# IADVL ACADEMY SPECIAL INTEREST GROUP (SIG) PSORIASIS

E-Newsletter, Issue 01, June 2016



In This Issue:

# A Few Thoughts to Introduce This

**Dr Murlidhar Rajagopalan MD**
**Senior consultant dermatologist and coordinator SIG psoriasis**
**docmurli@gmail.com**

Dear friends and colleagues

This is to introduce the first newsletter which we from the SIG psoriasis group have brought out.

The aim of this newsletter is to open a channel wherein the group brings out a newsletter like this regularly. The focus is on clinical medicine and also updating oneself with the latest in psoriasis.

For this we have asked our members to contribute case studies which can become a good learning point for all dermatologists.

In order to refine your skills, we have included a protocol which can be used for biologics

The literature search is up-to-date and brings out new areas of thought which will shape the future.

A newsletter is not good without a quiz to challenge you.

We hope this becomes a model to be perpetuated in future.

I thank all the contributors, the sig group and the iadvl academy which enabled this.

I am particularly grateful to our younger colleagues who are dynamic—Dr Brijesh and Dr Rajat for volunteering to take the lead and getting out this newsletter well ahead of the time we had wanted it.

With best wishes to everyone and do look out for the next issue

Dr Murlidhar Rajagopalan

Co-ordinator, SIG psoriasis

## IMPACT CME PROGRAMS

This is probably the highlight of the SIG activities this year. Sixteen CME meets have been planned with a common slide deck as a masterclass on psoriasis. The first four meets were successfully held in the four metros with the SIG and DSB of IADVL equally participating.

The next 12 meets will be held serially in various cities across the country using the same model but by May 2017.

## FIRST IMPACT CME AT NEW DELHI

The first IMPACT CME was held at New Delhi on August 9, 2016, under the aegis of Special Interest Group (SIG) psoriasis and Delhi State Branch (DSB) of IADVL. It was well attended, and more than 70 enthusiastic dermatologists from Delhi and nearby areas took part in it. The speakers were Dr. Paschal D'Souza, Dr. Kabir Sardana, Dr. Abir Saraswat, and Dr. Vinay Singh. Dr. Rishi Parashar, president, DSB, welcomed the audience and set the ball rolling. After four exhaustive talks on various aspects of psoriasis viz pathogenesis and epidemiology, topical therapy, systemic therapy, and biologic therapy, the audience interaction with the panel of speakers was the highlight of the meeting. There were scores of questions from the audience on all aspects of psoriasis therapy, and a lively discussion ensued, which went on for over an hour. The meeting ended with lunch, during which interaction between audience and speakers continued.





Organized by:
Indian Association of Dermatologists,
Venereologists and Leprologists


IMPACT


IMPACT

# A Man with Extensive Psoriasis, Tinea, and Deranged Liver Function

**Abir Saraswat**

**Consultant dermatologist, Indushree Skin Clinic**

**Lucknow, India**

## CASE STUDY

A 28-year-old, unmarried, male presented with an extensive itchy and scaly rash of 4 years duration. The rash had started from the scalp and had gradually spread to involve the entire body. He was applying some ointments on the rash and took chlorpheniramine tablets irregularly, which reduced the scaling and itch somewhat. There were irregular exacerbations and remissions correlated with changes in season, but the rash never cleared completely. About 1 year ago, he had developed a rash in the groin as well, which subsided with application of some topical agents prescribed by a general practitioner (GP), but recurred.

Past history was significant for the presence of essential hypertension for the past 3 years, which was well controlled with daily telmisartan. He consumed about 120 mL alcohol 4–5 days a week, and his body mass index (BMI) was 29.5. There was family history of diabetes mellitus as well. He was diagnosed to have psoriasis by a dermatologist 3 years ago and was prescribed methotrexate, which he did not take because he could not stop alcohol, and his liver function tests were deranged. He only applied clobetasol-salicylic acid ointment on it intermittently. His groin rash was treated with a cream containing clobetasol, terbinafine, ornidazole, and ofloxacin intermittently. He had also taken oral terbinafine 250 mg/day for 3–4 weeks, and fluconazole 150 mg/week for 3–4 months without relief.

