

Successful Guselkumab treatment in a psoriatic patient affected with Cornelia de Lange Syndrome, and prosecution during the COVID-19 pandemic.

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KEY WORDS: Psoriasis, Guselkumab, Cornelia de Lange Syndrome, intellectual disability, COVID-19

World counts: 1077

Figure: 2

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dth.13433

Founds: None

Conflicts of interest: None of the Authors have conflicts of interest to disclose.

Copyright: The authors certify that the manuscript is original, never submitted to other journal for publication before. All authors contributed equally to the manuscript and had the opportunity to revise and approve the final text.

ABSTRACT

Psychomotor delay and intellectual disability are potential limitations in psoriasis management, due to low compliance, and strict dependence from care givers intervention. We report our successful experience with a 58-year-old woman, who was genetically affected by Cornelia De Lange syndrome, which causes intellectual disability and psychomotor disorders. The patient had been already treated with topical and traditional therapies, without any clinical benefits. Eventually she adhered to guselkumab treatment. The compliance was excellent, significant improvements were observed after only 3 months of treatment, without adverse effects. During follow-up, the COVID-19 pandemic address concern on the possible increased risk of infection due to immunosuppression. In agreement with current Italian recommendations, risk and benefits profile was discussed with the patient's legal tutor and the decision to continue the treatment was taken. Psoriasis complete clarification was maintained during the most difficult period of the Italian outbreak, allowing the patient to remain safely at home.

INTRODUCTION

Psoriasis is a chronic disease with a high psychosocial impact, on body image and self-esteem, thus compromising the patient's quality of life.¹ Well-planned treatments are important to achieve the best outcome, but they could be a challenge in patients with psychomotor delay and intellectual disability, because of adherence loss.^{2,3} We present a woman affected with Cornelia de Lange Syndrome (CdLS), a rare genetic disease characterized by psychomotor delay and intellectual disability,⁴ with a 10 years' history of psoriasis. All previous treatments had been discontinued because of low compliance and compulsive scratching. When she eventually came to our clinic, we proposed to the legal tutor to initiate parenteral treatment with guselkumab, which was accepted, and induced significant improvement in only 3 months, without adverse effects. The compliance was so high that treatment prosecution was accepted even during the COVID-19 outbreak.

CASE REPORT

A 58-year-old woman affected with CdLS presented to our Department with extensive psoriatic plaques on her trunk and limbs, accounting for a Psoriasis Area and Severity Index (PASI) score of 12.7. Due to her syndrome, the patient did not enjoy any autonomy in the treatment adherence, needing constant care by her sister, who was also her legal tutor. Previous topical and systemic treatments, including cyclosporine showed little improvement, and were rapidly interrupted due to patient's low compliance. The patient was intolerant to ointments application and refused oral

capsules and solutions if proposed repeatedly on a daily base for months. With aging, the behavioral difficulties, including anxiety, depression and aggression shots had worsen, and psoriasis symptoms were among trigger factor of compulsive self-harm behaviors. The sister felt discouraged by many years of unsuccessful therapies. The patient was assessed to evaluate a possible treatment with biotechnological drugs, and an extensive work-up was performed including routine blood clinical chemistry, neoplastic markers, viral hepatitis markers, autoimmunity panel and quantiferon test that resulted in normal ranges. Among the new active principles, the choice felt on an anti-IL23 agent, guselkumab for its rapid induction phase and the spaced doses of administration (100 mg subcutaneous injection at week 0, 4 and then every 8 weeks). In order to allow enough time for her sister to become confident with the injection technique, the first doses were performed in our out-patient office. After only 3 months, the clinical improvement of her psoriasis was so impressive, achieving PASI 100 (Fig.1, 2), that also the patient's behavior had improved, with more stabilized mood, and the sister enthusiastically adhered to handle the treatment at home. After 6 months of follow-up, psoriasis was always under complete remission, and the compliance was excellent, without any adverse effects. At the beginning of March 2020, safety concern aroused due to COVID-19 pandemic and the unpredictable risk of infection in immunocompromised patients. Telephone consultation with the patient's sister allowed treatment prosecution, with the agreement of prompt referral in case of any symptom occurrence.

DISCUSSION

Cornelia de Lange syndrome is a rare genetic syndrome, characterized by growth and psychomotor delay, intellectual disability, distinctive facial features, limb malformations, and hirsutism.

Moreover, it can affect other systems, such as the nervous, the gastrointestinal and the cardiovascular ones, as well as sight and hearing.⁵ Dermatological diseases are not characteristics, and a retrieval of current literature found no significant association with psoriasis. The skin pathology, which has a strong impact on the quality of life of any patient,¹⁻³ could further compromise the delicate psychosocial balance of person with such severe behavioral disorders, worsening obsessive-compulsive and self-harming traits in response to severe itching, and plaque

development. Although treatment is mandatory, efficacy is limited due to loss of adherence, especially with long-term daily administration of drugs. Our patient was extremely suffering from her psoriasis, as well as discouraged was her sister, legal tutor and caregiver, who could no more handle with patient's aggressive reactions to ointments and oral drugs administration. The proposal for a parenteral regimen was welcomed, and the assessment of risk-benefit profile for guselkumab resulted favorable. This novel fully human immunoglobulin G1 λ (IgG1 λ) interferes with the psoriasis inflammatory pathogenic pathway, inhibiting interleukin (IL) 23.⁶ The monoclonal antibody selectively binds the p19 subunit of IL-23, and several clinical trials have demonstrated its efficacy and safety in patients with moderate-to-severe plaque psoriasis. Guselkumab regimen is very manageable, with a short induction, and delayed doses, every 8 weeks. We were quite impressed of the rapid improvement, and the symptoms relief further reinforce patient's excellent compliance. Six months after treatment initiation, the problem of novel coronavirus 2019 pandemic arose, with a huge Italian burden, that forced the President of the Council of Ministers to order the country lockdown from March 9, 2020.⁷ Concerns about the safety of biotechnological treatment aroused, although most of experts suggest that the benefit-to risk-ratio is in favor of maintaining effective treatments until a patient is diagnosed with COVID-19.⁸ Thus, we followed the recommendations of the Italian Society of Dermatology and Venereology,⁹ and arranged a telephone consultation with the patient's legal tutor, i.e. her sister who allowed Guselkumab treatment prosecution. In fact, she was aware that a psoriasis worsening would represent a critical issue in time of suspension of outpatients consultations for the epidemic outbreak, and that the risk of contagion is minimal when the isolation and preventive measures are respected in the household.

CONCLUSION

Psychomotor disorders and intellectual disability are potential limitations in the psoriasis management, as compliance might be undermined, especially with daily long-term administration. Our experience confirms the validity of biological therapies, whose subcutaneous injections are quite painless, and the device very comfortable, similar to an innocuous pen. Guselkumab was chosen for the favorable treatment schedule, and excellent safety profile to treat a very difficult multi-failure adult psoriatic patient, affected with Cornelia de Lange Syndrome. Clinical response

was very rapid, with PASI 100 achievement in only 3 months. Additional observation is that the treatment has been maintained during the actual COVID-19 pandemic, under careful monitoring by her care-giver, and the agreement of prompt referral in case of symptoms occurrence. Compliance is still excellent, allowing the patient to stay safe at home, in such a dangerous period.

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Legend to figures

Figure 1: Dorsal-lumbar region lesions before (a) and after 3 months of guselkumab treatment (b).

Figure 2: Posterior region of the lower limbs lesions before (a) and after 3 months of guselkumab treatment (b).



