

SHORT COMMUNICATION

Different Responses to Ustekinumab of Two HLA-Cw6-positive Homozygous Twins with Psoriasis

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The immunopathogenesis of psoriasis has been extensively reviewed in recent literature. Human leukocyte antigen (HLA)-Cw6 has been identified as the major psoriasis susceptibility genetic polymorphism and identifies early-onset (type 1) psoriasis (1). Recently Talamonti et al. (2) observed that the HLA-Cw6 allele is associated with a faster and better clinical response rate to ustekinumab. Ustekinumab is a human monoclonal antibody directed against interleukin 12 and interleukin 23; cytokines that regulate the immune system and immune-mediated inflammatory disorders. We describe here 2 HLA-Cw6-positive homozygous twins, both affected by psoriasis, who showed different responses to ustekinumab.

CASE REPORTS

The first of the homozygote twins, a 47-year-old obese man (160 kg, body mass index (BMI) 53.5) had had psoriasis since 1990. His medical history revealed that he had previously been treated with topical therapy (corticosteroid and calcipotriol) followed by cyclosporine, 3 mg/kg based on ideal weight, which was stopped after 6 months due to arterial hypertension. He then started methotrexate, 15 mg/week, for approximately one year, experiencing only a partial response (Psoriasis Activity Severity Index (PASI) 50). When assessed at our unit, he had moderate psoriasis (PASI 17). Before starting biological therapy, general laboratory, physical examination and an X-ray were performed. Surprisingly no sign of metabolic disease was found. As the patient's weight was more than 100 kg, we decided to start ustekinumab, 90 mg, using the standard protocol (time 0, after 4 weeks, and every 12 weeks thereafter). After only 3 injections a significant improvement was noted (PASI 9). Due to this positive result, the patient's brother, his homozygous twin, who had had psoriasis since 1992 requested similar treatment. He had previously been treated with topical steroids and, when his psoriasis worsened (PASI 22), he started cyclosporine, 3 mg/kg, with a positive response after 6 months of therapy (PASI 5), but he had to stop the treatment due to severe epigastralgia. Methotrexate, 15 mg/week, was then introduced, but stopped after 3 months due to lack of improvement. Due to the patient's weight (140 kg, BMI 43.21), and thinking that ustekinumab might also be efficient in the twin brother, we decided to start ustekinumab, 90 mg, following the standard protocol. After only 4 injections the PASI decreased from 22 to 7. All follow-up examinations for the 2 patients were within the normal ranges, but the clinical follow-up was different. After 2 years of treatment, the first twin showed progressive deterioration of the disease (final PASI score 33, increased from 9), while the second twin reached stabilization at PASI 5. To investigate the genetic psoriasis predisposition profile of our patients, we checked for the presence of the HLA-Cw602, which is linked to ustekinumab efficacy. The presence of the same HLA-Cw602 allele was found in both twins.

DISCUSSION

Few articles have been published concerning psoriasis among twins (1). Psoriasis in concordant, monozygotic twin pairs tends to be similar with respect to age of onset, distribution pattern, severity and course. The therapeutic response has not been completely studied in the literature. The largest twin study on psoriasis was published in the British Journal of Dermatology in 2013 (3). The Danish Twin Registry, involving 10,725 twin pairs, was used. However, the article does not report how the twins responded to the therapy. It states that homozygotic twins have more probability of both developing psoriasis than heterozygotic twins, thus confirming the contribution of genetics to psoriasis, but also suggesting that genetics is not the only factor.

Our patients responded in the same way to ustekinumab, but after 2 years their response to the treatment changed.

HLA-Cw6 is the major psoriasis susceptibility genetic polymorphism and identifies early-onset (type 1) psoriasis. Talamonti et al. stated that patients carrying the HLA-Cw6 allele had a greater response to ustekinumab (achieving a PASI score of less than 5) than patients without this allele. Moreover, HLA-Cw6-positive patients responded more quickly to ustekinumab than did HLA-Cw6-negative patients, with almost 90% of HLA-Cw6-positive patients achieving significant improvement within 4 weeks, compared with only 60% of patients without the allele (2).

Surprisingly, after an effective and rapid response in both twins, who had a compatible genetic profile, the first patient deteriorated. This suggests that other factors influenced the development of psoriasis in our patients. We therefore investigated the personal life of the patients for triggering factors. The non-responsive twin is a truck driver, who works night shifts and is married with children. Although he weighs 160 kg and is considered obese, no metabolic syndrome was found. The second twin, who still responds effectively to ustekinumab, is employed in an office 40 h/week. He is single and weighs 135 kg. The difference in weight between the twins might be a triggering factor for the difference in response (4). However, since both twins weigh more than 100 kg, we would expect that both would show an attenuated response to ustekinumab over time (4).

One possible explanation is that the first patient developed an immune response to the drug, conditioning faster clearance of ustekinumab, thus reducing its blood levels and, as a consequence, reducing its efficacy. However, this hypothesis could not be confirmed, since neither anti-ustekinumab antibodies nor serum drug concentration were tested because these techniques are not used on a daily basis (5).

In conclusion, we emphasize the importance of the presence of HLA-Cw6 in order to obtain a fast response in patients treated with ustekinumab. However, for a stable PASI over time, other factors, such as immune response, can influence ongoing treatment. The different immune response observed in the homozygous twins described here may depend on their different lifestyles; however, further research is needed to confirm this hypothesis.

The authors declare no conflicts of interest.

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