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Pathogenesis, Treatment and Impact on Quality of Life in Psoriasis

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ABSTRACT

Background: psoriasis is a papulo-squamous disease with different morphology, severity, distribution and course of disease**.** The aim of the treatment was to reduce disease activity to a level that permits an acceptable quality of life with negligible toxicity from the treatment itself. About 25% of patients experience major psychological distress due to the disease. Its long duration along with comorbidities have a negative impact on quality of life. **Aim of the work:** we tried to understand the types, pathogenesis and management of psoriasis, and also try to understand its effect on the quality of life**. Methodology:** we conducted this review using a comprehensive search of MEDLINE, PubMed and EMBASE from January 1994 to March 2017. The following search terms were used: psoriasis, psoriasis classification, psoriasis management, quality of life in psoriasis patients. **Aim of the work:** we tried to understand the types, pathogenesis, and management of psoriasis, and also try to understand its effect on the quality of life**. Conclusion:** due to the chronic course, and its noticeable visibility on skin, many patients suffer from major social and psychological ill effects. In majority of the time the health care providers fail to recognize or treat such comorbidities. Healthcare providers must be educated to offer ways to tackle such issues in the management plan for better results

Keywords: psoriasis, pathogenesis of psoriasis, management of psoriasis, impact on quality of life in psoriatic patients.

INTRODUCTION

Psoriasis is a papulo-squamous disease with different morphology, severity, distribution, and course of disease. Differential diagnosis other papulo-squamous diseases that must be considered include tinea infections, lichen planus and pityriasis rosea. The lesions of psoriasis are different from these other types and are characteristically very well circumscribed, round, red papules, or plaques with a grey or dry silvery-white scale. At the same time, the lesions are classically scattered symmetrically on the scalp, knees, elbows, body folds and lumbosacral area [1]. Psoriasis may also grow at the location of precious trauma or injury. This phenomenon is known as Koebner's phenomenon. Progressive or uncontrolled psoriasis can end up as a generalized exfoliative erythroderma. Nail may be involved, predominantly if case of psoriatic arthritis. Sporadically psoriasis may cause lesion in the oral mucosa or the tongue. The dorsal surface of the tongue may have gyrate red patches, sharply circumscribed with a white yellow border. The patches can grow and spread, can have a discrete annular pattern and may look a lot like a map, therefore the term geographic tongue [2].

Although psoriasis normally does not disturb survival, it undoubtedly has various major negative effects on patients, evident by a substantial disadvantage to quality of life. Due to the chronic and incurable nature of psoriasis, its accompanying morbidity is weighty. About one in four patients experience and note chief psychological distress and the degree to which they feel socially stigmatized and left out is massive. Unfortunately, doctors, including dermatologists, and other medical staff usually fail to analyze the magnitude of this disability [3]. Therefore, we attempted to understand the types, pathogenesis, and management of psoriasis, and also try to understand its effect on the quality of life.

METHODOLOGY

- Data Sources and Search terms

We conducted this review using a comprehensive search of MEDLINE, PubMed and EMBASE, from January 1992 to March 2017. The following search

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terms were used: psoriasis, psoriasis classification, psoriasis management, quality of life in psoriasis patients.

- **Data Extraction**

Two reviewers have independently reviewed the studies, abstracted data and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

This study was done after approval of ethical board of Umm Alqura University.

CLASSIFICATION OF PSORIASIS

Psoriasis can be greatly different in morphology, distribution and severity. The morphology can vary from small tear shaped papules called guttate psoriasis, to pustules which are called pustular psoriasis and generalized erythema and scale known as erythrodermic psoriasis. Furthermore, these various forms of psoriasis can be classified as localized or widespread and disabling. Additionally, psoriasis can present with a variable course as chronic, stable or acute rapid progression with widespread involvement. Psoriasis can be symptomatic where the patients complain of extreme pruritus with burning [4]. The different types and presentations of psoriasis are classified as below:

1. Plaque Psoriasis

The plaque psoriasis is the most common form of psoriasis in which patients have sharply bordered, round to oval shaped or coin-sized plaques. The lesions might primarily arise as erythematous macules or papules, spread peripherally, and eventually coalesce to form plaques of a few centimeters in diameter [5]. A Woronoff's ring, which is a white blanching ring, can be seen in the skin around a psoriatic plaque. The plaque then gradually extends peripherally and may develop various configurations such as [6]:

- psoriasis gyrata—curved linear patterns predominate
- annular psoriasis—ring-like lesions grow secondary to central clearing
- Psoriasis follicularis—minute scaly papules present at the openings of pilo-sebaceous follicles.

