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Successful pregnancy under benralizumab: a case of severe eosinophilic asthma

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Dear Editor,

Monoclonal antibody therapy has revolutionized the management of eosinophilic disorders and severe asthma (SA). However, its increasing use among women of childbearing age raises concerns about safety during pregnancy [1,2]. Benralizumab, an IgG1k IL-5 receptor antagonist, is widely used and effective for SA treatment [3,4]. Safety and efficacy data during pregnancy are limited due to the exclusion of pregnant women from clinical trials [2,4,5]. Current recommendations for benralizumab use during pregnancy are uncertain. Early pharmacovigilance data and published cases do not suggest adverse outcomes with asthma biologics, but caution is advised due to potential eosinophil depletion (ED) in newborns [2]. Conversely, uncontrolled asthma and systemic corticosteroid use are well-established risks for adverse perinatal outcomes [2,5,6]. We report a case of a patient with SA who became pregnant while on benralizumab and successfully delivered a healthy infant.

A 37-year-old non-smoker woman with adult-onset asthma and no relevant comorbidities or exposure factors, presented to a SA consultation due to worsening symptoms post-pneumonia. Over two years, she had persistent wheezing, dyspnoea on exertion, and five exacerbations requiring antibiotics and oral corticosteroids, evolving into a corticosteroid-dependent asthma phenotype despite GINA STEP 5 treatment (ACT:12; CARAT:10/4). She underwent a comprehensive diagnostic workup after optimization of therapy (Table 1). Following the diagnosis of uncontrolled eosinophilic asthma with rhinitis, and after SA multidisciplinary discussion (MD), she initiated benralizumab therapy (30mg subcutaneously via pre-filled autoinjector pen, every 4 weeks for the first 3 doses, then every 8 weeks), leading to significant clinical improvement (ACT: 21; CARAT: 9/12), reduce to GINA STEP 3 and discontinuation of corticosteroids. After one year of benralizumab treatment, she was unexpectedly found to be pregnant during follow-up. After careful consideration with her obstetrician, she decided to continue benralizumab therapy until the end of the second trimester (ie, 26-30 weeks of gestation), based on recommendations for discontinuing certain biologics before the third trimester in immunomodulatory anti-rheumatic drug guidelines [2,7,8]. Her asthma symptoms remained well-controlled until 20 weeks of gestation, when she experienced an exacerbation due to a bacterial infection following *Influenza A*. This has required treatment with oseltamivir, antibiotics, transient intensification of inhaled therapy and an oral corticosteroid course. Persistent post-infectious symptoms and difficulty discontinuing corticosteroids led to a second MD at 22 weeks of gestation. After risks and benefits evaluation, continuation of benralizumab through the third trimester was agreed with the patient, with a transition from domiciliary to inhospital administration. At 38 weeks of gestation, the patient delivered a healthy male neonate (2920 grams) via cesarean section due to failure to progress. APGAR scores were 9 and 10 at 1 and 10 minutes, respectively. The physical examination was unremarkable. During

initial breastfeeding, the neonate exhibited hypoactivity, hypoglycemia, and a diminished sucking reflex, requiring glucose supplementation; breastfeeding subsequently normalised with adequate growth. At 8 weeks, blood count revealed eosinophils of 0.3% (0.02×10^9/L). By 18 months, the child remained healthy with no signs of atopic diseases. Routine vaccinations, including live-attenuated vaccines, were administered without delay after confirming absence of ED. During postpartum and breastfeeding, the mother continued benralizumab with well-controlled asthma symptoms.

Human data on asthma biologics during pregnancy is limited. Placental transfer of IgG antibodies accelerates at 17 weeks of gestation [8]. Due to concerns about immunosuppressive effects of anti-TNF biologics, some specialties recommend discontinuing biologic therapy before the third trimester [2]. However, biologics targeting the type 2 inflammatory pathway are not broadly immunosuppressive [2,9]. The EXPECT study found no increased risk of preterm delivery or major congenital defects in women exposed to omalizumab during pregnancy [10]. Information for other biologics, including benralizumab, is mainly from clinical cases/series [1,6,9,11,12]. In 2018, a case reported no adverse events after benralizumab initiation during pregnancy as a glucocorticoid-sparing agent in a woman with a life-threatening eosinophilic disorder [9]. Recent case-series have focused on maternal and neonatal outcomes with benralizumab continued throughout pregnancy [1,6,9]. No maternal adverse effects have been reported with benralizumab treatment, similar to our case. Regarding neonatal outcomes, benralizumab has been associated with transient ED [1,6,12]. Manetz *et al*. described ED persisting until 7 months, while Naftel *et al*. reported transient ED during the first 7 weeks, normalizing by the 8th week [1,6]. These findings align with preclinical nonhuman studies, which demonstrated transient ED following maternal benralizumab exposure and no teratogenicity, even at higher dosages [1]. In our case, as the newborn remained clinically stable with no signs suggestive of immune or haematological abnormalities, and in line with the case described by Naftel *et al*., analytical studies were performed only at 8 weeks, at which point the infant showed no evidence of ED. While the normal eosinophil range in neonates remains unclear, the absence of prolonged ED is reassuring and suggests that placental transfer of benralizumab did not result in lasting suppression. Also, regarding neonatal outcomes, transient neonatal hypoglycaemia, consequent hypoactivity, and reduced suck reflex, occurred but were considered more consistent with common caesarean-related neonatal effects rather than in-utero drug exposure, as such findings have not been reported with benralizumab or other asthma biologics, including mepolizumab [1,6,9,11-14]. Although transient corticosteroid course during the second trimester may represent a potential confounder, its duration and timing are unlikely to have contributed to major adverse perinatal outcomes, though it may have contributed to the