## CLINICAL EXAMINATION

Examination revealed plaques of psoriasis over almost 15% of body surface area, including the scalp. Further examination revealed extensive broad and livid striae extending from the knee to the groin and extending up to the lower abdomen. Erythematous papulopustules and some arcuate plaques were also present. One stria had broken down to form a shallow 5 × 3.5-cm irregular ulcer with livid edges, which was extremely tender on palpation.

## INVESTIGATIONS AND TREATMENT

KOH preparation from the groin revealed plenty of septate hyphae. A biopsy from the edge of the ulcer revealed nonspecific changes in the dermis, but showed fungal elements in the epidermis on periodic acid–Schiff (PAS) staining. A swab from the ulcer floor grew mixed flora of no significance. Blood investigations were significant for raised transaminases, both 2.5 times above the upper range of normal. Serum triglycerides were 220 mg/mL. Blood glucose, renal function, and urinalysis were within normal limits. Further investigation was deferred in view of the extreme discomfort caused by the ulcer and widespread tinea.

He was advised to stop alcohol immediately and was given itraconazole 400 mg/day with sedative antihistamines and nonsteroidal anti-inflammatory drugs (NSAIDs). The ulcer was dressed with ionic silver gel, and a multivitamin with high-dose zinc was prescribed. The psoriasis was treated with bland emollients and a tar-based shampoo. With this treatment, his tinea subsided and the ulcer healed completely within 4 weeks. Itraconazole was continued for a further 2 weeks and stopped. His liver enzyme levels came down marginally, but were still nearly 2 times above normal. At this point, he was investigated further for initiating active treatment of his psoriasis with biologics. It was then that he was discovered to be hepatitis B surface antigen positive. Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) serology was negative. His hepatitis B virus (HBV) DNA count was more than 68,000 copies/mL. He denied any sexual activity and had not received any blood transfusions.

He was referred to a gastroenterologist for treatment of his hepatitis, where after further

investigations, he was started on entecavir 1 mg/day and propranolol 40 mg/day. After 2 weeks of this treatment, his viral counts were 5800 copies/mL. After discussion with his gastroenterologist, he was started on injection secukinumab 300 mg/week subcutaneously for 4 weeks, after which it was reduced to once a month. His psoriasis cleared rapidly, and he was completely clear after 10 weeks of starting this treatment. He remains on this treatment, and a dose reduction of secukinumab is planned after 16 weeks are completed.

## DISCUSSION

This case exemplifies the situations that can arise in the treatment of psoriasis in real-life scenarios. This patient had a history of chronic alcohol abuse and hypertension, which was complicated by extensive tinea and signs of prolonged topical steroid abuse. This made the use of conventional systemic agents like methotrexate and cyclosporine problematic. Acitretin was not considered because of the rapidity of spreading of the disease, and phototherapy was not feasible due to the distance of the patient's house from the clinic. Subsequent detection of active hepatitis B infection further complicated matters.

As this case demonstrates, viral hepatitis whether HBV or HCV is not an absolute contraindication for biologic therapy in psoriasis. If the liver infection is adequately treated and the liver function is stable, biologics for the treatment of psoriasis can be given safely and effectively. Of course, constant communication with the gastroenterologist and proper monitoring are necessary.

# Biologics for Psoriasis: Ready Reckoner

**Dr Vinay Singh**
**Consultant Dermatologist**
**Delhi, India**

To be considered eligible for treatment, psoriasis patients must have

a. Severe disease defined as a Psoriasis Area and Severity Index (PASI) score of 10 or more (or a body surface area (BSA) of 10% or greater where PASI is not applicable) and a Dermatology Life Quality Index (DLQI) >10.

and

b. Fulfill at least one of the following clinical categories:
   - Where phototherapy and alternative standard systemic therapy are contraindicated or cannot be used due to the development of, or risk of developing, clinically important treatment-related toxicity
   - Are intolerant to standard systemic therapy
   - Are unresponsive to standard systemic therapy
   - Have significant, coexistent, unrelated comorbidity that precludes the use of systemic agents such as cyclosporine or methotrexate
   - Have severe, unstable, life-threatening disease

An adequate response to biologic treatment is defined as either

- 50% or greater reduction in baseline PASI (PASI 50 response) (or % BSA where the PASI is not applicable) and a 5-point or greater improvement in DLQI

**or**

- 75% reduction in PASI score compared with baseline (PASI 75 response)

