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Severe relapse of generalized psoriasis in a young patient with Löfgren syndrome history

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Abstract

Psoriasis and sarcoidosis are two systemic inflammatory diseases characterized by elevated Th1 and Th17 lymphocyte activity and overlapping genetic components. Although psoriasis often accompanies known comorbidities, the simultaneous presence of acute sarcoidosis (Löfgren syndrome) is uncommon. A 23-year-old Caucasian male patient with a history of mild psoriasis without relapse since childhood presented with generalized psoriatic plaques. In May 2020, he experienced symptoms compatible with Löfgren syndrome (LöS), which followed complete resolution after three months of systemic corticosteroid therapy. After one year of treatment with adalimumab, the Psoriasis Area and Severity Index (PASI) decreased from 25.3 to 4.2, while sarcoidosis remained stable.

The common pathogenic mechanisms between psoriasis and sarcoidosis warrant further investigation. This case emphasizes the importance of vigilance for respiratory symptoms in psoriasis patients and the potential for psoriasis reoccurrence post-sarcoidosis. Dermatologists need to be aware of these associations, promoting comprehensive management strategies for psoriatic patients with a history of sarcoidosis.

Introduction

Psoriasis is a systemic inflammatory disease characterized by increased activity of Th1 and Th17 lymphocytes. Sarcoidosis is a chronic disease of poorly understood etiology, characterized by sarcoidal granulomas with aggregates of Th1 and Th17 cells.[1] It affects many organs, mimicking a great majority of pathologies, and one distinct phenotype is called Löfgren syndrome.[2,3] The studies indicate that sarcoidosis, including Löfgren's syndrome, is more prevalent in specific populations, such as African Americans and individuals of Scandinavian descent. However, the exact global prevalence of LöS remains undetermined, probably because of diagnostic challenges, underreporting related to benign prognosis, and discrepancies in diagnostic practices across medical specialties.[1-4] LöS has been observed in 33% of sarcoidosis cases in Sweden, 19% in Turkey, 44.7% in Spain, and infrequently in Asian populations.[4,5] Löfgren syndrome is characterized by acute onset of fever and symptoms consisting of bilateral hilar lymphadenopathy, erythema nodosum, and/or bilateral ankle arthritis or periarticular inflammation and has a benign prognosis.[6]

Increased activity of specific immunity pathways, common genetic factors, and the promising results obtained in both sarcoidosis and psoriasis patients after applying anti-TNF-α agents support the hypothesis of their common pathogenic mechanisms.[7] In this case, we will discuss the rare association of psoriasis and Löfgren syndrome. We aim to raise consciousness and knowledge about the possibility

of late reoccurrence of psoriasis in patients with an episode of acute sarcoidosis.

Case Report

A 23-year-old Caucasian male patient, while in complete remission for approximately 14 years, presented to the Dermatology clinic with a severe flare of psoriasis. It appeared with generalized, well-circumscribed, erythematous, and infiltrated plaques exhibiting thick scales on the surface. He had been successfully managed with local glucocorticosteroids and emollients in childhood without relapse. He was a smoker and overweight.

The patient referred that during the COVID-19 pandemic, in May 2020, he sought consultation with a primary care physician, presenting with symptoms including high temperature, cough, ankle joint pain and swelling, and painful erythematous plaques localized to the shin regions. Routine laboratory examinations were within normal range except for antistreptolysin O=634 IU/mL, C-reactive protein (CRP)=35.7 mg/L, angiotensin-converting enzyme (ACE)=161.8 U/L, and leukocytosis. Sars CoV-2 rapid test and Manthoux test resulted negative. Serology for autoimmune diseases, infections, and hemomalignancies was unremarkable. The lung computed tomography (CT) scan showed aortopulmonary lymph nodes up to 1.3 cm, bilateral hilar lymph nodes up to 1.4 cm, and subcarinal lymph nodes up to 2.2 cm, without parenchymal changes. Unfortunately, broncho-alveolar lavage and lymph node biopsy were not performed at that time because of pandemic restrictions in hospitals dedicated to patients with respiratory symptoms. Based on the clinical presentation and the presence of bilateral hilar lymphadenopathy, Löfgren syndrome was confirmed, accompanied by elevated levels of ACE. He was prescribed cephalosporin, NSAIDs, and prednisone 50 mg orally for 10 days, tapering 5 mg every 5 days. After three months, laboratory examinations became normal, and the CT scan showed no lymphadenopathy.

