Efficacy of Secukinumab in the Treatment of Paediatric Psoriasis: A Case Report

Giovanni Palazzo*

Outpatient Dermatology Department Tinchi Pisticci District Hospital, Matera Health Authority, Matera, Italy

Corresponding Author*

Giovanni Palazzo,
Outpatient Dermatology Department
Tinchi Pisticci District Hospital, Matera
Health Authority, Matera, Italy
E-mail: giovannipalazzo60@virgilio.it

Received date: 27 October 2022, Manuscript No. DMCR-22-19857; Editor assigned: 31 October 2022, Pre QC No. DMCR-22-19857 (PQ); Reviewed: 02 November 2022, QC No. DMCR-22-19857 (Q); Revised: 05 November 2022, Manuscript No. DMCR-22-19857 (R); Published date: 08 November 2022 doi. 2684-124X .2022.7.(1).10001

Abstract

Introduction: This case report documents the efficacy and safety of secukinumab in severe paediatric psoriasis (PP) with serious comorbidities and quality of life (QOL) implications, and it contributes data to the body of evidence supporting its use in routine clinical practice.

Main symptoms: A 14-year-old female with severe plaque psoriasis manifesting as small seborrheic plaques affecting her scalp, face, trunk, and the rest of her body (100% of body surface area). Her Psoriasis Area Severity Index score was 12, her Children Dermatology Life Quality Index score was 20, and her Visual Analogue Scale score was 7.

Main diagnoses, treatments, and outcomes: Upon considering available treatment options, it was concluded that conventional disease-modifying antirheumatic drugs (cDMARDs) were contraindicated. Also, because the condition severely affected the patient's QOL, biologic disease-modifying antirheumatic drugs with a rapid onset of action were preferred. The patient was offered treatment with secukinumab, a humanised, recombinant monoclonal anti-IL-17A antibody.

Once treatment was initiated, the patient's condition started improving within two weeks of the first dose. Three weeks after the start of treatment, the patient's trunk, buttocks, thighs, and legs were scarcely affected, while her face presented mild residual lesions. Four weeks after the start of treatment, only slight residual lesions remained on the patient's face.

The patient's haematologic and blood chemistry profile remained normal throughout her treatment and her examinations at each follow up visit were consistently normal.

Conclusion: This case shows an optimal clinical response and rapid cutaneous clearance with good safety when secukinumab is administered to an adolescent with severe plaque psoriasis. During this period, the patient recovered her relational capacity, which plays a decisive role in the psychic development of adolescents.

Keywords: Case report • secukinumab • paediatric psoriasis • interleukin-17 • bDMARDs • real-world

Introduction

Psoriasis is an immune-mediated, non-communicable, inflammatory systemic condition that affects individuals chronically and tends to worsen with time and/or vary from periodic remissions to exacerbations. Its prevalence in children (individuals <18 years of age) is estimated at 0.13%–2.1% with higher prevalence among Europeans females, and adolescents (children <18 years of age). The most frequent subtype of paediatric psoriasis (PP) manifests as plaques, often presenting initially on the scalp, and showing a predilection for facial involvement. Its severity may go from only a few lesions to full-body involvement. Additionally, psoriasis causes considerable psychosocial disability and has a significant impact on quality of life (QOL) in the individuals affected by it [1-5]. Children with even mild psoriasis have a poorer QOL than normal children due to their symptoms, fatigue, and stigmatisation that affect their emotional well-being and progress at school. PP patients often have comorbidities observed in adult psoriasis, including diabetes mellitus, Crohn's disease, obesity, ischaemic heart disease, dyslipidaemia, and hypertension. Large-scale epidemiological studies have also found an increased risk for psychosocial comorbidities (psychiatric disorders, depression, and anxiety) with PP. Therefore, alleviating PP patients is especially important to ensure the optimal physical and psychosocial development of this vulnerable population. Many medications approved for adult psoriasis are used in children, sometimes off-label. This is because even though there is a large unmet need, studies evaluating the efficacy and safety of these treatments in children are scarce. As a result, approved treatment options are few as well.The primary topical treatments for all subtypes of psoriasis are corticosteroids, calcineurin inhibitors, vitamin D3 analogues, and keratolytics. These agents can be used with a relatively lower risk of adverse effects than systemic medications. Among them, corticosteroids are the most used due to their anti-inflammatory and anti-proliferative effects. Phototherapy is an option for refractory or diffuse plaque psoriasis in children, but its onset of action frequently takes >4 weeks [3,6]. Systemic agents such as methotrexate and cyclosporine (conventional disease-modifying antirheumatic drugs (cDMARDs)) have not been formally studied for PP and are not licensed to treat it[7]. Nevertheless, they are used to treat this condition based on literature that shows their advantages and risks for children experiencing ichthyosis, juvenile rheumatoid arthritis, and organ transplantation. One of the problems with methotrexate is the long time it takes to show its efficacy: its effect onset takes 5–12 weeks, and its full effect is reached after 34 months. It also has potentially dangerous pharmacologic interactions, contraindications, and it should be used carefully in obese children. Cyclosporine may be used in severe plaque psoriasis in children and has a rapid effect onset; however, it is not recommended for those who have had or are receiving phototherapy (PUVA) treatment due to its link with skin cancer [3].

