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Treatment of severe psoriasis during pregnancy and breastfeeding: A therapeutic challenging case

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Dear Editor,

What is known about this subject in regard to women and their families?

- In women with psoriasis, high disease activity during pregnancy has been associated with adverse pregnancy outcomes.
- The use of certolizumab pegol in pregnant and breastfeeding patients with moderate-to-severe psoriasis has been associated with minimal-to-no transfer across the placenta and breast milk.
- Concerns remain about active treatment during pregnancy of women affected by moderate-to-severe psoriasis.

What is new from this article as messages for women and their families?

- The optimal efficacy and safety profile of certolizumab pegol supports treatment initiation or continuation during multiple pregnancies and breastfeeding, when considered necessary, in case of psoriasis flares and a high disease burden.
- A complete clearance of a severe psoriasis during multiple pregnancies and breastfeeding was achieved throughout an active approach with certolizumab pegol.

Psoriasis management in fertile women needs special consideration because the disease is prevalent in women and often diagnosed and treated during the reproductive years (Gottlieb et al., 2019; Lambe et al., 2020). Psoriasis does not affect fertility, and an improvement in disease conditions is often observed during pregnancy. However, approximately 24% of women experience disease worsening during pregnancy, and postpartum flares and breastfeeding difficulties are common (Gottlieb et al., 2019; Lambe et al., 2020). Clinician awareness is relevant because high disease activity during pregnancy has been associated with adverse pregnancy outcomes, including miscarriage, preterm delivery, and low birth weight (Gottlieb et al., 2019; Lambe et al., 2020).

On the other hand, psoriasis is a systemic inflammatory disease that leads to disability and comorbidities (Gottlieb et al., 2019). The need to treat moderate-to-severe forms of psoriasis with systemic traditional and biologic agents in pregnant women or during breastfeeding raises concerns (Gottlieb et al., 2019) because pregnant patients with psoriasis are usually excluded from clinical trials, and the number of studies regarding systemic agent use during pregnancy are limited (Lambe et al., 2020; Porter et al., 2017). In addition, the U.S. Food and Drug Administration has classified antitumor necrosis factor (TNF) biologic agents that are approved for the treatment of moderate-to-severe psoriasis as pregnancy category B. In the last decade, case series and registry data of pregnancies exposed to biologics, including anti-TNF, anti-interleukin (IL) 12/23, and more recently anti-IL17 and anti-IL23 therapies, have

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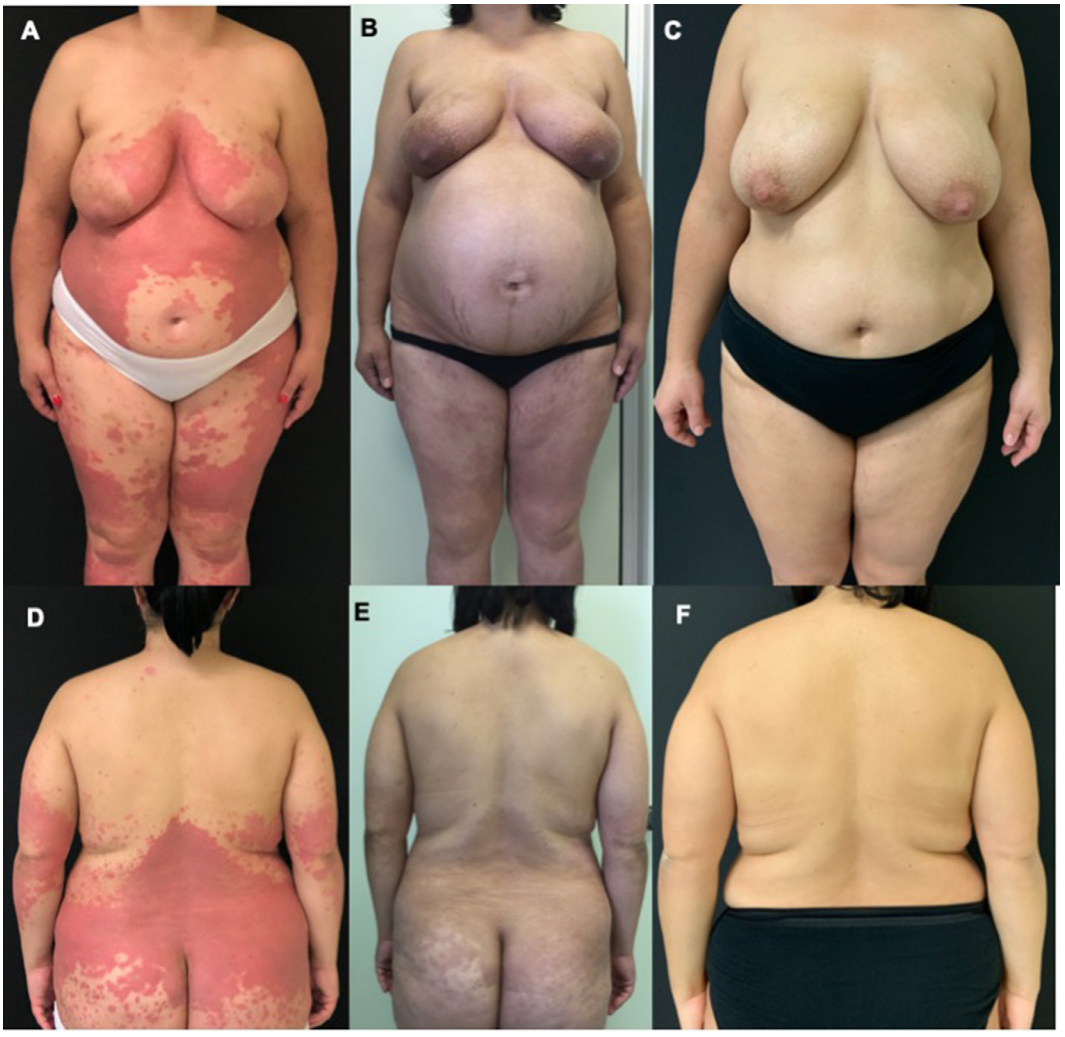

