Challenging Cases

SYMPOSIUM REPORT

A focus on pediatrics, comorbidities, infections, & biologics

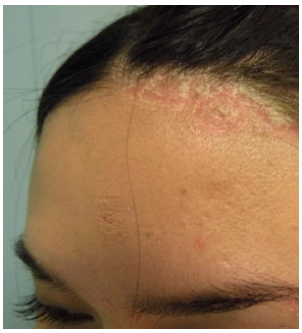
AN IPC SYMPOSIUM AT THE SKIN INFLAMMATION & PSORIASIS INTERNATIONAL NETWORK (SPIN) CONGRESS

Practical approaches to treating psoriasis were discussed through the lens of challenging cases at an IPC symposium presented during the Skin and Inflammation & Psoriasis International Network (SPIN) Congress in April in Paris, France. IPC Chief Medical Officer Peter van de Kerkhof, professor emeritus Radboud University, Njimegen, the Netherlands, chaired the symposium, entitled "Challenging Cases in Psoriasis: A focus on pediatrics, comorbidities, infections, and biologics."

Worsening of psoriasis under infliximab

In his lecture, IPC Councilor Errol Prens, Erasmus University Medical Center, Rotterdam, the Netherlands, presented a fascinating account of paradoxical manifestations to biologics in patients with immune-mediated disorders. Paradoxical reactions are defined as the new onset or exacerbation of a symptom/disease that usually improves with the biologic (TNF-α inhibitors).

Psoriasiform skin reactions are the most frequent and well-known paradoxical effects, but the list of other types is lengthy. They include autoimmune or autoinflammatory diseases such as lupus, uveitis, multiple sclerosis, vasculitis, sarcoidosis, hidradenitis suppurativa (HS), and Crohn's disease.[1] The mechanisms underlying these paradoxical reactions are still a matter of debate. One possible mechanism involves an imbalance of cytokines favoring Type 1 interferons, chemokines, and possibly interleukin-(IL)-23/IL-17 and Tregs, together with underlying genetic factors. Most paradoxical reactions are caused by TNF-α inhibitors, but cases associated with ustekinumab, secukinumab, and ixekizumab have been documented.[2]



Hair-line psoriasis, worsening after treatment with infliximab.

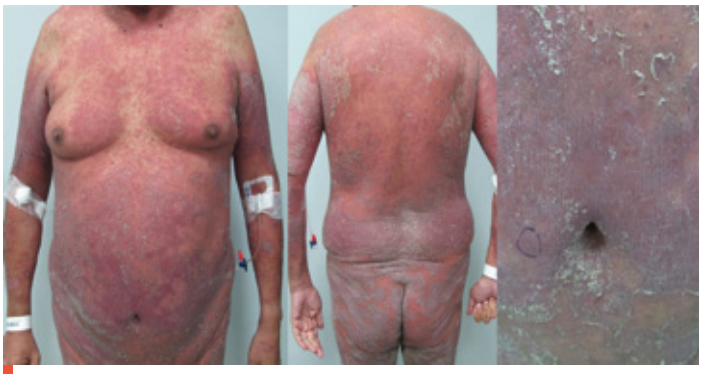
SPIN faculty from left: Fernando Valenzuela, Chile; Ron Vender, Canada; and Peter van de Kerkhof, Marieke Seyger, and Errol Prens, all of the Netherlands.

Professor Prens presented several cases of paradoxical reactions in patients with psoriasis, which included one case of worsening of the disease treated with infliximab. Most reactions clear upon discontinuation of the drug or by switching to another biologic. In some cases, additional therapies are required to manage the reaction. The underlying mechanisms, particularly genetic factors, require further research to identify patients at risk of developing paradoxical reactions.

Erythrodermic psoriasis and HIV infection

IPC Councilor Fernando Valenzuela, University of Chile, Santiago, Chile, discussed erythrodermic psoriasis, which is an uncommon, severe, inflammatory form of the disease.

Erythrodermic psoriasis usually manifests in patients with long-standing, unstable chronic disease. Triggering factors include HIV infection, emotional stress, intense ultraviolet light exposure, use of topical tar products, alcoholism, abrupt withdrawal of oral or topical corticosteroids, and methotrexate therapy. Erythrodermic psoriasis is associated with severe complications such as sepsis, acute kidney damage, respiratory distress, electrolyte imbalance, severe anemia, altered thermoregulation, protein depletion, and cardiac failure.[3]



Erythrodermic psoriasis as the first manifestation of HIV infection.

