Viewing Psoriasis as a Systemic Disease for Better Health Outcomes

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TO THE EDITOR

Recent guidelines published by the National Psoriasis Foundation (NPF) and the American Academy of Dermatology (AAD) highlight the importance of addressing the systemic nature of psoriasis in clinical management of patients to optimize health outcomes (Elmets et al., 2021, 2019a, 2019b; Menter et al., 2020, 2019). Related guidelines have been issued by the American College of Rheumatology-NPF and the American Heart Association. The comprehensive form of published clinical guidelines yields a voluminous document often difficult to distill into a resource bank, particularly for patients. To enhance the uptake of these long-awaited psoriatic disease guidelines, NPF and expert partners (see Acknowledgments section) created an infographic condensing these guidelines for clinicians and patients (Figure 1) (American Academy of Dermatology Association, 2020; Armstrong et al., 2017; Grundy et al., 2019; Kurd and Gelfand, 2009; Rachakonda et al., 2014). The graphical summary offers providers a tool for easy comprehension and prioritization of care and a resource for discussions with patients, a key highlight of the guidelines.

Psoriasis is an immune-mediated inflammatory disease affecting an estimated 8.3 million persons in the United States, including an estimated 600,000 persons living with undiagnosed psoriasis (Kurd and Gelfand, 2009; Rachakonda et al., 2014). Common signs and symptoms of psoriasis include raised, discolored, scaly patches on skin; persistent rash; itch; and swelling. These symptoms are the superficial manifestations of psoriasis, driven by a systemic inflammatory process. This process impacts the whole body, leading to higher rates of comorbidities that must be considered in the management of patients to optimize patient outcomes and QOL.

Comorbidities

The systemic inflammatory processes underlying psoriasis can manifest as, or contribute to the development of, comorbidities, including psoriatic arthritis (PsA), cardiovascular disease (CVD), metabolic syndrome, and mental illness. Psoriasis is a chronic disease prone to flares, making successful long-term management of patients difficult and increasing the burden of disease and the impact on QOL. Comorbid conditions further complicate effective disease management, inhibiting and even impairing patient outcomes. As per NPF-AAD guidelines, psoriasis and its related comorbidities are influenced by several lifestyle choices, such as smoking and alcohol consumption (Elmets et al., 2019a). Patients should be educated about the association between these behaviors and psoriasis severity and comorbid conditions and provided tools and resources to support behavioral change. Proactively screening patients for the presence of these comorbid conditions, referral to appropriate specialists, and initiating therapy as appropriate may decrease their impact on patient outcomes—especially in the instance of PsA (Elmets et al., 2019a).

CVD. Systemic inflammation promotes atherosclerosis, leading to an increased risk of CVD in individuals with psoriasis (Baumer et al., 2018; Mehta et al., 2010). Many studies demonstrate increased risk of heart attack, stroke, heart failure, and abnormal heart rhythm. Guidelines issued by the American Heart Association and the American College of Cardiologists identify psoriasis as a potent risk factor for CVD that warrants consideration of early statin initiation to prevent future CVD development (Grundy et al., 2019).

PsA. An estimated 30% of individuals with psoriasis develop a form of inflammatory arthritis known as PsA (Mease et al., 2013). PsA commonly involves enthesitis and dactylitis and lacks a definitive diagnostic test, complicating diagnosis and treatment. However, validated screening tools exist to screen patients (Mease et al., 2013). If left untreated, PsA can lead to functional impairment and disability in as little as 6 months, underscoring the importance of proactively screening patients (Haroon et al., 2015).

