Review Article

Update on psoriasis: A review

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Abstract

Psoriasis is a disease characterized by the presence of papules and plaques over the surface of skin with variable morphology, distribution and severity. The lesions of psoriasis are distinct from these other entities and are classically very well circumscribed, circular, red papules or plaques with a grey or silvery-white, dry scale. In addition, the lesions are typically distributed symmetrically on the scalp, elbows, knees, lumbosacral area, and in the body folds. The oral manifestations of psoriasis may involve the oral mucosa or the tongue. The dorsal surface of the tongue shows characteristic red patches surrounded with a yellow white border. The relationship between eye lesions and psoriasis are the current findings in the literature. The ocular complications along with the several extracutaneous manifestations are common complications seen in psoriasis. The pathogenesis of exact relationship between these two is still controversial. Immunological studies have shown a positive relationship between T helper cells and uveitis. Various signs and symptoms of ocular psoriasis may be overlooked. Thus, a complete understanding of ophthalmic involvement is important to the comprehensive care of patients with psoriasis. Almost any part of the body can be affected in psoriasis, but the ophthalmic complications of psoriasis usually remain clinically subtle. This review highlights the various manifestations of psoriasis with their clinical sign and symptoms.

Keywords: Inflammatory cells, manifestations, patches, psoriasis

Introduction

Psoriasis is an immune-mediated inflammatory disease with unknown etiology that may be associated with the defect in proliferation and differentiation of keratinocytes associated with inflammatory cell infiltration particularly consisting T-lymphocytes, macrophages, and neutrophils.[1] Psoriasis affects 1–3% of the adult population with various extra cutaneous manifestations. The psoriasis affected patients have ocular manifestations that are characterized by hyperproliferation of keratinocytes with abnormal differentiation along with infiltration of inflammatory cells mainly activated T cells in the epidermis and papillary part of dermis.[2,3] Ocular lesions are more common in males, and they often occur during psoriasis exacerbations.[4,5] Chandran *et al.* in their study found only one ophthalmic abnormality out of 67% patients with psoriasis, whereas 20% had more than one abnormality. The present figures seem to be higher as postulated by the authors than would be expected; this could be verified only in presence of a control group or population-based data for comparison.[6]

Various clinical findings associated with psoriatic eye include conjunctivitis, dry eye, episcleritis, and uveitis. Lambert and Wright in 1976 noted the presence of ocular inflammation with psoriatic arthritis, conjunctivitis iritis in patients suffering from psoriasis.[7]

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Psoriasis is a common chronic inflammatory cutaneous disease affecting 0.5% to 2% of children and adolescence. The disease affects 4% of all children younger than 16 years with all types of dermatologic disorders.[8]

Various forms of psoriasis have been known so far:

1. Plaque Psoriasis (characterized by dry scaly patches)
2. Pustular Psoriasis (contains pus like fluid mainly infiltrated with white blood cells)
3. Erythrodermic Psoriasis (characterized by exfoliation of fine scaly skin with pain and itching)
4. Guttate psoriasis (characterized by drop like dots)
5. Inverse Psoriasis (affects the flexure surfaces and characterized by smooth inflamed lesions)
6. Others including scalp psoriasis and nail psoriasis.

Oral Manifestations

Oral lesions can occur on the mucous membranes of the mouth, but it is not as common as on the skin and are usually accompanied by lesions on other parts of the body. Reports of oral psoriasis that are well documented show no consistent lesion pattern. Patterns range from raised, white, scaling lesions predominantly on the palate or buccal mucosa to well-demarcated, flattened, erythematous lesions involving the dorsal surface of the tongue with a slightly raised, white, and annular or serpiginous border. These latter lesions closely resemble geographic tongue. Patients with tongue lesions also show nail and genital involvement and it seems geographic tongue is more common in early onset psoriasis and maybe an indicator of disease severity. Nonspecific tongue lesions have also reported frequently in psoriatic patients.[9]

Oral lesions may disappear quickly, or they may undergo exacerbations or remissions concomitantly with skin lesions. Diagnosis of oral psoriasis is best made when the clinical course of the oral lesion parallels that of the skin disease and is supported by microscopic findings.

