Brodalumab Seems to Recover Its Therapeutic Efficacy After a Relatively Short "Washout" Period with Anti-TNF Agents: A Successful Pattern for Double-switch Therapy

Psoriasis is a lifelong disease with a chronic relapsing course, and treatment agent switching is a common and accepted practice in cases of primary or secondary inadequate response. Patients with prior biologic treatment failure or loss of response are a subset of individuals who most likely have more severe disease with a greater impact on quality of life. Additionally, switching between multiple biologics is associated with clinical consequences (e.g. development of anti-drug antibodies), which may limit efficacy of subsequent biologic therapies (1,2). Adalimumab and brodalumab were both shown to be highly specific and efficient while sparing the cumulative toxicity observed in conventional anti-psoriatic drugs use. An observational study on 5 patients suffering from severe plaque psoriasis provided a successful pattern on double-switching of the aforementioned biologic agents. Therapy was initiated with brodalumab, and after secondary failure or occurrence of arthritic comorbidities, a short washout period with adalimumab followed without striking results. Re-administered brodalumab showed retrieval of initial therapeutic efficacy on both skin and joints. Patients provided written informed consent.

Five Caucasian patients (mean age 53.2 years), with severe plaque psoriasis (mean baseline Psoriasis Area and Severity Index (PASI) score 18.58) and seriously affected Dermatology Life Quality Index (DLQI) (median score 19.3) underwent brodalumab treatment with excellent response. However, a secondary loss of efficacy occurred within an average period of 23 months, with intense arthritic implication in three patients. A switch to adalimumab followed, which lasted 4.2 months on average. Due to inadequate response, treatment with brodalumab was resumed (Figure 1).

Resumption of treatment with brodalumab, after a rather short "washout" period with adalimumab, led to immediate remission of psoriasis, reducing median PASI and DLQI scores to 1.84 and 2.3 respectively, while still maintaining this effectiveness for an average of 8.8 months (follow-up timepoint). The clinical course over time for patient 2 is presented from the start of brodalumab treatment to the first and second relapse before completing and maintaining treatment with this biologic agent (Figure 2). Interestingly, at the same time, comorbidities in 3 of 5 patients with the axial psoriatic arthritis type that had arisen earlier subsided with remarkable clinical amelioration.

Switch therapy in patients with severe psoriasis is a common clinical practice, due to the chronic and unpredictable course of the disease, both in nonre-

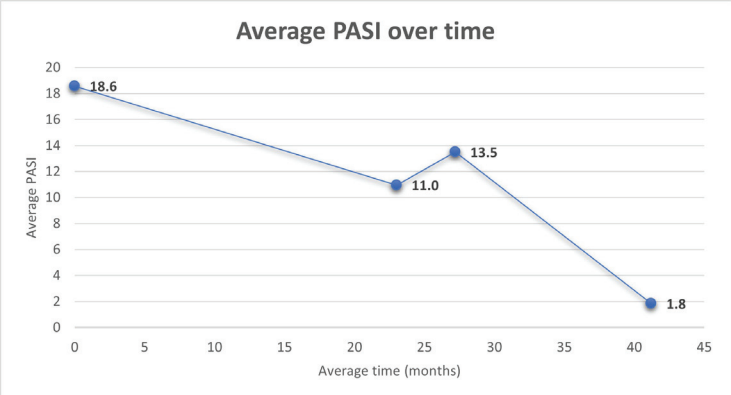

Figure 1. Average Psoriasis Area and Severity Index score at every phase of switch therapy from baseline to final follow-up.