The terms rupioid and ostraceous describe two separate morphological subtypes of plaque psoriasis. Rupioid plaques are small of 2–5 cm in diameter and are highly hyperkeratotic. Whereas, ostraceous psoriasis decide hyperkeratotic plaques with comparatively concave centers [7].

Scale is usually present in psoriasis, is habitually silvery white and varies in thickness. Removal of scale may disclose tiny bleeding points. This is called Auspitz sign. The amount of scaling the Greek word gutta which means droplet, shows the acute onset of a myriad of 2–10 mm diameter lesions. These are typically spread in a centripetal fashion although guttate lesions can also involve the head and limbs [8]. Classically, guttate psoriasis occurs soon after an acute group B hemolytic streptococcal infection of the tonsils and may be the presenting incident of psoriasis in children or, infrequently, adults. The number of lesions may vary from five or ten to over a hundred. Guttate psoriasis consists of 2% of the total cases of psoriasis. In children, guttate psoriasis is generally self-limiting; in adults, guttate flares may worsen chronic plaque disease. Even though few studies have evaluated the long term prognosis of children with acute guttate psoriasis, one such study discovered that 33% of patients with acute guttate psoriasis eventually transformed into chronic plaque disease [6].

2. Flexural (Inverse) Psoriasis

Psoriasis which affects the flexures, mainly infra-mammary, axillary and perineal, is different morphologically from traditional plaques anywhere else on the trunk and limbs. Flexural lesions lack scale and appear as red, shiny, well-marked plaques, and are sometimes confused with candida, intertrigo and other dermatophyte infections [9].

3. Erythroderma

Involvement of the skin by active psoriasis is called erythroderma and can take one of two forms. First, chronic plaque psoriasis might gradually progress and become confluent and extensive. Second, erythroderma may be an indicator of unstable psoriasis triggered by infection, tar, drugs, or corticosteroid withdrawal. Erythroderma may harm the thermoregulatory capability of the skin, causing hypothermia, high output heart failure, and metabolic variations which includes hypo-albuminemia and anemia because of loss of iron, vitamin B12, and folic acid [10].

4. Generalized Pustular Psoriasis

Generalized pustular psoriasis is infrequent and signifies active, unstable disease. Triggers include withdrawal of systemic or strong topical corticosteroids and infections. The patient is

pyrexial, and has red, inflamed, and painful skin studded with monomorphic, sterile pustules, which may join together to form sheets. Patients with generalized pustular psoriasis often need to hospital admission for management [11].

5. Palmoplantar Pustulosis

Palmoplantar pustulosis starts as sterile, yellow pustules with a background of erythema and scaling and it often affects the palms and soles. The pustules are painful and die away to form dark brown coloration with scale/crust stuck to it. Palmoplantar pustulosis is often associated with psoriatic nail participation. Roughly 25% of cases are linked with classic psoriasis vulgaris, but it is now understood that palmoplantar pustulosis could not be a form of psoriasis. This assumption is derived from genetic studies showing no link with HLA-Cw6 or other markers on chromosome 6p—which are associated to chronic plaque and guttate psoriasis. The demographics of palmoplantar pustulosis are noticeably dissimilar from those of chronic plaque psoriasis in that it more frequently affects women (9:1), presents most often between the ages of forty and sixty years, and has a very striking link with smoking, either recent or in past, in up to 95% of patients [12].