Metabolic disorders. Metabolic syndrome (obese waist, hypertension, high glucose, high triglycerides) refers to a group of metabolic-related diseases that increase risk of heart disease, stroke, and type 2 diabetes (Esser et al., 2014). Recent research has provided insight into the immunological components connecting psoriasis and metabolic syndrome (Patrick et al., 2020). Metabolic syndrome is associated with chronic systemic inflammation that impacts adipose tissue, liver (increased steatosis), and pancreas (increased insulin production owing to peripheral insulin resistance) (Esser et al., 2014). Thus, patients with psoriasis have a higher prevalence of metabolic syndrome than the general population, which also increases risk of atherosclerosis (Armstrong et al., 2013).

Mental illness. Individuals with psoriasis are more likely to have clinical

Abbreviations: AAD, American Academy of Dermatology; BSA, body surface area; CVD, cardiovascular disease; NPF, National Psoriasis Foundation; PsA, psoriatic arthritis

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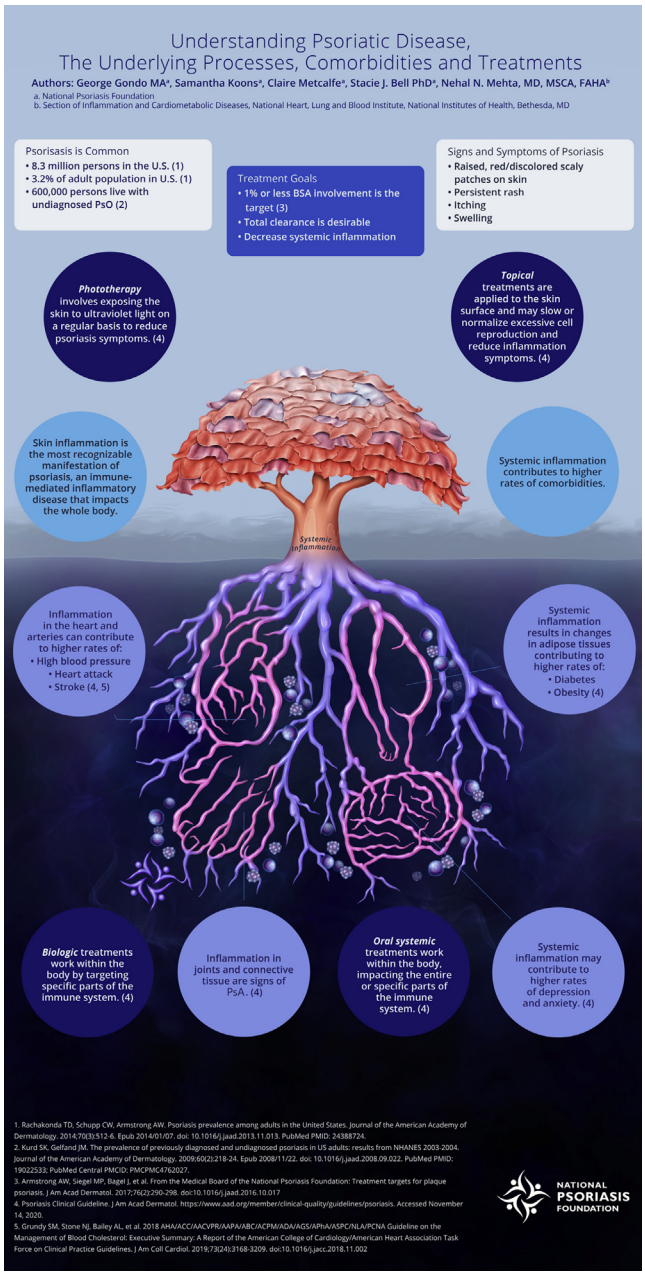

Figure 1. Infographic: Understanding psoriatic disease. The infographic of a tree and root system is a representation of psoriatic disease as an immune-mediated inflammatory disease with underlying systemic inflammation contributing to various comorbidities, while also outlining treatment options. The leaves of the tree represent the skin manifestations of psoriasis (e.g., raised, discolored scaly patches) that are the visible presentation of systemic inflammation. This systemic inflammation is depicted by the root system of the tree, which connects to visual depictions of associated comorbidities. The heart represents CVD. The enlarged belly represents metabolic syndrome. The brain represents mental health disorders, and the hand represents PsA. BSA, body surface area; CVD, cardiovascular disease; PsA, psoriatic arthritis. Image published with permission from the National Psoriasis Foundation.