## RECOMMENDATIONS (ASSESSMENT AND MONITORING FOR TUBERCULOSIS [TB])

- Pretreatment chest X-ray and Mantoux skin test currently remain the preferred screening tests.
- Tuberculin testing is not valid in patients already established on immunosuppressive therapy (e.g., methotrexate). Interferon gamma release assay (IGRA) tests may have a role in this group and can be used if practicable, although the positive and negative predictive values are unknown. The T-SPOT-TB test is more sensitive in patients on immunosuppressive drugs.
- Patients with signs to suggest TB or a history of previous treatment should be referred to a specialist.
- Patients with latent TB should be considered for prophylactic anti-Koch's therapy.
- When antituberculous therapy is indicated, patients should complete 2 months of treatment before commencing biologic therapy with either isoniazid (total treatment course 6 months) or rifampicin plus isoniazid (total treatment course 3 months) or rifampicin alone (total treatment course at least 4 months).
- During Rx, and for 6 months following discontinuation, a high index of suspicion for tuberculosis should be maintained, especially in those at high risk.
- For patients on biologics for duration longer than 1 year, who have negative screening tests for TB on initiation of therapy, annual assessment for tuberculosis may be considered in high-risk patients using IGRA.

## USE IN PATIENTS WITH CHRONIC VIRAL INFECTIONS

- Insufficient evidence to recommend biologics in patients with chronic, potentially harmful viral infections, and clinicians should seek specialist advice on a case-by-case basis.
- In patients who are hepatitis C carriers, there is limited evidence to support the use of biologics provided they are appropriately evaluated and monitored during therapy.
- Tumor necrosis factor (TNF) antagonist therapy should be avoided in chronic carriers of hepatitis B because of the risk of reactivation.

## USE OF BIOLOGICS AND VACCINATION

- Vaccination brought up-to-date prior to initiation of biologics.
- Patients should NOT receive live or live attenuated vaccinations less than 2 weeks before, during, and for 6 months after discontinuation of biologic therapy.
- Inactivated vaccines are safe to administer concurrently with biologics.
- TNF antagonists reduce antibody responses to influenza vaccine, and TNF antagonists and methotrexate may lead to reduced antibody responses to pneumococcal vaccine.
- Patients should be advised to receive the pneumococcal vaccine and annual influenza vaccine while on biologic therapy.

## BIOLOGICS AND INFECTION RISK

- Patients on biologics should be monitored for early signs and symptoms of infection throughout treatment.
- Patients on biologic interventions should be warned against risk factors for *Salmonella* and *Listeria* and should not consume raw or partially cooked dairy, fish, or meat produce or unpasteurized milk or milk produce. Salads should be washed thoroughly before consumption.
- It may be advisable to avoid public baths, saunas, and swimming pools and wear masks when in crowded places while on treatment with biologics.

## BIOLOGICS AND MALIGNANCY

- Patients should be fully assessed prior to and during treatment with biologics with respect to their past or current history of malignancy and/or any future risk of malignancy.
- Biologics must be avoided in patients with a current/past history of malignancy (unless malignancy is more than 5 years old and treated).
- Regular, comprehensive dermatological assessment for skin cancer, including melanoma, is recommended before and at regular intervals during therapy.
- Biologics are contraindicated in patients who have had prior therapy with >200 psoralen and ultraviolet A (PUVA) and/or >350 UVB treatments, especially when it has been followed by cyclosporine.

## BIOLOGICS AND MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACES)

- Preliminary reports of MACEs (a composite end point of myocardial infarction, cerebrovascular accident, or cardiovascular death) in patients receiving TNF-α antagonists (infliximab and etanercept) and in randomized controlled trials (RCTs) of psoriasis patients treated with ustekinumab and briakinumab have raised concerns.
- Clinicians must take proper history, identify and document risk factors associated with cardiovascular disease (tobacco/alcohol consumption, obesity, dyslipidemia, etc.).
- Caution should be used when considering TNF inhibitor use in patients with Chronic heart failure (CHF):
  - Patients with New York Heart Association class III or IV CHF should avoid all use of TNF inhibitors.
  - Patients with class I or II CHF should undergo echocardiogram testing; if the ejection fraction of these patients is <50%, then TNF inhibitor treatment should potentially be avoided.
- Clinicians should be aware that
  - New-onset heart failure or exacerbation of preexisting heart failure may occur in patients who begin TNF antagonist therapy independent of risk factors.
  - Patients receiving TNF-α inhibitors may be at higher overall cardiovascular risk.