Upon his arrival at the dermatology clinic, the skin lesions were clinically (Figure 1) and histologically (Figure 2) compatible with psoriasis vulgaris. A skin biopsy was required to exclude psoriasiform cutaneous sarcoidosis in this patient with an acute sarcoidosis history. The pathologist excluded the presence of granulomas. Psoriasis Area and Severity Index (PASI) was 25.3. Different therapeutical alternatives were discussed, taking into account the clinical severity of psoriasis, its side effects, and the patient's history. After one year on the adalimumab regimen, his clinical signs improved, and his PASI decreased to 4.2 (Figure 3).

Discussion

Strauss described for the first time the association of comorbid disease (diabetes) among psoriatic patients in 1897.[8] Nowadays, psoriasis is described as a systemic inflammatory disease related to many well-known comorbidities: cardiovascular, neuropsychiatric, respiratory, gastrointestinal, endocrine, renal, and rheumatological diseases.[9]

Recent studies have proved a statistically significant association between psoriasis and sarcoidosis. A Danish nationwide study indicated for the first time a strong association between psoriasis and sarcoidosis. This association increased with increasing psoriasis severity and remained statistically significant after adjustments for potential confounding factors.[1] In another population-based study in the USA, sarcoidosis was found to be significantly associated with psoriasis, underlying the need for screening psoriasis patients for the development of new cardiopulmonary symptoms.[8-10] Comorbidome of psoriasis in a wide Israeli patients study revealed that sarcoidosis was one of the inflammatory diseases with strong association.[11] Due to the rare co-occurrence of these conditions, there is currently a lack of statistical data regarding the risk of LöS in patients with psoriasis within the existing literature.

Common inflammatory mechanisms combined with a complex interplay with genetic factors are likely to explain their occurrence. Their systemic immunologic response includes the activation of Th1 and Th17, resulting in the release of IFN-γ and proinflammatory cytokines, including IL-12, IL-17, IL-18, and TNF-α.[12,13] Th17 cells participate in the phase of alveolar granuloma and progression to the fibrous phase of sarcoidosis. Th1 and Th17 cells are involved in the pathogenesis of psoriasis by releasing inflammatory cytokines that promote the recruitment of immune cells, the proliferation of keratinocytes, and the maintenance of the inflammatory response.[14]

Moreover, an enhanced TNF-α secretion by BAL macrophages is observed in sarcoidosis, mediating granuloma formation and maintenance. TNF-α activates Th17 cells to lead IL-17 production, and IL-17 inflammatory pathway has been suggested to be important in psoriasis.[12]

It has also been reported that the pso p27, a protein detected in mast cells in psoriatic lesions and extractable from psoriatic scales, is markedly increased in the lungs of patients with pulmonary sarcoidosis.[7] Their pathogenesis is driven by distinct yet overlapping immune mechanisms involving the JAK-STAT signaling pathway. In psoriasis, the JAK-STAT3 axis is primarily activated by IL-23, promoting Th17 cell differentiation and the release of pro-inflammatory cytokines (IL-17 and IL-22) that induce keratinocyte hyperproliferation and chronic inflammation. In contrast, sarcoidosis is driven by Th1 responses where IL-12 and IFN-γ activate JAK2/STAT1 signaling, facilitating granuloma formation and tissue damage, with IL-23 further amplifying inflammation via STAT3 activation. Therapeutically,

psoriasis is managed with JAK inhibitors like tofacitinib, baricitinib, and upadacitinib, which target specific JAK family members to suppress the pro-inflammatory cytokines involved in skin inflammation. Biologics targeting IL-23, such as guselkumab and tildrakizumab, also indirectly regulate the JAK-STAT pathway. In sarcoidosis, JAK inhibitors show potential in modulating the Th1-driven inflammatory response, particularly by inhibiting JAK2/STAT1 signaling to reduce granuloma formation.[15]

From the genetic perspective, polymorphisms in the IL-23 receptor gene have been reported as a factor associated with both sarcoidosis and psoriasis.[13] Clinically, in sarcoidosis, the systemic immune response produces psoriasiform granulomatous skin lesions; therefore, a cutaneous biopsy is needed to differentiate psoriasiform sarcoidosis from psoriasis.[14]

The treatment of these diseases has continuously evolved over the years, and new treatments are available. Adalimumab, a fully human monoclonal anti-TNF antibody, is applied to treat plaque psoriasis and sarcoidosis. A 52-week trial of adalimumab in the treatment of refractory sarcoidosis results in a successful outcome with no severe adverse incidents reported.[16] A paradoxical response, so-called sarcoid-like granulomatosis, was reported in 10 patients with rheumatologic diseases receiving anti-TNF-α agents, including adalimumab.[17] Mazur *et al.* described a 51-year-old female who developed Löfgren syndrome while treated with etanercept for psoriatic arthritis.[18] Therefore, we are monitoring our patient through periodical laboratory and imaging examinations. Adalimumab provides a dual therapeutic benefit by targeting both cutaneous and systemic inflammatory processes, thereby reducing the risk of cardiovascular, cerebrovascular, and gastrointestinal complications, as well as preventing the progression of arthritis.[19,20] To date, our experience with adalimumab has yielded positive outcomes. After one year of treatment, we observed a reduction in the PASI score, stability in pulmonary sarcoidosis, and no occurrences of immunogenicity or infectious diseases.

