Pregnancy outcomes following tofacitinib use for SAPHO syndrome: a case report

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Abstract

Tofacitinib, an oral Janus kinase inhibitor, has demonstrated teratogenic effects in animal models. However, there is a lack of data on its effects during human pregnancy, especially in the context of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome, a rare disease. We report a case of a 31-year-old female patient with SAPHO syndrome who became pregnant unexpectedly after 5 weeks of continuous tofacitinib treatment during the first trimester. Tofacitinib was immediately discontinued upon discovering the pregnancy. The patient successfully delivered a healthy full-term male infant under vigilant monitoring, and her SAPHO syndrome symptoms ameliorated during gestation but exacerbated 40 days postpartum. Given the limited clinical data available, further monitoring of pregnancy outcomes in patients treated with tofacitinib is still warranted.

Introduction

Tofacitinib, an oral Janus kinase (JAK) inhibitor, has been increasingly over-scheduled for the treatment of rheumatologic disorders, particularly for challenging rheumatologic conditions that exhibit resistance to conventional treatment regimens.[1-2]Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome is a rare autoinflammatory disease characterized by osteoarticular and dermatological manifestations, for which there is a lack of standardized treatment. Notably, tofacitinib has demonstrated substantial multidimensional improvements in pain, skin lesions, systemic inflammation, quality of life, and magnetic resonance imaging remission in patients with SAPHO syndrome. Consequently, it is increasingly being employed in refractory SAPHO syndrome cases where biologic therapy has proven ineffective.[3-4] However, limited data exist regarding its use during human pregnancies. Here, we report a case of an unintended pregnancy in a patient with SAPHO syndrome who was treated with tofacitinib.

Case report

A 31-year-old woman presented in 2022 with persistent anterior chest wall pain and palmoplantar pustulosis (PPP, **Figure1A**). Whole-body bone scintigraphy revealed abnormal radioactive uptake at the sternoclavicular joint **(Figure 2**). The diagnosis of SAPHO syndrome was made based on clinical manifestations and imaging examinations. Initial treatment with diclofenac 75mg twice daily for one month did not lead to symptom improvement. Subsequently, the patient was treated with adalimumab at a dosage of 40mg every two weeks, resulting in an initial satisfactory remission. However, after 10 weeks of treatment, the patient experienced a recurrence of rash. In July, the patient initiated a trial of tofacitinib treatment at a dose of 5mg twice daily, which provided significant relief from the rash. Unexpectedly, after 10 weeks of tofacitinib therapy, the patient discovered a 5-week pregnancy and promptly discontinued the use of tofacitinib.

During the patient's pregnancy, regular monitoring was conducted to ensure the well-being and development of the fetus. The screening for chromosomal abnormalities showed the fetus to be at low risk for trisomy 13,

18, and 21. The second and third trimester of pregnancy, fetal growth parameters including skull length, biparietal diameter, abdominal perimeter, and femur length remained within the normal ranges. Continuous monitoring of the fetal heart rate and predicted weight were also normal. Ultrasound scans conducted at 20 weeks and beyond did not detect any external or internal fetal defects. At the 39th week of pregnancy, a cesarean section was performed, and a healthy infant was delivered. The baby had a birth weight of 2900 g and a length of 51 cm, with no congenital anomalies or dysfunctions detected.

The patient experienced a notable reduction in sternoclavicular pain and PPP (**Figure 1B**) during pregnancy. However, approximately 40 days after delivery, the symptoms resurfaced (**Figure 1C**). The patient continues to use tofacitinib 5mg twice daily as treatment for SAPHO syndrome and is still being followed up.

Discussion

Tofacitinib is a small molecule drug with the potential to cross the placenta. Animal studies have evaluated its teratogenic and fetotoxic effects in pregnant rats and rabbits. However, these studies used exposure doses significantly higher than those in humans.[5] Teratogenic effects include the development of membranous ventricular septal defects and cranial/skeletal malformations or deformations. To mitigate these risks, the manufacturer advises the use of effective contraception during tofacitinib treatment and for a period of 4-6 weeks after the last dose. Despite these recommendations, pregnancies can still occur during tofacitinib treatment.

A previous report has noted a case of preterm labor in pregnancies involving tofacitinib treatment.[6] Studies have also indicated a potential association between tofacitinib exposure and congenital malformations and spontaneous abortions. However, the frequency of these occurrences does not appear to be significantly different from that observed in the general population.[7] Based on limited clinical data, pregnancy outcomes related to tofacitinib have primarily focused on patients with RA and psoriasis. The comprehensive analysis of pregnancy outcomes in these populations has shown similarities to the general population and to patients receiving biologic therapies for inflammatory diseases, and no definitive conclusions can be drawn.[8]

To the best of our knowledge, this case report presents the first documented instance of using tofacitinib during pregnancy in a patient with SAPHO syndrome. Interestingly, it was observed that the patient experienced an improvement in SAPHO syndrome symptoms during pregnancy, despite discontinuation of the drug and symptoms recurred 40 days after delivery. It is well-established that several immune disorders, including RA, often exhibit significant improvement during pregnancy due to physiological changes in the hormonal status and immune system of pregnant women.[9] Thus, pregnancy appears to confer a protective effect in the management of SAPHO syndrome. Currently, the adverse pregnancy outcomes observed in patients with rheumatic diseases are primarily attributed to autoimmune disease activity during pregnancy, underscoring the importance of appropriate antirheumatic medications to control disease activity and minimize side effects in pregnant patients.[10] While unintended pregnancies cannot be completely avoided in the treatment of tofacitinib, this may not interfere with SAPHO syndrome therapy. In the case, the patient successfully delivered a healthy newborn after timely discontinuation of tofacitinib and continued using the medication for SAPHO syndrome without breastfeeding. Importantly, no abnormalities were detected in either the mother or the baby.

We report a case of SAPHO syndrome in which an unintended pregnancy occurred after 5 weeks of continuous tofacitinib treatment during the first trimester. Following the discontinuation of the drug, a healthy newborn was delivered. Although the pregnancy outcome in this case was favorable, given the short duration of tofacitinib exposure, further monitoring of pregnancy outcomes in tofacitinib -treated patients is warranted.

Declarations

Ethics approval

This work was approved by the medical ethics committee of Fangshan Hospital of Beijing University of Chinese Medicine with the following reference numbers: FZJ JS-2021-002. Participants gave informed

consent to participate in the study before taking part.

Consent statement

Written informed consent was provided by patient to have the case details and any accompanying images published.

Disclosure of interest

The authors report there are no competing interests to declare.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Contributors

CL and XJH designed this study. CZ produced the images used in the manuscript and wrote the manuscript. XJS and YHD collected the patient data. TLQ and XPL was responsible for editing. All authors approved the final manuscript.

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