Biologic disease-modifying antirheumatic drugs (bDMARDs), immune modulators targeting specific cell signalling pathways and regulating the inflammatory response, are indicated for serious or recalcitrant psoriasis cases. Compared to other systemic therapies, these agents tend to have better efficacy and more convenient dosing, require less laboratory testing, and have a lower risk of systemic toxicity[3, 8]. However, severe side effects such as opportunistic infections, malignancies, latent tuberculosis, and autoimmune disease have been identified. Consequently, patients should undergo tuberculosis and comprehensive evaluations, including haematology and blood chemistry laboratory tests, before initiating treatment with bDMARDs. Safety and efficacy data supporting bDMARD use in PP are rapidly accumulating, and regulatory agencies have progressively approved their use in children [3]. So far, the European Medicines Agency has approved adalimumab, etanercept, ustekinumab, ixekizumab, and secukinumab. In a systematic review five studies to evaluate treatments for PP were identified involving etanercept, adalimumab, ustekinumab, ixekizumab, and secukinumab. Although all these agents were efficacious, the probability of achieving Psoriasis Area Severity Index (PASI) 75 and 90 was higher for the last three, and improved responses were observed with them. Anti-IL-17 agents seemed to be superior to anti-TNF-alpha agents in treating PP, matching the efficacy observed when they are administered to adults [7]. As summarised by Blair as part of an Adis Drug Evaluation, the Joint American Academy of Dermatology and National Psoriasis Foundation guidelines for PP recommend biologics as effective therapies for paediatric patients with moderate to severe psoriasis. The European consensus-based guidelines for treating PP recommend adalimumab as first-line treatment, and etanercept, ustekinumab, ixekizumab, and secukinumab as second-line treatments for moderate to severe psoriasis in children that do not respond sufficiently or do not tolerate other systemic treatments or phototherapy. The National Institute for Health and Care Excellence recommends secukinumab for children with severe plaque psoriasis that do not respond to other systemic treatments, or when these are contraindicated or not tolerated [8,9].

Secukinumab is a fully humanised, monoclonal anti-IL-17A antibody with sustained efficacy, a good safety profile, and a more rapid onset of action (approximately 4 weeks) in adults with psoriasis
[6]. The development of psoriasis involves many cytokines, but IL-17A has been identified as a major driver in this condition. Thus, inhibiting this cytokine

disrupts pathways critical to the development and progression of psoriasis, and agents that target it improve psoriasis rapidly and significantly [10]. In children, it improved psoriasis with a similar safety profile in a phase 3 double-blind, randomised, controlled trial. It was approved in July 2020 for moderate to severe plaque psoriasis in children >6 years of age who are candidates for systemic therapies [6].

The case reported herein documents the efficacy of secukinumab in severe PP with QOL implications, and it contributes real-world data to the body of evidence supporting its use in routine clinical practice.