6. Psoriatic Nail Disease

Fingernails are more frequently affected than toenails. The most common finding is minor pits in the nail plate, resulting from flawed nail formation in the proximal part of the nail matrix. The nail can also separate from the bed at its distal or lateral attachments and this is known as onycholysis. Orange-yellow areas may be present underneath the nail plate and are called oil spots'. Furthermore, the nail plate can become, thickened, discolored and dystrophic. Yellow, keratinous substance may be collected under the nail plate and is termed as subungual hyperkeratosis [13].

PATHOGENESIS

Psoriasis can be activated by many reasons, comprising injury and trauma (due to Koebner effect), medication, infection, and a topical biological reaction modifier, also known as imiquimod (a TLR7 agonist). Several studies have revealed that topical imiquimod may cause psoriasiform skin inflammation, mediated by interleukin IL-23 and IL-17. Damage to the skin causes cell death and that causes the making of the AMP LL37 by keratinocytes. DNA/LL37 complexes then associate and bind to intracellular TLR9 in plasmacytoid dendritic cells, which leads to stimulation and production of type I interferons IFN-α and -β. LL37/RNA complexes can activate plasmacytoid DCs with the help of TLR7, while myeloid DCs are activated by this complex with the help of TLR8 [14]. Hereafter, myeloid DCs can be activated by the LL37/RNA complex and additionally by type 1 interferons, causing T cell activation and the formation of cytokines found in psoriasis. Extracellular DNA has been seen in the epidermis in association with neutrophil extracellular traps, thus explaining this model of psoriasis initiation [15].

Genetic Factors

Scans of the human genome show a minimum of nine different loci with predisposition to psoriasis (PSORS1-9). PSORS-1, a region on the gene of the major histocompatibility complex on chromosome 6p2, is the key genetic determinant of psoriasis, and is responsible for up to 50% of genetic predisposition to the disease, while the absolute gene has not yet been recognized. Several of the associated loci are mutual to the other autoimmune and inflammatory diseases for example inflammatory bowel disease, multiple sclerosis, type1 diabetes and atopic dermatitis. This proposes that similar mechanisms motivate many common genetically complex inflammatory diseases [16].

It is noted in a study that through NexGen sequencing of patients with familial psoriasis, a mutation in the Caspase Recruitment Domain-Containing Protein 14 (CARD14) gene was seen at this site, which isolated with psoriasis. CARD14 mRNA was noticed to be elevated 2.7 times in the psoriasis transcriptome, and a *CARD14* SNP was also newly discovered. In a patient with this mutation as well as in classic psoriasis, CARD14 protein was expressed in the epidermis and dermis of psoriasis plaques. CARD proteins a play a role in scaffold formation for inflammation activation, while wild-type CARD14 activates Bcl10 and NF-κB [17]. Mutations in the CARD14 gene change the CARD14 protein. This gene in presence of an inflammatory trigger may initiate increased activation of NF-κB, causing transcription of several genes including major chemokines which are increased in psoriasis for example CCL20, CXCL8/IL-8, and IL-36γ/IL-1F9. These chemokines bring other cells such as neutrophils and T cells that then secrete their own

inflammatory mediators. All of the above events add to the vicious cycle of inflammation as seen in psoriasis [14].

Mutations are also seen in other genes, namely IL36RN. This gene, also known as IL-1F5, encrypts for an anti-inflammatory protein IL-36Ra, which is a known antagonist of IL-1F9. Henceforth, a mutation in this to causes an altered protein with lessened effect and to unopposed IL-1F9 effects of NF-κB and MAPK activation by IL-1Rrp2 and IL-1RacP. Peripheral blood mononuclear cells from a suffering patient compared with another healthy volunteer displayed increased amount of cytokines downstream of NF-κB. These reviews indicated that a loss of function in IL36RN could be the genetic basis for generalized pustular psoriasis [18].

Immunological and Environmental Factors

Recent studies have indicated that both and acquired (antigen specific) immune mechanisms are altered in clinically uninvolved skin. In this environment key primary cytokines such as for example, tumor necrosis factor α and interferon α, are released, possibly as a result of environmental triggers, comprising infection, stress, drugs, and trauma. This suggestion is supported by the reflective efficacy of agents that block the actions of TNF α, for example infliximab, in treatment and the therapeutic potential of agents that inhibit pathways linking innate and acquired immunity [19].