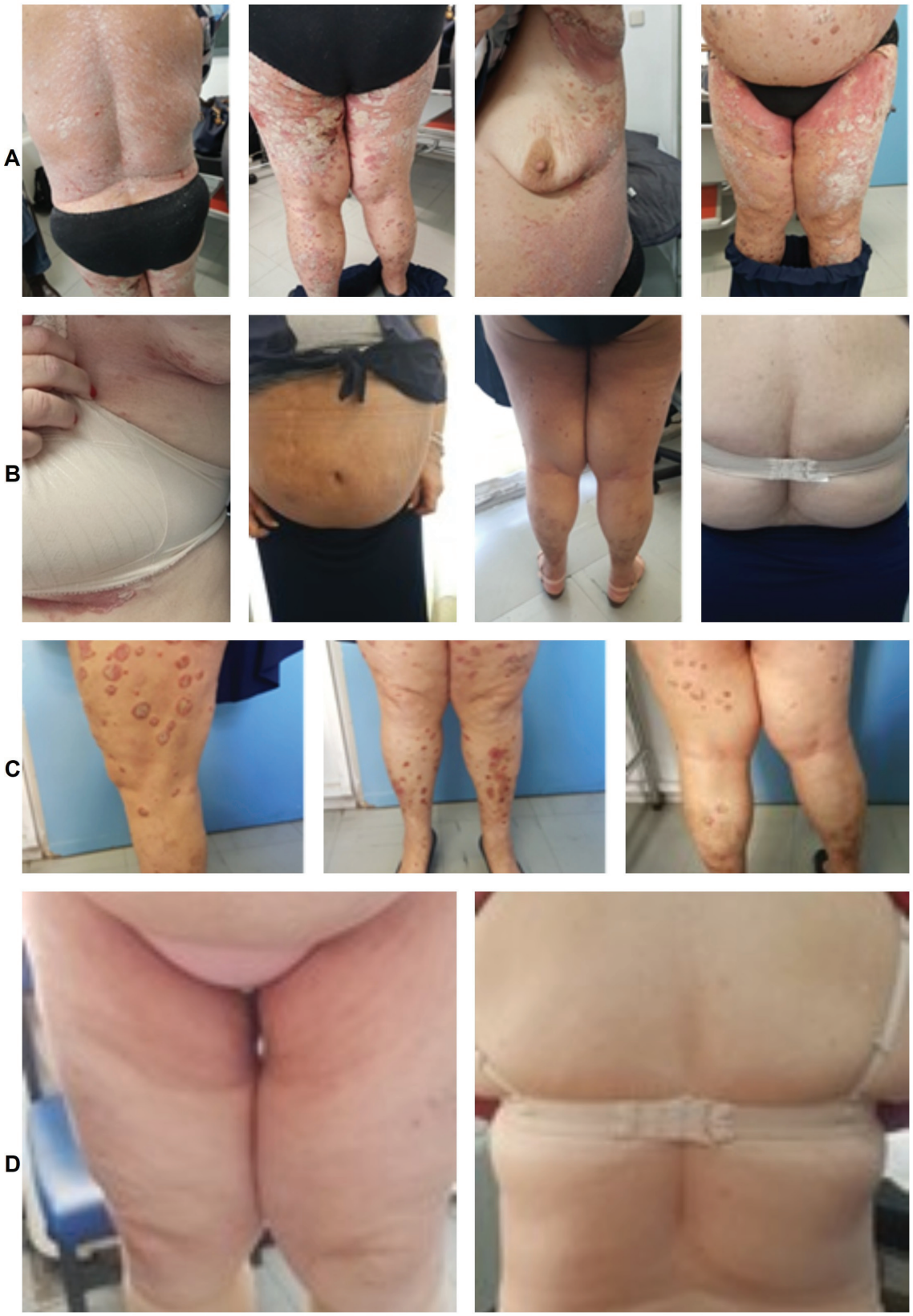

Figure 2. Patient 2 outcomes over the treatment period: (A) Baseline (brodalumab initiation); (B) clinical appearance after brodalumab initiation and maintenance up to 12 months; (C) 12 months since brodalumab initiation – 1st switch – adalimumab initiation; (D) 2nd switch – 26 months since reinitiating brodalumab.

sponsive or relapsing cases, and few studies have assessed the efficacy of a second line biologic treatment in this population. A real-life, multicenter, prospective study in Italy supported the switch from anti-IL 17 to adalimumab or ustekinumab as a safe and effective therapeutic strategy, but there was a gap for patients with loss of efficacy after failure of the second biologic treatment (3). The mechanism for secondary loss of efficacy of a biologic agent is still unclear, possibly due to altered immunogenicity closely connected to complex cytokine imbalance and activation of secondary pathways in disease induction and/or exacerbation. Brodalumab, having a unique mechanism of action inhibiting the receptor of the central cytokine implicated in the pathogenesis of psoriasis, not only has a broader effect on downstream inflammatory pathways but also overcomes the loss of response to anti-TNF inhibitors. The immunogenicity profile of brodalumab may supports its potential efficacy, which overlaps with the other biologic therapies (4-6). The present observational study described an unobserved successful management of severe psoriasis in which, for some reason, the initially administered brodalumab temporarily lost its effectiveness. It seems that the interference of adalimumab for a relatively short period enables the full healing capacity of brodalumab to be restored, with a positive rebound-like therapeutic outcome. The observed model may be worth studying in a larger number of patients in order to elucidate the underlying mechanisms and provide a pattern for a more efficient approach in cases of primary or secondary resistance.

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