Dr. Valenzuela presented an interesting case of a patient with a long history (50 years) of chronic mild psoriasis who then presented with dramatic worsening of psoriasis severity, fever, and weight loss. The patient tested positive for HIV infection. Psoriasis can appear as the first manifestation of HIV infection; therefore, HIV testing should be carried out in some new severe cases and in patients with sudden worsening of previously stable psoriasis, particularly in countries where HIV is prevalent. Psoriasis severity is proportional to the degree of immunosuppression, being most severe when CD4 counts <100 cells/mL.[4] Even though HIV-associated psoriasis can present with any phenotype, erythrodermic, guttate, and acral psoriasis, as well as psoriatic arthritis tend to be more common. Treatment of moderate to severe HIV-associated psoriasis poses a therapeutic challenge, as most systemic treatments are immunosuppressive and could lead to severe complications. Anti-retroviral therapy, phototherapy (narrowband ultraviolet light B [UVBnb] or ultraviolet light A with psoralen [PUVA]) and oral retinoids are considered first treatment options.

Treatment-resistant psoriasis

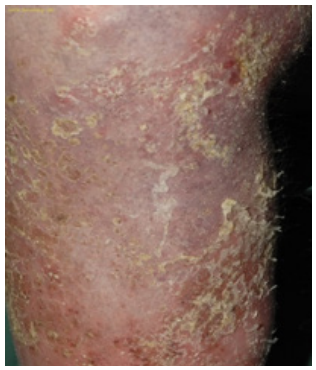
Professor van de Kerkhof addressed the challenging topic of treatment-resistant psoriasis in a patient with contraindication to biologics due to active infection.

In his presentation, Professor van de Kerkhof discussed the case of a 75-year-old man with a 30-year history of classical chronic plaque psoriasis, with no signs or symptoms of arthritis or of metabolic syndrome/cardiovascular disease. After 20 years of mild involvement, during the subsequent 10 years, this patient presented with unstable phenotype that included remissions and exacerbations. Previous treatments with topical therapies had resulted in adequate control; however, during the next 10 years, he received several courses of UVB treatment, at times in combination with acitretin, with adequate control for approximately 2 years. He then received methotrexate, which was well tolerated but not effective to control symptoms, and he experienced remissions and exacerbations. The patient then started on a round of ciclosporin and within two weeks developed fever and generalized pustular psoriasis.

The pustular psoriasis diagnosis, with transition from plaque psoriasis to unstable psoriasis, should be regarded as psoriasis with pustulation. In fact, it is unstable psoriasis. This is different from pustular psoriasis with no transition into plaque psoriasis. The latter can be regarded as a distinct disease entity with a different genotype.[5] In this patient, urinary tract infection with pyelonephritis and urosepsis was also diagnosed. The urinary tract condition remained an increased infection risk and constitutes the triggering factor.

Professor van der Kerkhof discussed to what extent all biologics are contraindicated in patients affected by infection. Recent analyses of the Psoriasis Longitudinal Assessment and Registry PSOLAR cohort (11,466 patients with psoriasis) suggested a higher risk of serious infection with adalimumab and infliximab, whereas, with ustekinumab and etanercept, no increased risk was observed.[6] So far, active infection remains a contraindication for all biologics in published guidelines. Therefore, this patient was contraindicated for treatment with biologics.

Another finding in this patient was liver test abnormalities. The increases of transaminases occurred in this patient synchronously with exacerbations of psoriasis. In the literature, patients with unstable psoriasis and pustular psoriasis may have abnormal liver enzyme function independent from the medication and dependent on relapses of psoriasis.[7,8]



Unstable plaque psoriasis with pustules.

Psoriasis comorbidities

In his presentation, IPC Councilor Ron Vender, Dermatrials Research Inc., Hamilton, Ontario, Canada, discussed the importance of addressing psoriasis comorbidities with the patient during clinic visits.

Patients with psoriasis often have comorbidities that can determine which biologic is best for them or which to avoid. Many psoriasis-related comorbidities are contraindications to traditional systemic medications as well.

Dr. Vender presented a case of a 54-year-old male patient with psoriasis who exhibited with many comorbidities, including obesity and depression. He was initially prescribed 300 mg of secukinumab at weeks 0-1-2-3-4, then 300 mg every 4 hours. The patient was quite pessimistic about treatment success, but his treatment response was as expected. However, continued clinical follow-up revealed a small amount of regression in his clinical response, and optimization of treatment was required by increasing the secukinumab dose at week 24 to 450 mg q 4. Importantly, his depression and depressive symptoms improved during his treatment, enhancing his quality of life with a reduction in DLQI to zero. This case can encourage dermatologists to take a "head-to-toe" treatment approach that would manage the signs and symptoms of psoriasis and also improve their patients' quality of life.

Pediatric psoriasis algorithm

Nowadays, many effective and safe treatments are available to treat children and adolescents who have psoriasis, and many more will be approved soon. IPC Councilor Dr. Marieke Seyger, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands, presented a treatment algorithm that can be used as general guidance for the treating physician (Figure 1).