DIAGNOSIS

Psoriasis is diagnosed based on clinical findings which include skin rash, nail changes and joint involvement. Seldom patients can also complain of a typical skin lesions which needs to be discriminated from tinea, seborrheic dermatitis, mycosis fungoides, discoid lupus, or non-specific skin findings such as minimal scalp scaling, isolated flexural erythema, or lesions on genital area. Cautious assessment of all body sites can show undeclared, diagnostically valuable features, and a skin biopsy may sometimes be indicated [5]. Chronic plaque psoriasis is the most common type, but other morphological variants consist of guttate psoriasis, flexural or "inverse" forms, sebopsoriasis, erythrodermic psoriasis and pustular psoriasis. Sometimes mixtures of the different types develop concurrently or successively over time in the same patient [20].

TREATMENT

The study aim of the treatment is to reduce disease activity to a level that permits an acceptable quality of life with negligible toxicity from the treatment itself. Antibiotics and tonsillectomy have often been encouraged for patients with recurrent guttate psoriasis or in case of chronic plaque psoriasis, but good indication is lacking for either intervention being advantageous. Interventions include topical therapy, phototherapy, systemic immunosuppressant agents, and other biological treatments [21].

Topical Therapy

Compliance to topical therapy regimens is not good. Even when patients were informed that drug use is monitored, treatment is adhered to just over half the time. Therapeutically active topical agents approved for psoriasis include corticosteroids, tar, vitamin D analogues, dithranol and tazarotene. Evaluation of agents in studies showed that vitamin D analogues were of similar effectiveness to strong corticosteroids and more beneficial than dithranol due to fewer reported adverse effects. Of the three vitamin D derivatives presently accessible is calcipotriol which is slightly more effective than tacalcitol or calcitriol. Furthermore, when given together with a potent or very potent steroid, it more effective than calcipotriol alone [22].

In practice topical corticosteroids are extensively used because they are effective and onset of action is quick. Mild to moderate strength corticosteroids, provided it is for limited periods only, can be recommended for facial and flexural disease. Alternating use as twice weekly or once at weekends or use combined with non-steroidal agents such as calcipotriol, may preserve remission and at the same time minimize risks that can occur with uninterrupted use. Those risks include loss of efficacy, skin atrophy, and rebound or more severe psoriasis [23]. The vitamin D analogues are also commonly used, but even though efficacy is equivalent to that of potent corticosteroids without the attendant risks, their onset of action is sluggish and skin irritation is common (reported in about 20%-25% of users). Therefore, the utility of combination therapy with corticosteroids has the potential to abrogate both these problems. The calcineurin inhibitors tacrolimus and pimecrolimus are prescribed sometimes for challenging flexural or facial psoriasis, while no good indication exists for size of benefit [24].

Phototherapy and Systemic Treatments

Firm, short term proof on the effectiveness of phototherapy ultraviolet B-light and photochemotherapy (Psoralen plus ultraviolet A light, PUVA) and many of the systemic treatments for psoriasis are studied through randomized controlled trials. However, very few comparative studies have inspected the relative efficacy along with safety of the various interventions. The existent studies have failed to talk about clinically important questions including length of remission when treatment is paused or whether effectiveness is preserved with continuous or intermittent routine [25]. Approaches to decrease toxicity from long term management comprise rotational or sequential use of systemic treatment, drug holidays, and combination therapy. Multidisciplinary teams with experience in several drug therapies provide specialist care for a small number of patients with severe, refractory disease [24].

Methotrexate is yet believed to be the ideal treatment for moderate to severe psoriasis, especially if arthritis or nail is involved, as it is highly effective over prolonged periods. 50% reduction in disease severity in 75% of patients was noted. Methotrexate use has been discouraged because of the need for routine liver biopsies to detect, although rare, but silent liver fibrosis and cirrhosis. Lately, measurement of serum procollagen III once every 3 months during treatment has been accepted as a substitute marker of liver toxicity, which indicates that most patients can avoid liver biopsies [26].