## BIOLOGICS AND NEUROLOGICAL DISEASE

- Both peripheral and central demyelinating disorders, including MS, have been reported to not only develop but also worsen in patients taking TNF-α antagonists and previously with efalizumab.
- TNF-α antagonists should be avoided in the setting of a personal history of demyelinating conditions.
- TNF inhibitors should not be used in first-degree relatives of patients with MS.
- Signs and symptoms such as paresthesias, weakness, blurring, loss of vision, sensory loss, and back pain (band like or associated with paresthesias and/or weakness) should alert the clinician regarding onset of neurological disease.
- Onset of new neurologic symptoms in a patient on TNF-α inhibitors that suggest the development of a demyelinating disorder should be promptly evaluated by a neurologist while the TNF inhibitor is withheld.

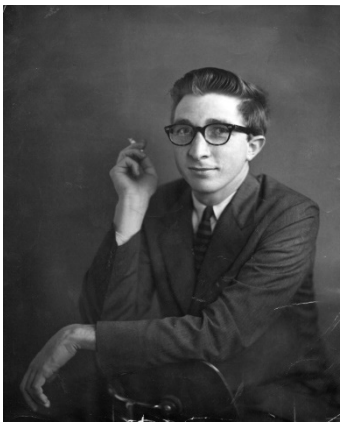
# Trivia and Quiz

**Dr Brijesh Nair**
**Consultant Dermatologist**
**INHS Sanjivani**
**Kochi**

While exploring for these psoriasis questions and trivia, I noticed this quote. "Patches of dead skin pile up like multiple-car collisions, bleeding sores stain the sheets, mounds of white flakes fill the house. It's the 'heartbreak of psoriasis'." This was from a blog called "Grad School Madness" and best spells out the predicament of a psoriatic patient. Let's have a few trivia now on this "nontrivial" affliction.

1. What is the drug of choice in the treatment of psoriasis in HIV-positive individuals?
   a. PUVA therapy
   b. Secukinumab
   c. Methotrexate
   d. Acitretin
2. Which antidiabetic drug has shown to be efficacious with a favorable safety profile when used in the treatment of chronic plaque-type psoriasis?
   a. Sitagliptin
   b. Exenatide
   c. Insulin detemir
   d. Pioglitazone
   e. Acarbose
3. Which is the first specifically expressed transcription factor after differentiation into Th17 cell lineage on conversion from naive T cells?
   a. STAT3
   b. JAK1
   c. RORγt
   d. MAPK
   e. p40
4. The presence of which disease along with psoriasis will be a contraindication for IL-17 A blockers?
   a. Nonalcoholic fatty liver disease
   b. TNF-blocker-induced paradoxical psoriasis
   c. Crohn's disease
   d. Rheumatoid arthritis
   e. ankylosing spondylitis
5. Which among the following supplements are found to be effective in lithium-induced psoriasis?
   a. Glutathione
   b. Polypodium leucotomos
   c. Ellagic acid
   d. Inositol
   e. Pilocarpine
6. Which among the following do not form part of the NAPSI scoring system for nail psoriasis?
   a. Red spots in the lunula
   b. Leukonychia
   c. Splinter hemorrhages
   d. Onychomadesis
   e. Nail plate crumbling
7. Which among the following medicines has potential interaction with methotrexate due to plasma protein binding?
   a. Colchicine
   b. Salicylates
   c. Leflunomide
   d. Ciclosporin
   e. Barbiturates
8. Which among the following assessment scores is nonspecific for psoriasis?
   a. BASDAI
   b. NAPSI
   c. PEST
   d. SPI
   e. PLSI
9. The role of the lymphocyte in pathogenesis of psoriasis was convincingly confirmed when a group led by James Krueger successfully treated psoriasis using the first-ever biological agent. What was that?
   a. Abatacept
   b. NF KB
   c. Alefacept
   d. Efalizumab
   e. DAB-IL-2

