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Treatment of Pustular Psoriasis with Infliximab during Pregnancy: Case Report and Review of the Literature

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ABSTRACT

Introduction: Infliximab is a chimeric monoclonal antibody to tumour necrosis factor alpha (TNF-Î±) inhibitor which crosses the placenta with resultant concerns regarding its use in pregnancy.

Case Report: A 31-year old Chinese lady with a history of generalized pustular psoriasis diagnosed at the age of 18 years old was admitted multiple times throughout her pregnancy for pustular psoriasis flare. After extensive discussion with the obstetricians and the patient, decision was made to continue infliximab throughout her pregnancy. A healthy female baby was delivered at 38 weeks of gestation had normal development and growth till the present age of 4 years old.

Conclusion: It is important to balance control of maternal pustular psoriasis with safety of the developing fetus during pregnancy. Inter-disciplinary management by dermatologists and obstetricians is vital to improve the quality of life of the mother and contribute to a favourable outcome for the fetus.

Keywords: Pregnancy; Pustular psoriasis; Fetus

INTRODUCTION

Infliximab is a chimeric monoclonal antibody to tumour necrosis factor alpha (TNF-α) inhibitor used to treat inflammatory disorders such as psoriasis, rheumatoid arthritis, ankylosing spondylitis and inflammatory bowel disease. Infliximab crosses the placenta with resultant concerns regarding its use in pregnancy. The existing guidelines and studies on the safety of use of infliximab in pregnancy are based on non-dermatological conditions and 7873 pregnant patients with chronic plaque psoriasis [1]. We report on the safety of use of infliximab in pregnancy in a patient with pustular psoriasis.

CASE REPORT

A 31-year old Chinese lady with a history of generalized pustular psoriasis diagnosed at the age of 18 years old was admitted multiple times throughout her pregnancy for pustular psoriasis flare. From the age of 18 years, various treatments for psoriasis included topical corticosteroids, phototherapy, dapsone, methotrexate and cyclosporine with varying efficacy. She was commenced on infliximab 18 months prior to conceiving; this was stopped due to plans for conception. She was then fairly controlled on cyclosporine (maximum dose 2.7mg/kg/day) up till week 16 of pregnancy. Her pustular psoriasis flares during pregnancy are summarized in Table 1.

DISCUSSION

Infliximab is a category III drug in pregnancy. Its full safety profile in pregnancy remains unknown due to lack of evidence and inconsistent data. TNF-α inhibitors crossing the placenta, especially in the 2nd and 3rd trimesters, and can be detected in serum of neonates up to 6 months of age after maternal exposure. Potential side effects to the new-born that TNF-α inhibitor exposure during pregnancy may impose include

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immunosuppression and clinical infectious disease if given live vaccines. Other risks stated in literature include early pregnancy loss, preterm birth, stillbirth, low for gestational weight and congenital malformations.

On the other hand, discontinuing infliximab during pregnancy can lead to exacerbation of underlying skin disease and reduced quality of life for the patient during pregnancy [2]. Evidence points towards poorer maternal outcomes in pregnant patients with active psoriasis - increased risks of gestational diabetes, gestational hypertension, pre-eclampsia and elective and emergency caesarean section [3].

However, data on fetal outcomes are conflicting - some show higher odds ratio for stillbirth, preterm birth, small for gestational age and fetal distress in mothers with active psoriasis in particular severe disease [3], while other studies showed no statistically increased risks of fetal complications in mothers with psoriasis overall [4,5].

The conflicting evidence on fetal outcomes after maternal exposure to TNF-α inhibitors during pregnancy is summarized in Table 2.

Both dermatological and non-dermatological guidelines advocate for continued use of TNF-α inhibitors during pregnancy. The non-dermatological guidelines, for example, the French society for rheumatology guidelines [6-9], are however more conservative in that they recommend cessation of TNF-α inhibitors if there are plans for pregnancy.

The table below (Table 3) summarizes both dermatological

Table 1: Pustular psoriasis flares during pregnancy of our patient.

