SHORT COMMUNICATION

Insights into New-onset Arthritis in Patients with Hidradenitis Suppurativa

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Immune-mediated inflammatory diseases (IMIDs), encompassing conditions such as psoriasis, hidradenitis suppurative (HS), and various forms of arthritis, share common underlying immunopathological targets and a treatment approach. This leads to the possibility of multiple IMIDs coexisting within the same individual, with a higher likelihood of experiencing a second IMID after the first occurrence compared with the general population (1). However, the exact etiopathogenic mechanism underlying this phenomenon remains elusive.

In this context, we present 3 distinct clinical cases of patients with HS who subsequently developed new-onset arthritis. Through these cases, we introduce various potential etiopathogenic hypotheses regarding the association of IMIDs, particularly HS and arthritis.

CASE REPORTS

The first case is a 39-year-old man diagnosed with Hurley stage II HS, who showed a mixed phenotype involving the axillae, trunk, groins, and perineum from the age of 16. Remarkably, he had not undergone any previous treatment or dermatological follow-up. At the age of 37, he sought an evaluation from the rheumatology department due to oligoarthritis affecting wrists, knees, and ankles, associated with global inflammatory axial involvement predominantly in the cervical region, buttocks, multiple enthesitic pain, and stiffness. The blood study revealed elevated acute phase reactants and negativity of autoimmunity parameters including human leukocyte antigen (HLA)-B27, rheumatoid factor (RF), and cyclic citrullinated peptide (CCP) antibody. However, antinuclear antibodies (ANAs) were positive at a titre of 1/640. The patient was diagnosed with axial and peripheral spondyloarthritis associated with HS. Due to the inefficacy of non-steroidal anti-inflammatory drugs and the absence of approved biologics covering both conditions at the time, infliximab (IFX) was initiated at a spondyloarthritis dosing of 5 mg/kg every 2 months to address both manifestations.

The second case involves a 61-year-old man with an extensive history of Hurley stage III HS, characterized by an inflammatory phenotype (2) affecting the axillae, groins, buttocks, and perianal region. After the inefficacy of topical and oral antibiotics, a 2-year course of adalimumab (ADA) was initiated in January 2020 without clinical improvement. Subsequently, in February 2022, intravenous IFX was started at a dosage of 10 mg/kg every 2 months. After the second IFX infusion, the patient developed asymmetric non-erosive peripheral arthritis involving the metacarpophalangeal and interphalangeal joints, and wrists. Serological analysis showed elevated acute phase reactants, with negative results for HLA-B27, RF, ANAs, and anti-CCP. Therefore, a diagnosis of paradoxical arthritis induced by IFX was established. The treatment plan involved IFX maintenance, a daily descending dose of steroids (0.5 mg/kg), and weekly oral methotrexate (15 mg) added to IFX, leading to sustained remission of both dermatological and rheumatologic domains.

The third case concerns a 29-year-old woman diagnosed with Hurley stage II HS since the age of 16, displaying a mixed HS phenotype in the groins and buttocks. She received a regimen of ADA 80 mg every 2 weeks from the age of 18 until 28 years old, when she developed asymmetric non-erosive subacute peripheral arthritis, mainly affecting proximal interphalangeal joints. Despite elevated acute phase reactants, no specific serological biomarkers were identified. Consequently, a diagnosis of peripheral seronegative arthritis was established. Due to a partial response to naproxen (550 mg twice daily) added to ADA, she was recommended to initiate treatment with the anti-IL17 agent secukinumab following approval by the European Medicines Agency (EMA) for HS.

DISCUSSION

Here, we have presented 3 distinct clinical scenarios involving the emergence of new-onset arthritis in patients with pre-existing HS. The first case depicts a spondyloarthritis associated with a long-term untreated HS, potentially attributable to the natural course of the disease. After a narrative review of the literature, the prevalence of spondyloarthritis in HS currently appears to be higher compared with that observed in the general population (0.93–28.2% vs 0.2–1.6%) (3). Moreover, in the systematic review of Hanna et al. (3), this manifestation was more frequent in males with earlier onset of the disease and severe HS. Furthermore, there is an increased occurrence of rheumatoid arthritis observed in HS patients (up to 4.8% vs 0.2–1%), while the prevalence of psoriatic arthritis mirrors the general population (0.3%) (3–5). Although the exact cause of the HS–arthritis association remains unknown, we suggest that immune dysregulation, particularly involving Type 1 and Type 3 immunity (6), along with dysbiosis, might play a role, similar to observations already described in inflammatory bowel disease–arthritis (7).

In contrast, the second and third cases involve the development of seronegative peripheral arthritis in patients undergoing anti-TNF treatment. Specifically, the second case reveals a new onset of arthritis following the introduction of IFX, which suggested a potential paradoxical arthritis induced by anti-TNF therapy. Indeed, a paradoxical reaction is defined as the occurrence of a condition typically responsive to a specific class of drugs during biological treatment (8, 9). Though the terminology is not clear, these reactions often demonstrate a cause-and-effect relationship between the initiation of a new drug and the development of the new condition, with approximately

70% occurring within the first year (10). Paradoxical reactions have been well documented in the literature, with psoriasiform (10) and HS-like lesions (9, 11) being reported during biological treatment in patients with diverse IMIDs, including rheumatologic disorders (11). On the other hand, paradoxical arthritis has also been described while undergoing treatment with TNF-α inhibitors (12, 13). While psoriatic arthritis during anti-TNF treatment for psoriasis is well documented (14), limited evidence exists regarding arthritis during anti-TNF treatment for HS (15). In the study of Megna et al. (14), new-onset psoriatic arthritis developed in 10 out of 118 patients (8.5%) during a 1-year follow-up period. The primary ongoing treatments in the new-onset psoriatic arthritis group were ADA, ustekinumab, and secukinumab. It is important to highlight that the real incidence of arthritis in ongoing biological therapy for HS remains unknown. Moreover, there is a lack of specific clinical or serological biomarkers to identify paradoxical reactions. Although the specific immunopathological features of paradoxical arthritis in HS remain unclear, it is plausible that the pathogenesis involves the overexpression of Interferon beta (IFN-β), Interferon alpha (IFN-α2a), and proinflammatory molecules associated with the IL-23/Th17 axis (14). The dysregulation of these cytokines may lead to aberrant immune responses, triggering and perpetuating arthritic symptoms in HS patients undergoing anti-TNF treatment.

Lastly, in the third case, a considerable time gap between the initiation of ADA and the onset of arthritis makes it challenging to establish direct causality. This stimulates a significant debate on whether arthritis could result from the natural course of the disease or emerge as a late-onset manifestation induced by anti-TNF therapy in an individual with underlying susceptibility. This hypothesis, suggesting a link between anti-TNF drugs and late-onset manifestations, may be explained by a chronic modulation of classical immunopathological processes favouring the appearance of new-onset IMIDs. However, additional research is mandatory to confirm this hypothesis. Thereby, considering that the first biological approval for HS by the EMA was ADA in 2015, conducting exhaustive follow-up could be of interest to evaluate the long-term effects of inflammation modulation in individuals with HS.

In conclusion, it is crucial to assess the development of arthritis in individuals with HS continuously, even during ongoing biological treatment. Further studies are essential to thoroughly understand the pathophysiological pathways behind the proposed clinical scenarios, promoting targeted therapeutic strategies. Adopting a multidisciplinary approach with rheumatologists is recommended to enhance our understanding and management of arthritis in individuals with HS.

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