10. Among the six phenotypes of psoriasis, which phenotype is associated mostly with palmoplantar psoriasis?
    a. Type 1
    b. Type 2
    c. Type 3
    d. Type 4
11. Which of these therapeutic options is comparatively safe during pregnancy?
    a. Calcipotriene
    b. NB UVB
    c. Coal tar
    d. Ustekinumab
    e. Dithranol
12. Corrona, Biobadaderm, Psobest, and PSOLAR are:
    a. Psoriasis guidelines
    b. Psoriatic arthritis criteria
    c. Psoriasis severity scores
    d. Psoriasis registries
    e. Psoriasis genetic trial groups
13. How long after initiation of TB prophylaxis does National Psoriasis Foundation recommend initiation of biological therapy?
    a. Simultaneously
    b. 1–2 months
    c. 3–4 months
    d. 6 months
14. What UV source was recommended by Goeckerman in his eponymous original regime?
    a. Ruby Laser
    b. UVA lamps
    c. UVB lamps
    d. Excimer light
    e. Hot quartz lamps
15. Which among the following HLA is associated with Type II psoriasis?
    a. HLA-DR7
    b. HLA–Cw6
    c. HLA-B57
    d. HLA-Cw2
16. Which surgery has been anecdotally associated with improvement in psoriasis?
17. Which nutritional supplement has highest published evidence in alleviation of psoriasis?
18. Which subtype of psoriatic arthritis is an absolute indication for initiation of biologicals?
19. This Pulitzer Prize–winning author was plagued from an early age with psoriasis. In his book, "*Self-Consciousness*," he devoted an entire chapter to his lifelong battle with psoriasis called "At war with my skin." He states: "Because of my skin I counted myself out of any of those jobs—salesman, teacher, financier, movie star—that demand being presentable. What did that leave? Becoming a craftsman of some kind, closeted and unseen—perhaps a cartoonist or a writer, a worker in ink who can hide himself and send out a surrogate presence, a signature that multiplies even while it conceals." Name him.



20. The eponyms for both annular pustular psoriasis and spongiform pustules are associated with the name of a French dermatologist. Name him.

## ANSWERS

1. d
2. d
3. c
4. c
5. d
6. d
7. e
8. a
9. e
10. b
11. b
12. d
13. b
14. e
15. d
16. Roux-en-Y gastric bypass surgery
17. Fish oils—eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
18. Axial involvement
19. John Updike
20. Lapierre (Psoriasis pustuleuxannulaire de Bloch-Lapierre, pustule de Kogôj-Lapierre)

# Literature

**Dr Brijesh Nair**
**Consultant Dermatologist INHS Sanjivani Kochi;**
**Dr Rajat Kandhari**
**Consultant Dermatologist**
**Delhi, India**

**Comparative effectiveness of biologic agents for the treatment of psoriasis in a real-world setting: Results from a large, prospective, observational study (Psoriasis Longitudinal Assessment and Registry [PSOLAR])**

**Strober BE, Bissonnette R, Fiorentino D, et al. *J Am Acad Dermatol*. 2016;74:851–861.**

In the future, advent of more biologic agents is going to make the task of the treating dermatologist very complicated, and choices have to be made. There is increasing demand for comparative effectiveness data in the current health care environment to better inform patients and physicians when choosing appropriate treatments for psoriasis (*J Am Acad Dermatol*. 2013;68:262–269). Selection of therapy depends on numerous factors, including efficacy, safety, response over time, convenience, affordability, and health-related quality of life (HRQoL). Results of biologics in clinical trials pertain largely to short-term outcomes and do not always reflect findings in typical practice. Psoriasis Longitudinal Assessment and Registry (PSOLAR) is an ongoing, longitudinal, prospective, international, observational study that follows patients with psoriasis who are receiving, or are eligible to receive systemic or biologic therapies. The objective of this study was to compare the effectiveness of tumor necrosis factor (TNF)-alpha inhibitors (infliximab, adalimumab, and etanercept) with effectiveness of ustekinumab (IL 12/23 antagonist) based on standard clinical and HRQoL measures (i.e., Physician Global Assessment [PGA], percentage of body surface area with psoriasis [%BSA], and Dermatology Life Quality Index [DLQI]) after 6 and 12 months of treatment.