Pathogenesis

Psoriasis is a hyperproliferative skin disease with increased rate of epidermal turnover. The pathogenesis of psoriasis is linked to various cellular mechanism and the role of T cells, antigen presenting cells (APCs), keratinocytes, Langerhans cell, macrophages, natural killer cells, an array of Th1-type cytokines, as well as certain growth factors like vascular endothelial growth factor (VEGF), keratinocytes growth factor (KGF), etc., have been suggested to play a key in the pathogenesis of psoriasis.[10] Psoriasis is an immunologically mediated disease, the activation of T lymphocytes leads to the inflammation in the dermal component and secondary to the inflammatory events there is also that epidermal hyperproliferation.[11]

Various mechanisms are hypothesized to be involved in the pathogenesis of psoriasis:

- T cell function
- Role of dendritic cell
- Hyperproliferation of keratinocytes
- Angiogenesis
- Cytokine mediators
- Reduced apoptosis
- Genetic factors
- Role of oxidants and antioxidants in psoriasis

1. T cell function
   T lymphocytes consist of a functionally distinct population of helper T cells and cytolytic T cells. The principal function of T cells is to recognize the processed peptide antigens that are attached to proteins encoded by the MHC class II genes. Therefore, for activation, T cells need APCs to process and present peptide fragments on the APC cell surface. T cells secrete various lymphokines. T cells may also inhibit immune responses; in this role, these are known as suppressor T cells. Distinct cell membrane proteins are expressed by different populations of T cells. CD4 positivity is shown by most of the helper T cells while cytolytic and suppressor cells are CD8 positive. Activation of T cells requires three steps:[12] a. Binding b. Antigen-specific activation (signal 1) c. Non-antigen-specific cell-cell interaction (signal 2)
2. Role of dendritic cells
   Dendritic cells serve as a major class of antigen presenting cells found in increased abundance in psoriatic skin lesions.[13] Langerhans cells are a type of immature dendritic cell (iDC) found in normal epidermis and can also be found in psoriasis lesions.[14] iDCs are derived from blood monocytes or other myeloid precursors and have a immunostimulatory role. These iDCs are further stimulated to become mature DCs (mDCs). Psoriasis lesions show a marked increase in dermal DCs. XIIIa and CD11c are expressed by myeloid DCs or iDCs, and CD83 and DC-LAMP proteins are positive for mDC.
3. Hyperproliferation of keratinocytes
   The skin provides a protective mechanism through its multilayered structure. The epidermis consists of five layers, stratum basale, stratum spinosum, stratum granulosum, stratum lucidium, and stratum corneum. Mainly the keratinocytes are formed in the stratum basale and further they migrate towards the stratum corneum. As cells move toward the surface, their organelles disappear and are filled with keratin. The topmost layer of keratin provides a protective feature. In normal conditions the epidermal cell cycle is completed in about four weeks. But in psoriatic skin, the epidermal cell cycle is accelerated. Cell division in the basal layer occurs every 1.5 days, and the migration of keratinocytes to the stratum corneum occurs within approximately 4 days. This results in hyperproliferation of keratinocytes.
4. Angiogenesis
   Keratinocytes produce proangiogenic cytokines (VEGF, IL-8), but the precise mechanism for angiogenesis in psoriasis is still unknown. In psoriasis the endothelial cells swell and become activated these activated endothelial cells migrate, sprout, and lay down a basement membrane with pericytes

for structural support to form novel vessel networks.[15] This results in widening of the intercellular spaces, and hence, dermal blood vessels dilate thus making it easier for leukocytes to migrate into the skin.[16]