Case history

A 14-year-old female with severe plaque psoriasis consulted the Dermatology Department at the Tinchi Pisticci District Hospital (Italy) starting in November 2020. She related that she started suffering from mild plaque psoriasis when she was 6 years of age, and she was initially diagnosed with this condition by her paediatrician. She experienced the first exacerbation at 10 years of age and her disease remained severe from the time of her menarche (11 years old). The lesions were initially located in her scalp and subsequently became seborrheic in the form of small plaques and extended towards her face, trunk, and the rest of her body, affecting 80% of her body surface area (BSA) (Figure 1). Her PASI score was 12. The disease caused significant QOL impairments: her Children Dermatology Life Quality Index (cDLQI) score was 20, and her Visual Analogue Scale (VAS) score was seven. When the patient first visited our centre, her weight was 72 kg as she compensated for her lack of social life with excessive dieting and consequent weight gain (height 150 cm, body mass index (BMI) 32). The chief complaints the patient expressed were the itching and her limited social life. Differential diagnoses were discarded because the patient presented a typical and characteristic case of severe plaque psoriasis.

The patient underwent a complete baseline assessment, including chest X-ray, haematology, and blood chemistry laboratory tests. The results of all the evaluations were normal. Until her consultation at our centre, the treatments the patient received included topical agents (cortisone and calcipotriol creams, hydration, and oil cleansing) and phototherapy, but the responses they elicited were unsatisfactory and transient. The patient was otherwise healthy, and her family history was negative for psoriasis.

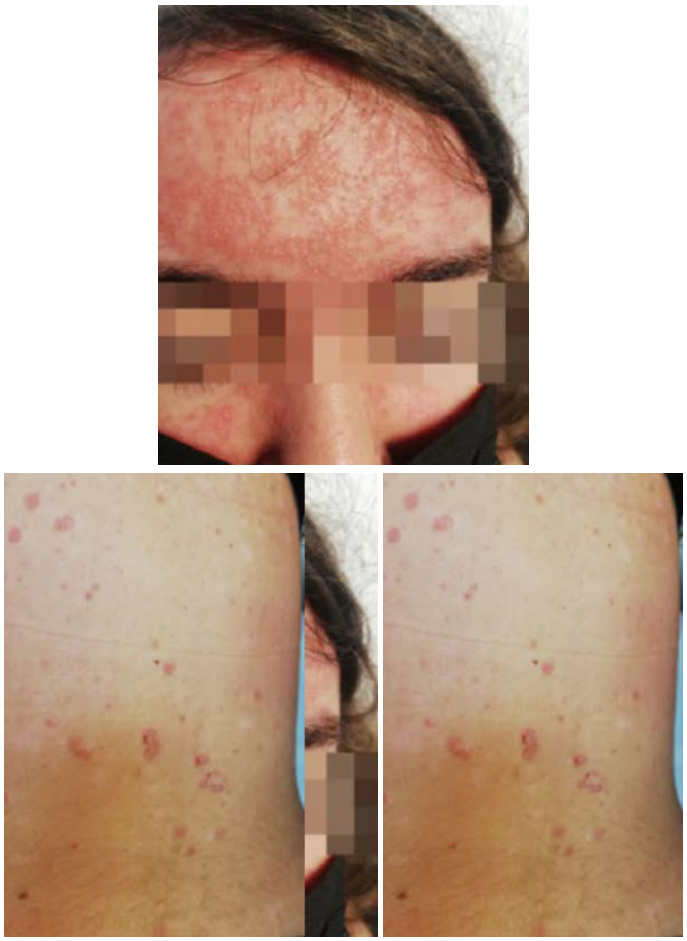

Figure 1. Psoriatic lesions at baseline on the face,abdomen and back.

Upon considering available treatment options, it was concluded that cDMARDs were contraindicated. Another factor was that in Italy this drug needs to be approved by regulatory authorities for use in paediatric patients. Also, because the condition severely affected the patient's QOL, bDMARDs with a more rapid onset of action than cDMARDs were preferred. Therefore, the patient was offered treatment with secukinumab, a humanised, recombinant monoclonal anti-IL-17A antibody. The posology indicated in the medication's information leaflet was followed to determine the dose and administration intervals (5 subcutaneous doses of secukinumab 150 mg weekly during the first month followed by maintenance with one dose every 4 weeks) [7-10].