Biological Treatments

Biological therapy includes agents that hamper molecular steps vital in the pathogenesis of psoriasis. Presently they include two main groups which are [27]:

- agents that target the cytokine TNF α such as, etanercept, infliximab, adalimumab and
- agents that target T cells or antigen presenting cells like efalizumab

In spite of the need for parenteral administration (intravenously every 8 weeks for infliximab, self-administered subcutaneous injections 2 times weekly), extensive disappointment of patients with standard managements has led to great demand. Their part in the context of prevailing standard systemic treatments is inadequate at the moment, because of the relative lack of data on long term safety and effectiveness. However, certainly for some patients with severe psoriasis these treatments can be lifesaving. Risks of infection such as tuberculosis with the anti TNF agent and potential future malignancy remain as concerns [28].

IMPACT ON QUALITY OF LIFE

Psychosocial Effect

Although psoriasis usually does not disturb survival, it surely has various major negative effects on patients, evident by a significant disadvantage to quality of life. Because of the chronic, incurable nature of psoriasis, the accompanying morbidity is significant. Patients in primary care and hospital settings have comparable declines in quality of life, similar to those recorded for major diseases such as cancer, diabetes, heart disease [3]. Reductions in quality of life include various aspects like psychological, functional, and social aspects. Symptoms precisely related to the skin which include, chronic itch, scaling, bleeding, nail involvement; problems related to treatments odor, mess, inconvenience, duration; arthritis; and the impact of living with a highly observable, disfiguring skin disease contribute to numerous difficulties with relationships, problems with securing employment, and a low self-esteem. All of these aspects add to morbidity. Even those with negligible involvement (less than the size of three palm areas) have expressed that psoriasis has massively negatively affected their lives [29].

About 25% of patients have reported major psychological anguish. The degree to which they sense socially stigmatized and excluded is massive. Doctors, including dermatologists, unfortunately, often fail to realize the extent of this disability. Even when it is correctly recognized, less than 33% of patients receive correct psychological therapy. Such aspects may affect management outcome, but they are possibly responsive to intervention. In one study the combination of cognitive behavioral therapy with the standard treatment led to considerably superior reductions in anxiety, stress, depression, self-reported disability, and in the clinical severity of psoriasis [30].

Associated Comorbidity: Cardiovascular Disease and Cancer

Psoriasis patients with severe form were reported to have at least a two to three times increase in mortality from cardiovascular causes. Numerous potentially inter-related influences are likely to add to this risk. The occurrence of obesity is two times

that of the normal population and also compared to those with other types of skin disorders. Weight gain has been reported to occur after disease onset, and is probably related to a sedentary lifestyle. The risk of psoriasis is greater in current smokers (relative risk of 1.7) and former smokers (1.9) compared to those who never smoked. High consumption (≥ 20 packs/ day) along with long duration of smoking predominantly was related to severe disease form in women. Patients with psoriasis demonstrate high rates of excess intake of alcohol, and high mortality due to alcohol related diseases [31]. Stress, as stated above, may be more common in people with psoriasis. It could also be a cause, as generally assumed by patients to be a trigger of psoriasis and flare ups. Increased rates of hyperlipidemia occur in patients with severe, chronic disease; somewhat iatrogenic due to prolipidogenic properties of antipsoriatic medications (ciclosporin, acitretin). Chronic inflammation is a documented risk factor in other diseases including rheumatoid arthritis and systemic lupus erythematosus. Numerous community and hospital based studies have presented an amplified risk for a number of malignancies. In patients with severe disease, the risk seems to be similar to that of patients post organ transplantation, displaying noteworthy increases recorded for lymphoma and non-melanoma type of skin cancer [32].

CONCLUSION

We have learned the various types and pathogenesis behind psoriatic skin disorder. There are several treatment options, localized and systemic and we discussed the risks and benefits for each. Unfortunately, due to its nature of being noticeable visible on skin and its chronic course, many patients suffer from major social and psychological ill effects. In majority of the time the health care providers fail to recognize or treat such comorbidities. Healthcare providers must be educated to offer ways to tackle such issues in the management plan for better results.

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