Despite the presence of the algorithm, however, managing the disease can be challenging. In order to personalize care in pediatric psoriasis, practitioners need to know patients' values and preferences, but, particularly in adolescents, it can be difficult to glean this information. The use of the Children's Dermatology Life Quality Index (CDLQI) is helpful.[9] In addition, showing and discussing a graph of the patients' quality of life (CDLQI) and severity of psoriasis (PASI) over time improves interactive consulting and facilitates shared decision-making.

Another challenge is determining which children should be treated with systemic treatments at an earlier stage and if they are at

Figure 1: Management of pediatric psoriasis[11-13]

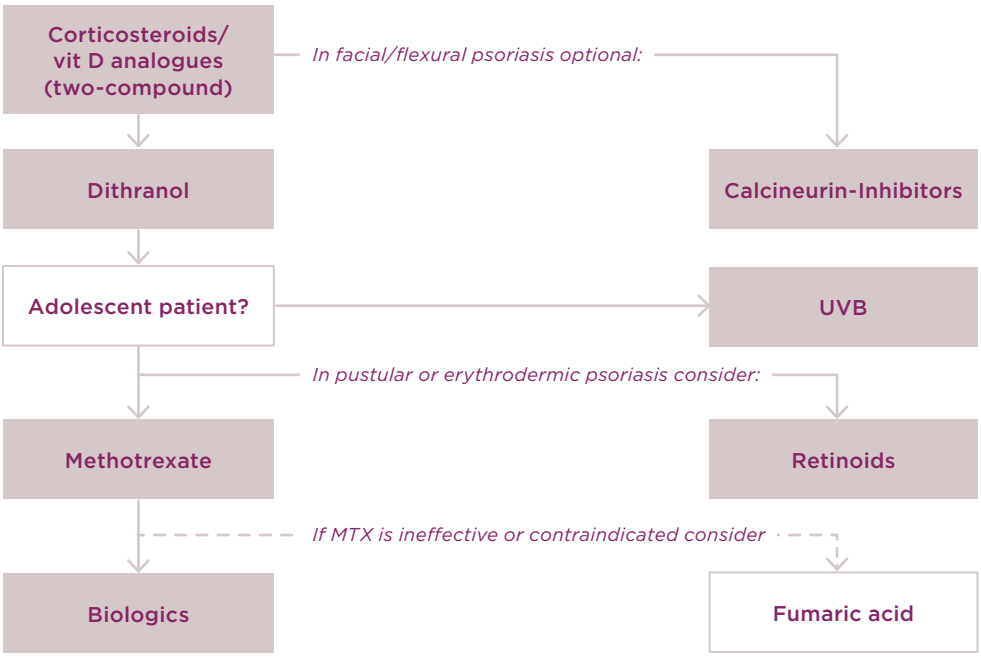
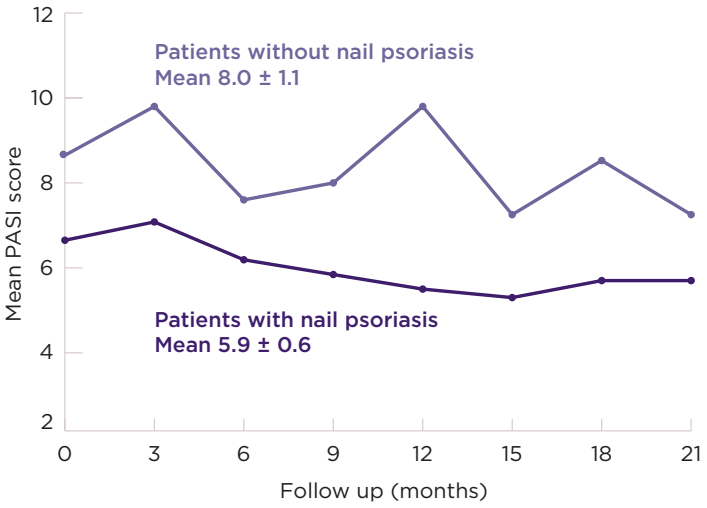


Figure 2: Estimated PASI scores during 2-year follow-up in pediatric psoriasis patients with nail involvement (n=65) and without nail involvement (n=278) at baseline (Bronckers et al. 2019)



risk of developing more severe disease course. In a study of 343 pediatric patients with psoriasis, nail involvement was associated with more severe disease during 2-year follow-up *(Figure 2)*.[10] These findings suggest that nail psoriasis is a potential clinical predictor for more severe disease over time in these pediatric patients. It is important to search for more severe-disease predictors for in pediatric psoriasis because it would help clinicians improve individualized treatment.

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