**Updates on cardiovascular comorbidities associated with psoriatic diseases: epidemiology and mechanisms**

**Yim KM, Armstrong AW *Rheumatol Int*. DOI: 10.1007/s00296-016-3487-2**

## COMMENTS

- This comparative effectiveness study was based on data from more than 2000 patients with psoriasis who initiated a new biologic during their participation in PSOLAR.
- At 6 months, 5 of the 6 comparisons for *PGA and % BSA showed significantly better effectiveness for ustekinumab versus the TNF-alpha inhibitors* taking into account several variables such as baseline psoriasis severity and prior treatment. At 12 months, 3 of the 6 PGA and % BSA comparisons demonstrated statistically significant better effectiveness for ustekinumab.
- More severity, more body weight, prior use of TNF-alpha inhibitor were factors associated with diminished efficacy.
- *The effectiveness of biologics in PSOLAR was less than what has been reported in randomized controlled trials, as is expected in actual practice*.
- A recent PSOLAR analysis comparing drug survival across biologic therapies found that ustekinumab had better drug survival compared with all three TNF-alpha inhibitors. This may reflect the findings of generally better effectiveness and patient-reported outcomes with ustekinumab in the current study.
- More such registry-based comparative effectiveness research is the need of the hour.

Psoriasis is associated with a significantly increased risk of certain comorbid diseases; some studies have shown a dose–response relationship between psoriasis disease severity and incidence of selected comorbidities (*JAMA Dermatol*. 2013;149(10):1173–1179). A preponderance of the literature suggests that psoriasis and psoriatic arthritis confer an independent risk of cardiovascular disease and death (*Eur Heart J*.

2010;31(8):1000–1006; *J Am Heart Assoc*. 2013;2(2):e000062). Specifically, patients with psoriasis and/or psoriatic arthritis are at an increased risk of myocardial infarction, stroke, and cardiovascular mortality. Cardiovascular disease is the most common cause of death among patients with severe psoriasis. This article tries to elucidate the epidemiology of cardiovascular diseases, and major adverse cardiovascular events (MACE) in psoriasis and psoriatic arthritis and tries to explain the mechanisms involved.

**Salient mechanistic explanations:**

1. Similar inflammatory pathways: Psoriasis and atherosclerosis involve the same T-cell-mediated inflammatory pathways, specifically T-helper 1 (Th1) and T-helper 17 (Th17) cascades.
2. Role of monocytes: Monocytes aggregate at psoriatic sites and are also incriminated in atherosclerotic plaque progression. Increased monocyte chemoattractant protein-1 (MCP-1) levels are associated with atherosclerotic plaque instability and rupture.
3. Role of adiponectin: Adiponectin is an adipokine that protects against inflammation, insulin resistance, and atherogenesis. Patients with psoriasis have deficient plasma adiponectin levels independent of cardiometabolic risk factors. Dysregulation of adipose tissue inflammation may be the underlying mechanism of psoriatic and cardiovascular comorbidities by promoting a systemic pro-inflammatory state.
4. Role of insulin resistance (IR): IR also increases with increasing psoriasis severity, and it seems the chronic inflammation associated with psoriasis induces the insulin resistance state due to the persistent secretion of tumor necrosis factor-alpha (TNF-α) and other pro-inflammatory cytokines such as interleukin-1 (IL-1) and IL-6. Moreover, inflammation-induced resistance to insulin may increase endothelial expression of adhesion molecules, promoting further inflammation. Insulin favors keratinocyte differentiation.
5. Role of lipids: High-density lipoprotein (HDL) efflux capacity is decreased in psoriasis patients and is correlated to increased atherosclerotic risk independent of HDL cholesterol concentration.
6. Endothelial dysfunction: It is exhibited by intimal thickening, increased stiffness, decreased vasodilation, or decreased elasticity of various parts of the vasculature that might be a part of the all-encompassing malady.

**COMMENTS**

- *Both psoriasis and psoriatic arthritis are associated with cardiovascular risk factors, as well as with MACE*.
- *Standard lipid profiling is not sensitive enough to unmask the important lipid changes that result from psoriasis*. Research on lipoprotein characteristics and function may be necessary to refine the mechanistic role of dyslipidemia in the development of cardiovascular diseases with psoriatic diseases.
- *Angiogenic factors like VEGF are thought to be critical players in the development of psoriatic and cardiovascular comorbidities*. Activation of the JAK-STAT, NF-κB, and MAPK signaling pathways are observed in both disease processes.
- Key links between psoriasis and cardiovascular comorbidity are inflammation, insulin resistance, dyslipidemia, angiogenesis, oxidative stress, and endothelial dysfunction.
- Deeper exploration of the mechanistic pathways of pathogenesis and better establishment of quality longitudinal data collection across different populations, potentially through the use of advanced electronic medical records.