depression than their peers (Dowlatshahi et al., 2014). Skin manifestations of psoriasis can contribute to patients feeling self-conscious and stigmatized, leading to altered social patterns, even avoiding social interactions. It is often assumed that these behavioral modifications facilitate the onset of depression. Yet, mental health disorders can both result from and contribute to progression of psoriasis. The presence of elevated proinflammatory cytokines suggest that psoriasis and mental health conditions (e.g., depression) may have overlapping biologic mechanisms (Koo et al., 2017).

Treatment goals and therapies for psoriasis

Treatment goals. Focusing treatment efforts on reducing body surface area (BSA) impacted and hence systemic inflammation is important, especially when considering comorbidities and optimizing health outcomes. Recent consensus work conducted by the NPF Medical Board yielded treatment targets for individuals with psoriasis when initiating therapy (BSA $\leq$3%), 3 months after initiation (BSA $\leq$1%), and during therapy maintenance (BSA $\leq$1%) (Armstrong et al., 2017). Treatment plan selection should be based on several factors, including disease severity, health status, patient preference and response to previous therapies, and acknowledging the systemic nature of psoriasis (Kaushik and Lebwohl, 2019a, 2019b). For a comprehensive list of available treatments for psoriasis, see the AAD-NPF Joint Guidelines for topical treatments, phototherapy, oral systemics, and biologics (Elmets et al., 2021, 2019b; Menter et al., 2020, 2008).

Topical treatments. Topical treatments encompass a variety of medications applied to the skin. These treatments may slow or normalize excessive cell reproduction andreduce inflammation symptoms and are appropriate for individuals with mild psoriasis (BSA $\leq$3%) or in combination with another treatment type. Topical treatments may impact systemic inflammation by impacting immune cell populations but may minimally impact risk of inflammatory-related comorbidities compared with other treatments (e.g., CVD, metabolic syndrome) (Ahlehoff et al., 2015; Elmets et al., 2019a; Wu et al., 2012).

Phototherapy. Phototherapy exposes the skin to UV light at prescribed intervals for a predetermined length of time to alter cytokine expression and immune response to reduce psoriasis symptoms (Wong et al., 2013). Similar to topical treatments, the impact of phototherapy on the risk of heart attack, stroke, and other cardiovascular comorbidities is lower than the impact of systemic psoriasis treatments(Ahlehoff et al., 2015; Strober et al., 2018; Wu et al., 2018).

Oral systemics. Oral systemic treatments refer to a broad class of treatments used to manage psoriasis that work within the body to impact the immune system through suppression of inflammatory

response, either in part or as a whole (Menter et al., 2020). Effect of oral systemic treatments on comorbidity risk is varied, making awareness of patient risk profile important when selecting these treatments(Hu and Lan, 2017).

Biologics. Biologics are a relatively new class of psoriasis treatments approved for individuals with moderate-to-severe psoriasis that target specific inflammatory pathways (Elmets et al., 2019a). Recent studies have shown salutary effects of biologic therapy on psoriasis-related comorbidities, such as PsA, metabolic disorders, CVD, and mental illness (Elmets et al., 2019a; Esser et al., 2014; Koo et al., 2017). Presence of risk factors or signs of comorbidities may influence the choice of a biologic therapy.

Conclusion

In conclusion, this letter and accompanying infographic provide a resource for providers to understand the systemic nature of psoriasis and comorbid disease and can serve to share this information with their patients and families. It is the hope that the information will be used to improve care and health outcomes and emphasize the importance of treating psoriasis as a whole-body disease.

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CONFLICT OF INTEREST

The authors state no conflict of interest.

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