5. Cytokine mediators
   In psoriasis, the production of cytokines result in epidermal hyperproliferation, vascular dilatation, and dermal inflammation. The cytokines involved in the development of psoriasis include granulocyte–macrophage colony stimulating factor (GMCSF), epithelial growth factor (EGF), IL-8, IL-12, IL-1, IL-6, IFN-γ, and TNF-α. These cytokines result in keratinocyte proliferation, neutrophil migration, potentiation of Th1 type of responses, angiogenesis, upregulation of adhesion molecules, and epidermal hyperplasia.
6. Reduced apoptosis
   In order to maintain a constant thickness of the epidermis proliferation of keratinocytes in normal epidermis is regulated by apoptotic cell death. The epidermal hyperplasia characteristic of psoriasis is suggested to be due to P53 overexpression and these proliferating cells typically express Bcl-2 that protects them against apoptotic stimuli, while terminally differentiated cells lose Bcl-2 expression.[17]

Psoriasis and the Eye

Psoriasis and the eye for patients with psoriasis, uveitis had been commonly thought to occur only in conjunction with psoriatic arthritis, however, there have been many case reports of psoriatic uveitis presenting independent of joint disease. Furthermore, the temporal relationship of these two entities has been disputed. Some recent studies suggest that inflammatory joint manifestations precede uveitis. Nevertheless, some cases of uveitis have been reported to occur even before psoriatic skin disease, and uveitis has been reported as the first presenting sign of psoriatic arthritis in 0% to 11.4% of cases. The severity of ocular inflammation does not necessarily correlate with extent of joint findings but may correlate with skin disease.[8]

Since the latency period for development of symptomatic ocular abnormalities may be longer than 5 years, continued surveillance and continued use of appropriate ocular protection by all patients treated with PUVA is indicated.[18]

Ocular Disorder

Psoriasis is a chronic inflammatory disorder which commonly manifests with various extra cutaneous manifestations of which eye involvement is important. Psoriasis may affect the lid, conjunctiva or cornea resulting in the development of ocular manifestations, including conjunctival hyperemia and conjunctivitis, ectropion and trichiasis and corneal dryness with punctate keratitis and corneal melting. Studies done by Chandran *et al.* and Erbagci *et al.* in Turkey had found prevalence of ocular manifestations in psoriasis to be 67% and 65%, respectively, which were in congruence with the present study, which showed prevalence of 70%.[2]

Conjunctivitis

Published articles have suggested conjunctivitis prevalence rates in psoriasis patients as high as 64.5%. Conjunctivitis is a commonly occurring eye condition that can be caused by psoriasis, but it is more commonly due to allergies, bacterial infection, or viral infection.[8]

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 xerotic appearance on the bulbar conjunctiva. Conjunctivitis can lead to xerosis, symblepharon, and trichiasis with further complications involving the cornea.[7]

Dry Eye (keratoconjunctivitis sicca)

Keratoconjunctivitis sicca has been cited at a prevalence rate of 2.7% of psoriatic arthritis patients. Some studies suggest prevalence rates of dry eyes as high as 18.75%of psoriasis patients.[8]

Episcleritis

Episcleritis (inflammation of the tissue layer covering the sclera) may also occur in conjunction with psoriasis and presents with hyperemia (increased blood flow) that may be pink or even blue, tenderness (although significant tenderness should cause to suspect scleritis, a more serious condition), and watering.

Blepharitis

Psoriasis may affect the eyelids by several means. Blepharitis, a common inflammatory condition of the eyelids, has been suggested by Cram to be the most prevalent ocular finding in patients with psoriasis. Symptoms such as burning and itching may cause considerable discomfort. The mechanism of this dysfunction in psoriasis is not known, but Zengin *et al.* proposed that increased epithelial turnover leads to high volumes of cell production and subsequent shedding that may ultimately lead to a mechanical block through the meibomian duct. Blepharitis can usually be controlled with adequate lid hygiene including warm compresses, eyelid massage, and lid scrub traditionally with baby shampoo-based formulas.[7]

Uveitis

Uveitis is a loose term that refers to a large group of diverse diseases. The International Uveitis Study Group classifies intraocular inflammation into anterior (iris or ciliary body), posterior (choroid or retina), intermediate (vitreum, peripheral retina, and pars plana of the ciliary body), or panuveitis (generalized inflammation of entire uvea).[8]