## Palmoplantar pustulosis and palmoplantar pustular psoriasis are highly related diseases that appear to be distinct from psoriasis vulgaris

**Bissonnette R, Suárez-Fariñas M, Li X, et al. *PLoS One*. 2016;11(5):e0155215.**

Diseases such as pustular palmoplantar psoriasis (PPPP) and palmoplantar pustulosis (PPP) localize specifically to palms and soles. There have been arguments that PPPP and PPP are distinctive dermatoses from psoriasis vulgaris (*J Dermatol Treat*. 2011;22(2):102–105). PPP is usually defined as a chronic skin disease characterized by crops of sterile pustules with erythema and occasional scaling on palms and soles, whereas PPPP is usually defined as a variant of plaque psoriasis present on palms and soles with the presence of sterile pustules. Many patients have a palmoplantar morphology that is an intermediary between these two extremes of PPP and PPPP. In addition, the presence of psoriasis outside palms and soles has been reported in up to 24% of patients with a

typical presentation of PPP, making matters more confusing.

This landmark study from a renowned open-source journal uses gene expression microarray technique to compare gene expression in lesional skin of patients with PPP (defined as active palmoplantar morphology suggestive of palmoplantar pustulosis without lesions of psoriasis outside palms and soles and without history of psoriasis) and PPPP (defined as active palmoplantar disease morphology suggestive of psoriasis with at least one plaque of typical psoriasis outside the palms and soles or a history of typical plaque psoriasis outside the palms and soles) to normal acral and non-acral skin and to skin from psoriasis vulgaris located outside hands and feet.

### COMMENTS

- *Increased expression of GPRIN1 and ADAM23 at the gene and protein level differentiates PPP and PPPP*, and these might prove to be potential therapeutic targets in the future.
- *Th17 inhibitors seem to be better therapeutic options than IL-12/23 blockers in PPP/PPPP*.
- Further efforts are needed to differentiate or unify these two morphological entities in the future.

**Impact of pregnancy and oestrogen on psoriasis and potential therapeutic use of selective oestrogen receptor modulators for psoriasis**

**Lin X, Huang T *J Eur Acad Derm Venereol*. 2016;30(7): 1085–1091.**

The natural course of psoriasis is modulated by pregnancy, menstruation, and the menopause, suggesting a modulatory role for female sex hormones in the pathogenesis of psoriasis. A few reports have proposed a role for estrogen in the pathogenesis of psoriasis.

Selective estrogen receptor mediators (SERMs) are a group of compounds that function as ligands for estrogen receptors (ER) with mixed agonism/antagonism profile that affords the beneficial estrogenic actions in target tissues and avoids adverse, off-target effects. Tamoxifen is capable of inducing a shift from Th1 to Th2 immunity, and is antiangiogenic, in addition to its hormonal action (*Curr Med Chem*. 2009;16:3076–3080). There have been instances where treatment of the breast cancer with tamoxifen cleared the coexisting psoriatic skin lesions for several months, even after suspension of the hormonal treatment. This purported benefit in psoriasis may be counterbalanced by risk of endometrial cancer, deep vein thrombosis and alteration in liver enzyme levels. Experimental animal studies have been done to study antipsoriatic activity of topical tamoxifen encapsulated in phospholipid-based vesicular and micellar systems (*Pharm Dev Technol*. 2014;19:160–163). Raloxifene is a second-generation SERM with risk mitigation of adverse effects in comparison to tamoxifen. Raloxifene therapy inhibited lipopolysaccharide-stimulated production of IL-12 p40 and TNF-a in ex vivo and in vitro studies, which might be beneficial for psoriasis. Raloxifene treatment significantly decreased erythrocyte malondialdehyde level in postmenopausal osteoporosis subjects, which is an indicator of oxidative stress.

### COMMENTS

- Psoriatic systemic therapies are predominantly immunosuppressant, and hence, there is a felt need to have less immune suppressant oral options for treatment. The impact of estrogen on psoriasis is complex.
- Estrogen shows a biphasic effect with low concentrations activating and high concentrations suppressing T-cell functions, with overall benefit in psoriasis.
- Estrogen therapy cannot be continued long term due to adverse events, and hence SERMs with its agonist/antagonist dichotomy might offer a safer option with raloxifene preferable over tamoxifen in women with psoriasis. However, there is a caveat that such speculation can be implemented in a clinical scenario after carefully planned in vivo studies. But, harnessing the hormones to control psoriasis is an interesting thought, nevertheless.