Gestation period (weeks) during admission for pustular psoriasis flare	BSA (%)	Treatment	Progress
16	10	• After discussion with patient and obstetricians, decision made to continue infliximab throughout pregnancy with close monitoring of fetal health: restarted on infliximab 2.5mg/kg • Intensive topical therapy • Increased dose of cyclosporine to 3mg/kg/day then slowly tapered	• Controlled pustular psoriasis flare but remission was not achieved
20	15	• Cyclosporine increased to 3mg/kg/day • Infliximab was continued • Started oral prednisolone 10mg per day	
25	20	• Continued cyclosporine 3mg/kg/day • Continued infliximab • Intensified topical therapy • Oral prednisolone slowly tapered	• Remission of pustular psoriasis from week 25 to week 36 of gestation
38	10	• Elective Caesarian section (lesions did not involve abdomen) after discussion with obstetricians	• A healthy female baby was delivered • The baby was adviced against the Bacillus Calmette-Guerin (BCG) vaccination by neonatology in view of increased immunosuppression • The patient was advised against breastfeeding in view of the passage of cyclosporine into breast milk • The patient did not have any flares of pustular psoriasis during her immediate post-natal period and her daughter had normal development and growth till the present age of 4 years old

Table 2: Conflicting evidence on fetal outcomes after maternal exposure to TNF-α inhibitors during pregnancy.

No increase in risk to fetus	Increase in risk to fetus
• Population study analyzing the national health registries in Denmark, Sweden and Finland [3], of 1,633,909 women with inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and psoriasis, and their infants born from 2006 to 2013: higher risk of Caesarean section, small for gestational age and pre-term birth for babies delivered to mothers who were on TNF-α inhibitors while pregnant as compared to mothers who were on other systemic immunomodulatory treatment • Meta-analysis in 2020 [5]: the rate of adverse pregnancy outcomes (early pregnancy loss, preterm birth, still birth, low birth weight and congenital malformations) in inflammatory bowel disease patients with infliximab-exposed pregnancies is similar to those treated with other systemic immunosuppressants.	• Prospective study of 1875 [4], infliximab-exposed pregnancies reported that the prevalence of adverse pregnancy, birth and infant outcomes is consistent with that of the general population. Amongst infliximab-exposed pregnant women who had adverse pregnancy outcomes such as spontaneous abortion, intrauterine death, ectopic pregnancies, molar pregnancies, low birth weight and intrauterine growth retardation, there was a higher proportion of these outcomes in women who reported concomitant use of other systemic immunosuppressants (especially methotrexate) than those observed in the overall infliximab-exposed population.

Table 3: Dermatological and non-dermatological guidelines for the use of infliximab during pregnancy.

	Dermatological guidelines	Non-dermatological guidelines
Maternal considerations	• TNF-α inhibitors are safe for use in the treatment of psoriasis in pregnancy [1].	• Contraception is advised when taking TNF-α inhibitors, but should patients wish to become pregnant while on TNF-α inhibitors, they can continue up to the 2nd trimester but stop in the 3rd trimester [6]. • If clinically indicated, TNF-α inhibitors can be continued throughout pregnancy [7-8]. • In select pregnant women at low risk of relapse of IBD who have a compelling reason (patient preference) to discontinue TNF-α inhibitor therapy, the last dose should be administered at weeks 22-24 of pregnancy to minimise risk of placental transfer and any hypothetical long-term effects to the newborn [8].
Fetal considerations (as TNF-α inhibitors (except certolizumab) cross the placenta, neonates and infants born to mothers who were on TNF- α Inhibitors during pregnancy should be considered immunosuppressed)	• Live vaccines should be delayed until after 3-6 months of age [1,9]	• Live vaccines should be delayed for 3-6 months of age [6,8-9]

and non-dermatological guidelines for the use of infliximab during pregnancy, with respect to maternal and fetal considerations.

Till date, there is only 1 case report in 2010 [10] of infliximab use in a pregnant lady with pustular psoriasis, which reported the safe delivery of a healthy female baby at week 39 with normal development, while the patient was being kept on infliximab infusion throughout pregnancy.

CONCLUSION

It is important to balance control of maternal pustular psoriasis with safety of the developing fetus during pregnancy, especially as pregnancy is a known triggering factor for pustular psoriasis. From a humanistic point of view, a detailed discussion with the patient is to be done on a by case basis.

Our patient was a successful case of infliximab-exposed pregnancy with good outcomes, and we present this case as the second case of known infliximab-exposed pregnancy in a patient with pustular psoriasis. We emphasize that inter-disciplinary management by dermatologists and obstetricians is vital to improve the quality of life of the mother and contribute to a favourable outcome for the fetus.

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Nil.

STATEMENT OF ETHICS

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Ethics approval was not required for this study in accordance with our local IRB guidelines.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception, analysis, drafting and finalization of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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