Conclusions

The common underlying factors linking psoriasis and sarcoidosis remain an area of limited knowledge. We must be attentive to the appearance of respiratory symptoms in a psoriatic patient due to the known association with sarcoidosis and the possibility of psoriasis relapse after the episode of sarcoidosis. This case highlights the need for continuous awareness and education among dermatologists to comprehensively manage psoriatic patients with a history of sarcoidosis.

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Figure 1. Generalized psoriasis before treatment.

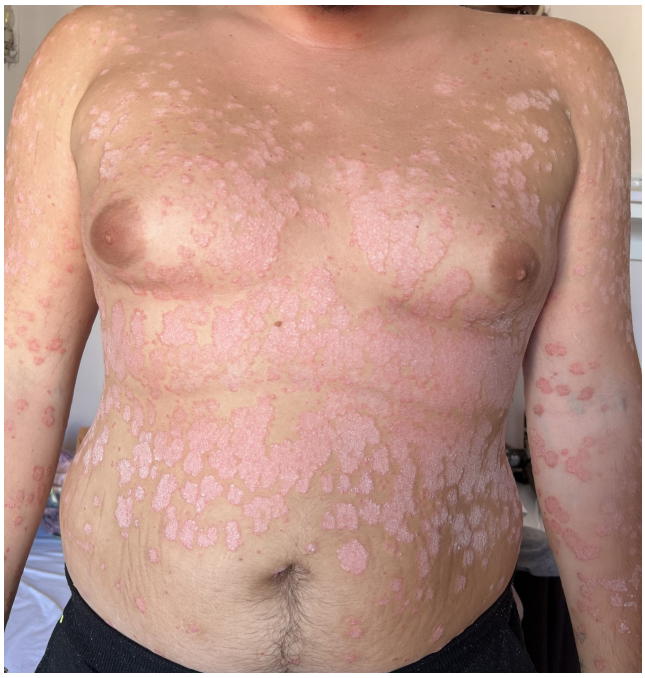

Figure 2. Typical findings of psoriasis with acanthosis (red arrow), parakeratosis (white arrow), spongiosis, intraepithelial neutrophils, perivascular lymphocytic infiltrates (black arrow) in papillary derma without granulomas. H&E staining, x20.

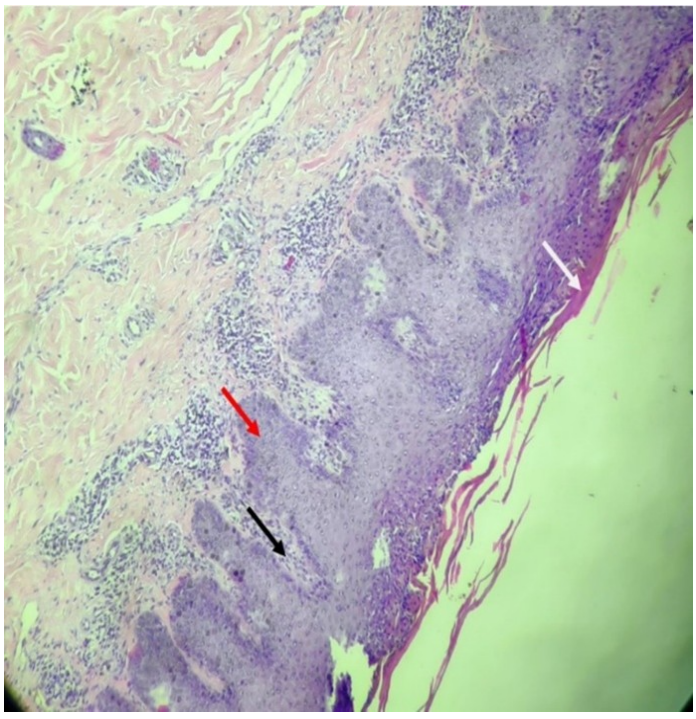

Figure 3. Clinical improvement after adalimumab therapy.