Fig. 1. (A, D) Intensely erythematous confluent psoriasis plaques involving the trunk and extremities at baseline. (B, E) Consistent clinical improvement after certolizumab treatment at week 8 (32nd week of gestation) and (C, F) week 96.

been published (Gottlieb et al., 2019; Porter et al., 2017; Strain et al., 2021). Monoclonal antibodies can be actively transported across the placenta, with an increasing rate and a peak in the third trimester, except for certolizumab pegol (CZP). CZP is an anti-TNF monoclonal antibody, approved for the treatment of psoriasis and psoriatic arthritis. It lacks the Fc-region, which plays a key role in active materno–fetal placental transfer by binding to the neonatal Fc receptor (Clowse et al., 2017; Mariette et al., 2018). Human placenta appears to be permeable to the immunoglobulin G Fc portion belonging to monoclonal antibodies, except for CZP, leading to active transport and high blood levels of immunoglobulin G in newborns after exposure during the late second and third trimesters (Clowse et al., 2017; Gottlieb et al., 2019; Mariette et al., 2018; Porter et al., 2017). This can result in therapeutic levels of monoclonal antibodies that persist for several months in newborns, creating concern for acquired infections and vaccination with attenuated live vaccines.

We report on a 34-year-old Caucasian woman affected by psoriasis since the age of 10. She failed to respond to various therapies, including ciclosporin, methotrexate, and etanercept, and interrupted treatment with adalimumab to plan a pregnancy. During the first trimester of gestation, the patient presented a gradual worsening of psoriasis, which was poorly controlled with topical and systemic steroids. At 24 weeks of gestation, the psoriasis worsened to a severe and diffuse disease with vulvar and folds involvement. After a gynecologic consultation, we prescribed CZP according to the summary of the product characteristics recommendation. At baseline, the patient's Psoriasis Area Severity Index score was 26.5, itch visual analogue scale was 7, and Dermatology Life Quality Index was 18, indicating severe skin disease associated with consistent quality of life impairment and psychological discomfort (Figs. 1A and D).

After 8 weeks of treatment (32nd week of gestation), fast and complete remission of psoriatic lesions and associated symptoms was observed (Figs. 1B and E). At 38 weeks of gestational age, the patient underwent an elective cesarean section for fetal malpresentation. The infant was healthy, weight at birth was 3.7 kg, and length was 50 cm. The patient showed maintenance of complete disease remission after 108 weeks of treatment (Figs. 1C and F) without adverse events. Thereafter, the patient planned a second pregnancy, and during the first weeks of gestation, a multidisciplinary consultation led to the decision to avoid CZP interruption during pregnancy due to the patient's instable disease activity and high risk of flares. At 39 weeks of gestation, the patient underwent an elective Cesarean section, the infant was healthy, weight at birth was 2.9 kg, and length was 48 cm. CZP treatment was temporarily interrupted 2 weeks before the Cesarean section to prevent surgical risk of infections and restarted after 4 weeks to avoid a postpartum flare during breastfeeding.

In routine dermatological practice, a watchful waiting approach for mild disease is often followed, but this is not suitable for patients with moderate-to-severe psoriasis or in case of rapidly worsening manifestations needing an active approach.

CZP is only able to cross the placenta by passive means (Clowset et al., 2017; Mariette et al., 2018), and cord blood studies showed CZP levels much lower than other anti-TNF agents. Clinical evidence is also available to support minimal/no transfer into breast milk (Clowset et al., 2017; Mariette et al., 2018). Although limited experience and lack of controlled studies may generate concerns regarding safety, the use of CZP in pregnant and breastfeeding patients with moderate-to-severe psoriasis, as in our case, may be an effective, fast, and safe therapeutic option. The optimal efficacy and safety profile of CZP, as demonstrated in this case, supports treatment initiation or continuation during multiple pregnancies and breastfeeding, when considered necessary, in cases of psoriasis flares and high disease burden.

Pregnancy registries and large prospective studies, including recently introduced agents, are needed to draft formal treatment guidelines.

Conflicts of interest

Dr. Maria Esposito has served as a speaker/board member for Abbvie, Almirall, Biogen, Celgene, Eli Lilly, Janssen, Leo Pharma, and Novartis. Dr. Gianluca Calianno has served as a speaker for Mylan. Dr. Maria Cconcetta Fargnoli has served on advisory boards and received honoraria for lectures and research grants from Almirall, Abbvie, Galderma, Leo Pharma, Mylan, Medac Pharma, Celgene, Pierre Fabre, UCB, Eli Lilly, Pfizer, Janssen, Novartis, Sanofi-Genzyme, Roche, Sunpharma, and MSD. Dr. Astrid Lappi declared no conflicts of interest.

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Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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