Uveitis is a potentially serious ocular complication that can occur in patients with psoriasis. Anterior uveitis has been reported to occur in 7%–20% of patients with psoriasis. Uveal involvement tends to be bilateral, prolonged, and more severe. Uveitis can be controlled effectively using corticosteroids and cycloplegic agents with possible adjunct therapy with conventional immunomodulatory therapy. In patients who are refractory to these therapies or cannot tolerate these agents' anti-tumor necrosis factor-alfa therapy is another option.[7]

Psoriatic uveitis may be anterior or posterior or both and thus may require different treatment strategies. Acute anterior uveitis may often be treated with a dilating eye drop to keep the pupil mobile and prevent formation of synechiae (adhesions between the iris and lens). Posterior uveitis, although it may be difficult to appreciate on examination, is more commonly responsible for the loss of vision, increasing the urgency for inflammation treatment. Recommended pharmacotherapy has evolved as understanding of the pathogenesis has improved and as specific inflammatory mediators have been identified. Although the traditional treatment has involved corticosteroids or immuno modifying drugs, in recent years, the use of drugs that target the TNF pathway has been suggested for use in the more intractable cases.[8] Uveitis in patients with psoriasis may have distinguishing clinical features.[19] Uveitis is frequently the first indication of a previously undiagnosed HLA-B27–associated extraocular disease.[20]

Cataract

Lens abnormalities in patients with psoriasis are generally thought to be incidental findings. Chandran *et al.* found that 63% (63 of 100) of patients had bilateral cataracts although. An association between with corticosteroid or phototherapy use was not found.[7] But some case reports have suggested that PUVA therapy in humans may be associated with an increased risk of ocular lens abnormalities but this is not well established.[21]

Corneal Lesion

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, but lesions can include superficial or deep opacities, stromal infiltrates, neovascularization, erosions, scarring, and even stromal melts.[7]

Ophthalmological Examination of Psoriatic Patient

All complaints should be referred to an ophthalmologist for evaluation. Non ophthalmologists can assess a patient's visual acuity and examine the external eye for circumcorneal injection. Referral to an ophthalmologist is essential for definitive diagnosis and treatment.[7] Routine eye examinations are necessary in patients with psoriasis of all types, for early detection of subclinical eye pathologies.[22]

Implications for Clinical Practice

The primary care physician is the first contact of a patient for the consultation of illness. Early diagnosis and a multi-disciplinary approach are key components of managing the various types of psoriasis. Increased awareness and research in this field have facilitated identification of risk factors and causation pathways. Certain therapies have shown a promise that needs evaluation in prospective clinical trials. The topical corticosteroids are commonly used in painful oral inflammatory conditions such as erosive lesions of the oral mucosa. Oral psoriasis has been successfully managed with topical steroids with complete remission.[23] Drugs like Infliximab and ustekinumab have proven to be effective for psoriatic lesions.[24]

Due to low incidence of psoriatic lesions in the oral cavity knowledge of psoriasis remains limited. Bruce *et al.* explained that the asymptomatic nature of these lesions is the reason for the lower prevalence of oral lesions in psoriasis compared to other papulosquamous diseases.[25] Furthermore, normal epithelial turnover is 28 days, but in psoriatic cutaneous plaques it decreases to 3 to 7 days, which is close to the normal regenerative time of the oral epithelium, thus, this phenomenon may be the cause of the lower prevalence of apparent changes in the oral mucosa of patients with psoriasis.[26,27]

Conclusion

The eye manifestations in psoriasis can lead to various complications including vision loss. These manifestations or complications can be seen more commonly in psoriasis patients with arthritis, but have also been associated in psoriasis patients without arthritis. These signs and symptoms can be easily be neglected by the physician is not specifically looking for them. Psoriatic eye manifestations may precede articular changes. Thus, the patient should consult the doctor at regular intervals and the specialist should remain mindful of a known history of psoriasis when evaluating ocular symptoms. Therefore, to rule out the common associated ophthalmic conditions including dry eyes, blepharitis, conjunctivitis, and uveitis regular eye examinations are recommended in psoriasis patients by the expert dermatologist and ophthalmologist.

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Conflicts of interest

There are no conflicts of interest.

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