated only at joints level. However, the associated ocular affections can lead to visual loss even before the entire course of collagen diseases. They concluded that, ophthalmological evaluations and the study of visual function using either standard automated perimetry (SAP) and optical coherence tomography (OCT) could allow the detection of early changes in visual function even before the appearance of other manifestations of psoriasis.

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