Once treatment was initiated in March 2021, the patient's condition evolved as follows:

• Two weeks after the first dose (14 days from baseline), the patient's face and trunk lesions were visibly attenuated (Figure 2 and Figure 3. Her PASI, cDLQI, and VAS decreased to 2, 5, and 2.

• Two weeks after the second dose (21 days from baseline), the patient's trunk, buttocks, thighs, and legs were scarcely affected, while her face presented mild residual lesions representing 10–15% of her BSA [Figure 3]. The patient also started recovering her relational capacity.

• Two weeks after the third dose (28 days from baseline), only slight residual lesions remained on the patient's face, and the rest of her body was completely free of lesions (Figure 4).

The patient was assessed at subsequent visits up to 10 weeks (70 days) and continues being followed up via telephone contact. The patient's haematologic and blood chemistry profile remained normal throughout bDMARD therapy, including metabolic functions. In addition, no organ toxicity was detected and the patient's examinations at each follow up visit were consistently normal. In July 2020, the patient presented the following parameters: PASI 100; VAS 0; DLQI 2. Personal wellbeing was once again confirmed by the patient.

The patient expressed that the therapy brought her emotional relief in terms of self-perception and social interactions. She said, "finally my skin is clear if it was not for my face. Within two months, I regained my composure, confidence, and the will to live my adolescence like everyone else." In addition, the patient reached a weight closer to normal limits (65 kg, 156 cm, BMI 26.7) through dieting and exercise guided by a professional nutritionist, but especially by gaining self-confidence and returning to a normal life.

In this patient, biological therapy with secukinumab had a rapid onset of action, was effective, and provided long-lasting relief reaching complete remission that persisted for >1 year without relapses (last follow-up being in July 2022).

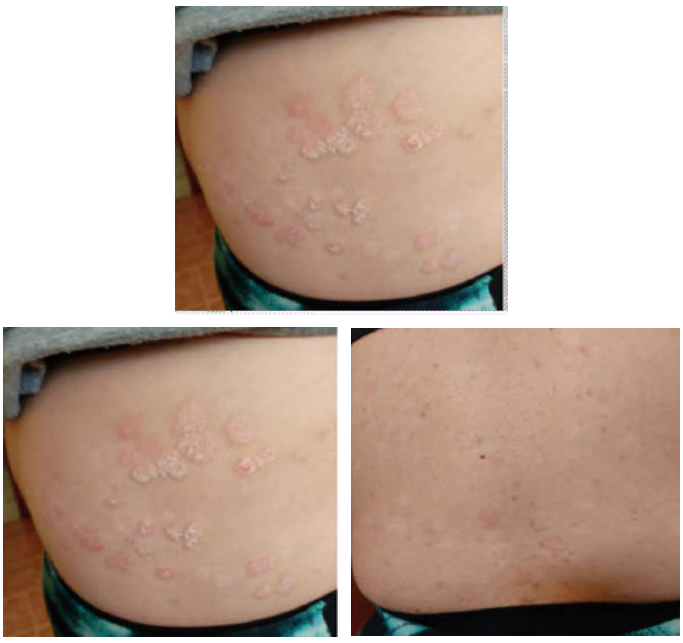

Figure 2. Psoriatic lesions two weeks after the first dose on the face, abdomen and back.

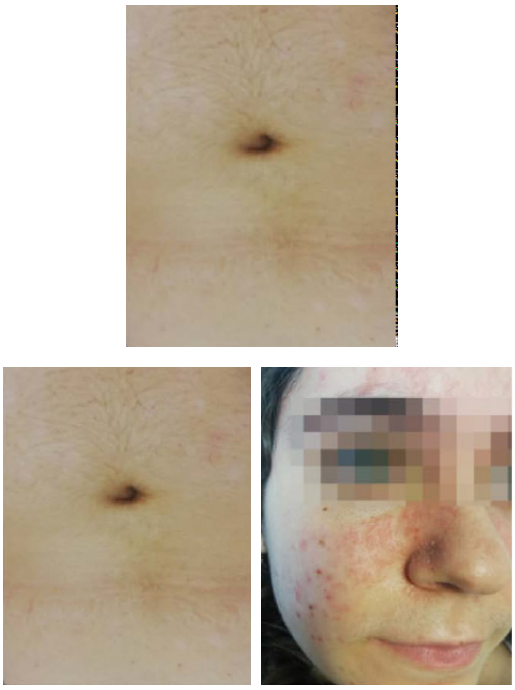

Figure 3. Psoriatic lesions two weeks after the second dose on the face, abdomen, and back.

