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BRIEF REPORT

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Successful use of tralokinumab for the treatment of atopic dermatitis on the genitals

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ABSTRACT

Background: Genital involvement in atopic dermatitis(AD) can have a significant impact on the patient's quality of life. However, inspection of genital areas is not usually conducted during routine examination and patients may be reluctant to inform the clinician or show this area.
Objective: to evaluate the efficacy of tralokinumab in AD patients with genital involvement.
Methods: Adult patients with moderate/severe AD and genital involvement receiving tralokinumab have been analyzed. Primary endpoints were EASI, DLQI, PP-NRS, genital-IGA (g-IGA) and genital itching (GI) at week 16.
Results: out of 48 patients with moderate/severe AD under treatment with tralokinumab, 12 patients (25%) showed a genital involvement. Seven patients reported itching in the genital area (58%), while none reported a positive history of genital infections. Median scores at T0 were EASI 17.5, PP-NRS 8 and DLQI 14. After 16 weeks of treatment, we observed a median EASI of 3, a median PP-NRS of 1 and a median DLQI of 1. Finally, concerning the genital response, after 16 weeks of treatment, we observed a statistically significant decrease in mean GI and g-IGA scores.
Conclusion: despite the small size of our sample, tralokinumab can be considered as a valid treatment option for AD with genital involvement.

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KEYWORDS
Atopic dermatitis; tralokinumab; genitals

Introduction

Atopic dermatitis (AD) is a chronic inflammatory disease that can affects any part of the skin, including the genital area. The presence of AD in the genital area can have a significant impact in the quality of life of patients. Nevertheless, routine physical examinations of AD patients seldom include an inspection of the genitals, and patients may exhibit reluctance in disclosing or exposing this area to their healthcare provider. Consequently, genital AD occurrences frequently go unnoticed and are inadequately documented (1–4). Given the potential for substantial impacts on patients' quality of life associated with this anatomical location, identifying appropriate therapy holds paramount importance for this patient cohort.

Tralokinumab is a fully humanized IgG4 monoclonal antibody, binding with high affinity the interleukin (IL)-13, preventing its interaction with the receptor, subsequently down streaming the signaling and improving AD (5). Therefore, we investigated to ascertain the frequency of genital AD among patients exhibiting moderate to severe AD, and to evaluate the efficacy of treatment using the interleukin IL-13 inhibitor, tralokinumab.

Materials and methods

The study was performed across three distinct medical centers located in Northern Italy. Our study employed a noninvasive approach, relying on data acquired during routine patient consultations. As the study's procedure did not deviate from good clinical practice, no instituinal review board was required. The study was conducted following the Helsinki declaration of 1964 and its later amendments. Written informed consent was obtained from all study participants. We included patients (≥ 18 years old) with moderate/severe AD involving also the genital areas, under treatment with tralokinumab. We excluded patients with also concomitant other chronic inflammatory conditions in genital area.

Severity of AD was assessed by means of Eczema Area and Severity Index (EASI; scoring range 0–72, with higher scores indicating greater severity); Dermatology Life Quality Index (DLQI; 0–30, with higher scores indicating worse quality of life) and Peak Pruritus Numerical Rating Scale (PP-NRS; 0– 10, with higher scores indicating worse itching). Moreover, we assessed specific genital involvement evaluating the patient's reported GI on a

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scale from 0 up to 10. Furthermore, g-IGA (from 0 up to 5) was used to define the severity of the genital component at T0 and after 16 weeks of treatment. Mann-Whitney U-test was used for statistical analysis and $p < 0.05$ was considered statistically significant.

Results

A total of 48 patients (median age 37; 24 M:24F; EASI = 19; PP-NRS = 8; DLQI = 23) with moderate to severe AD undergoing treatment with tralokinumab, were enrolled. Among them, 12 patients (25%) had involvement of the genital area (6 female, 6 male), with a median age of 44.5 years (range 20-71). (Table 1) Of these 12 patients, 9 had other comorbidities (such as rhino-conjuncitivitis 4, hypertension 2, leukemia 1, asthma 2, allergic contact dermatitis 1, headache 1, celiac disease 1, atrial fibrillation 1, sideropenic anemia 1). Concerning previous treatments, 5 patients had received systemic steroids, 2 patients cyclosporin, 1 patient upadacitinib and 1 patient dupilumab. While, topical steroids had been prescribed in 10 patients and topical calcineurin inhibitors in 7 patients. The main associated anatomical areas were the head/neck region ($n = 10$), trunk ($n = 8$) and limbs ($n = 10$). Specifically, among the limb involvement cases, hands were affected in 2 female patients. In term of symptoms, 7 patients reported itching in the genital area (58%), while none reported a positive history of genital infections. Median scores during the first visit were EASI 17.5 (range 15–35), PP-NRS 8 (range 6–10), DLQI 14 (range10–25) (Table 1).

Table 1. Clinico-pathologic features at baselines.

	n≠	%≠	n±	%±
Gender				
M	24	50	6	50
F	24	50	6	50
Age	37		44.5	
Anatomic area				
Trunk	43	95	8	66
Limbs	47	100	10	83
Head/Neck	15	29	10	83
EASI	19		17.5	
NRS	8		8	
DLQI	23		14	

≠general population; ±patients with genital involvement.

After starting treatment with tralokinumab, 2 patients did not show improvement (both genital and cutaneous). Among the 12 patients, only 1 necessitated the continuation of topical treatments for genital involvement (topical steroids and emollients). Therefore, excluding the two therapeutic failures, among the remaining 10 patients, by week 16, we observed a median EASI of 3 (range 0-9), a median PP-NRS of 1 (range 0-6). All patients reported a

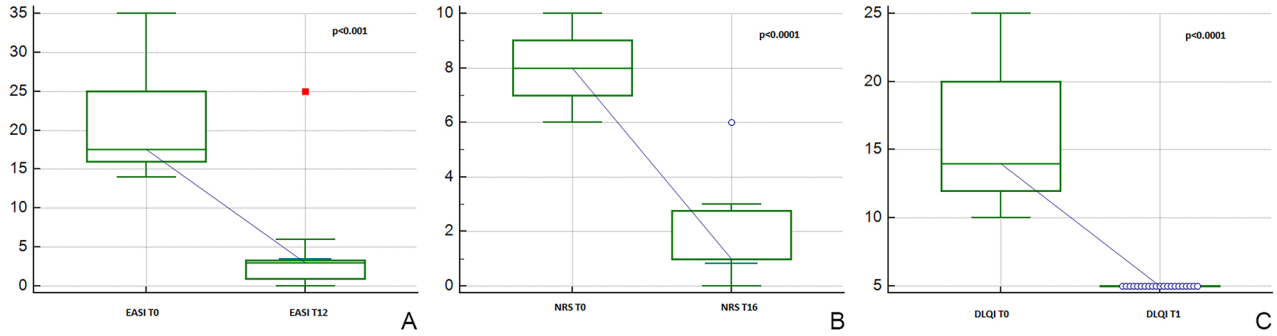

Figure 1. (a-c) Box-plot graphs showing mean EASI (a), PP-NRS (b) and DLQI (c) scores at T0 and after 16 weeks of treatment with tralokinumab. In particular, mean EASI score (a) decreasead from a 17.3 score at baseline at a score of 3 at week16; PP-NRS mean score (b) decreased from 8 to 1 after 16 weeks of tralokinumab therapy; mean DLQI (c) showed a reduction from a baseline value of 16 to a week16 value of 1; The statistical significance was assessed through Mann-Whitney U-test and was reached for EASI ($p < 0.001$), PP-NRS ($p < 0.0001$) and DLQI ($p < 0.0001$).