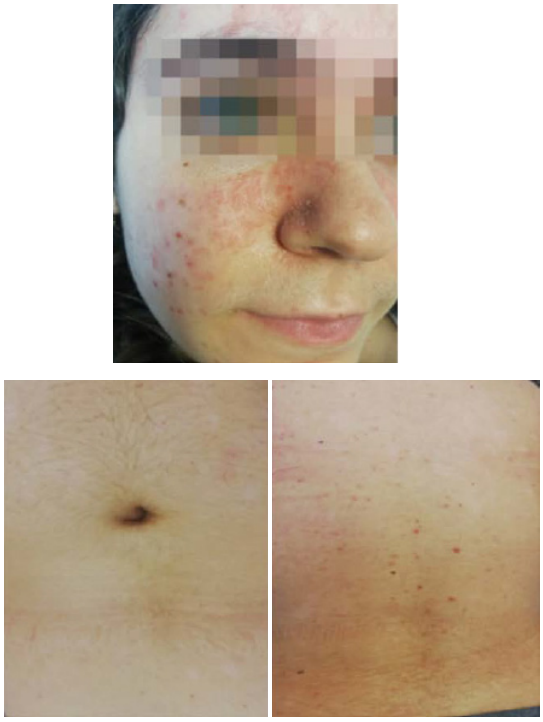

Figure 4. Psoriatic lesions two weeks after the third dose on the face, abdomen, and back.

Discussion

Since psoriasis has a chronic course, it often requires long term treatments. However, most treatment options for PP are used off-label and research supporting their use is lacking. As targeted biologic therapies are increasingly being used in PP this case report provides an example of the efficacy and safety of secukinumab that could be useful for clinicians facing PP in daily practice [3]. It also helps complement the existing literature on the subject. However, its main limitations are those common to case reports such as lack of generalisability, its retrospective nature, and the possibility of publication bias.The main studies that have evaluated the usefulness of secukinumab in PP [4]. The first was a phase 3 multicentre, randomised, and controlled study of secukinumab in children with severe chronic plaque psoriasis that found this bDMARD was effective for up to 52 weeks with a favourable safety profile. It included 162 patients that were randomised to receive low or high dose secukinumab, etanercept, or placebo. Secukinumab showed greater and more sustained efficacy compared to placebo and etanercept, and it improved QOL. No new safety signals were detected relative to the corresponding studies in adults. The second study was a phase 3 open-label, randomised, multicentre study of secukinumab in paediatric patients with moderate to severe plaque psoriasis that found that secukinumab was efficacious and well tolerated. In both studies, secukinumab improved PASI 75 and 90 [4,6].

Conclusion

As detailed previously in this text, treatment options for severe plaque psoriasis in children are limited, and secukinumab is a valuable new agent to treat severe PP, a hard-to-treat and chronic disease [8]. This condition usually requires continuous systemic treatment that should be effective and safe in the long term. Although long term data is not available yet in children, secukinumab has shown a good clinical profile. The case of this 14-year-old female shows an optimal clinical response and rapid cutaneous clearance reaching PASI 100 with good safety with continued secukinumab treatment. The patient's quality of life was greatly improved, she recovered her self-confidence and social life, which during adolescence is strongly conditioned by self-perceived physicality and plays a decisive role in the psychic development of these individuals.

Acknowledgements

Editorial assistance in the preparation of this article was provided by María Carolina Rojido(Medical Writing Consultant). Proofreading and editing assistance, as well as support for submission was provided by Laura C Collada Ali (Medical Writing Consultant). This support was funded by Novartis Farma SpA. The study investigators thank the patients object of this study for their involvement in the study.

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Cite this article: Palazzo."Efficacy of secukinumab in the treatment of paediatric psoriasis: a case report". *Dermatol Case Rep*. 2022, 7 (1), 001-003.