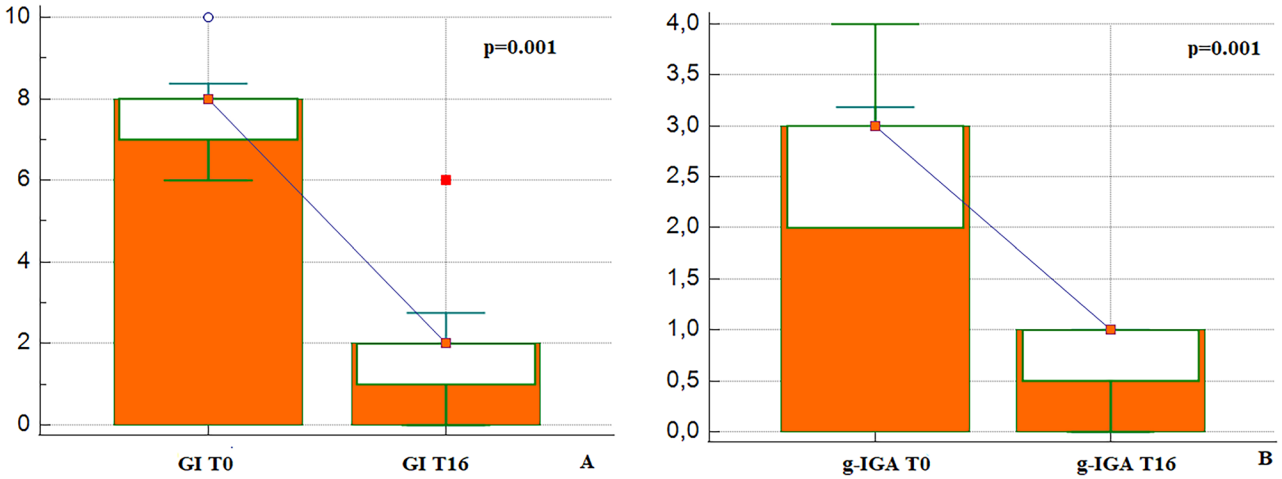

Figure 2. (a, b): Box-plot graphs showing the improvement on GI and g-IGA after 16 weeks of tralokinumab treatment. In particular, GI mean score (a) showed a reduction from 8 at baseline to 1 at week 16 while mean g-IGA (b) decreased from 3 to 1 at week 16.

reduction in DLQI, with median values of 1 (range 0-4). Summarizing, after 16 weeks of treatment with tralokinumab, median score on all three scales showed a statistically significant reduction, as reported in Figure 1(a–c).

Finally, for what concerning the genital response after 16 weeks of treatment, we observed a statistically significant decrease in mean GI from 8 to 1 and a reduction in mean g-IGA score from 3 to 1. The results regarding GI and g-IGA are reported in Figure 2(a, b).

Discussion

The incidence of genital lesions in AD ranges between 10.3% and 45% (1,2). In our analysis, we observed genital involvement in 25% of cases. Considering that genital presentation of AD is frequently neglected and under-reported, the incidence of genital involvement in patients with AD could be even higher than the values reported in the literature to date.

Consistent with our prior findings (1), but in contrast to Woo et al. (3) we noted a heightened prevalence of limb involvement, with two cases displaying hand involvement. While, we did not observe an elevated incidence of recurrent genitourinary infections. Notably, the majority of patients exhibited both atopic and non-atopic comorbidities, with two patients experiencing treatment failures with upadacitinib and dupilumab. Following a 16-week treatment period, generalized improvement in disease severity, including the genital area, was evident in 83% ($n = 10$) of cases. Interestingly, only one patient needed to continue topical treatments (steroid and emollient), highlighting how the systemic treatment (e.g. tralokinumab) can alone improve AD even in genital areas, thus avoiding patients the application of topical creams, which could create difficulties and social problems in daily life.

We acknowledge the small size of our sample, but patients usually exhibit resistance in considering or exposing this area to their specialist. According to our analysis, we found that genital involvement in AD can be observed in a considerable percentage of patients and remains still underreported in the literature. This study also highlights the efficacy of tralokinumab as a valid treatment option for AD with genital involvement, even in cases where patients have previously undergone systemic immunosuppressive or immunomodulatory treatments.

Disclosure statement

AN: has served on advisory boards, received honoraria for lectures and research grants from Almirall, Abbvie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Genzyme, Amgen, and Boehringer Ingelheim. PM has been a speaker for AbbVie, Lilly, Novartis, Janssen-Cilag, Celgene, Leopharma, and Almirall. ACo has served as an advisory board member, consultant and has received fees and speaker's honoraria or has participated in clinical trials for Abbvie, Almirall, Biogen, LEO Pharma, Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB-Pharma. MV has been a consultant and/or speaker for Sanofi, Leo Pharma, Eli Lilly, Novartis, Janssen, AbbVie, Almirall, UCB, and Boehringer-Ingelheim. The other authors have nothing to declare.

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