transient neonatal hypoglycaemia. Conversely, systemic corticosteroids are known to reduce the risk of complications secondary to poorly controlled asthma (e.g., pre-eclampsia, preterm birth, growth restriction and fetal hypoxia), making their precise contribution to the absence of these complications in this case difficult to establish [11,12]. Benralizumab continuation during breastfeeding was uneventful, consistent with literature. IgG1 transfer into breast milk is limited and oral bioavailability of monoclonal antibodies is low, suggesting minimal infant exposure to benralizumab [8]. A recent international Delphi consensus on asthma biologics during pregnancy emphasized the need for risk-benefit discussions and multidisciplinary decision-making [2]. The study concluded that most asthma biologics seem safe during conception, pregnancy (including the third trimester), breastfeeding and inactivated vaccination. The authors agreed that asthma biologics can be initiated during pregnancy, following national criteria for non-pregnant individuals, particularly for those with frequent exacerbations (4 in 12 months). Recent asthma-related admissions and steroid side-effects can lower the initiation threshold. No consensus was reached regarding live-attenuated vaccines, but in our case, these were administered at the usual schedule following paediatric evaluation. To our knowledge, this is the first reported case in Portugal of a healthy infant born to a mother who continued benralizumab throughout pregnancy. The case reinforces positive maternal and neonatal outcomes, including breastfeeding, growth, and vaccination, with no harm associated with benralizumab. It highlights the importance of multidisciplinary review and shared decision making for biologics use during pregnancy when benefits outweigh risks. Although no significant adverse effects have been identified, more data is needed to better characterize asthma biologics' safety profile and to establish consensus guidelines on its use during pregnancy.

References

1. Manetz S, Maric I, Brown T, et al. Successful pregnancy in the setting of eosinophil depletion by benralizumab. J Allergy Clin Immunol Pract 2021;9:1405-7.
2. Naftel J, Jackson D, Coleman M, et al. An international consensus on the use of asthma biologics in pregnancy. Lancet Respir Med 2025;13:80-91.
3. Ferguson GT, FitzGerald JM, Bleecker ER, et al. Benralizumab for patients with mild to moderate, persistent asthma (BISE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med 2017;5:568-76.
4. Middleton PG, Gade EJ, Aguilera C, et al. ERS/TSANZ Task Force Statement on the management of reproduction and pregnancy in women with airways diseases. Eur Respir J 2020;55:1901208.

5. Ramos CL, Namazy J. Monoclonal antibodies (biologics) for allergic rhinitis, asthma, and atopic dermatitis during pregnancy and lactation. Immunol Allergy Clin North Am 2023;43:187-97.
6. Naftel J, Eames C, Kerley S, et al. Benralizumab treatment of severe asthma in pregnancy: a case series. J Allergy Clin Immunol Pract 2023;11:2919-21.
7. Russell MD, Dey M, Flint J, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology 2023;62:e48-88. Erratum in: Rheumatology 2023;62:2021.
8. Beltagy A, Aghamajidi A, Trespidi L, et al. Biologics during pregnancy and breastfeeding among women with rheumatic diseases: safety clinical evidence on the road. Front Pharmacol 2021;12:621247.
9. Saco T, Tabatabaian F. Breathing for two: a case of severe eosinophilic asthma during pregnancy treated with benralizumab. Ann Allergy Asthma Immunol 2018;121:S92.
10. Namazy J, Cabana MD, Scheuerle AE, et al. The Xolair Pregnancy Registry (EXPECT): the safety of omalizumab use during pregnancy. J Allergy Clin Immunol 2015;135:407-12.
11. Shakuntulla F, Chiarella SE. Safety of biologics for atopic diseases during pregnancy. J Allergy Clin Immunol Pract 2022;10:3149-55.
12. Jang W, Jo H, Park J, Kim S, et al. Use of biologics to treat asthma during pregnancy and adverse events in pregnant women and newborns: a global pharmacovigilance analysis. Int Arch Allergy Immunol 2025;186:875-88.
13. Wang D, Zhou X, Ning J, et al. Risk factors for neonatal hypoglycemia: a meta-analysis. BMC Endocr Disord 2024;24:166.
14. Aksu K, Yağdıran M, Çelik Tuğlu H et al. Mepolizumab and pregnancy: a case of severe eosinophilic asthma in a patient who conceived during mepolizumab treatment. Eurasian J Pulmonol 2025;27:62-4.

Table 1. Patient diagnostic workup under GINA STEP 5 treatment (high doses of fluticasone-formoterol, montelukast and tiotropium bromide) and prednisolone 20 mg.

Nurse	Assess adherence and inhalers technique Questionnaires Education
Eosinophils blood count	0.36x10^9/L
Total IgE	96 UI/mL
Autoimmune panel	Negative
Prick tests	Negative
Fractional exhaled nitric oxide (FeNO)	9 parts per billion
Spirometry	Positive response to bronchodilator, with 2.12L (78.9%) of FEV1.
Chest computed tomography	Small area of ground-glass opacity in right lower lobe, likely related to an inflammatory process, with no other associated alterations.
Computed tomography of paranasal sinus	Enlarged turbinates and mild mucosal thickening of the maxillary sinus
ENT observation	Ear, oral cavity and oropharynx without alterations. Fibreoptic transnasal endoscopy without alterations.
Ventilation/perfusion scan	Excluded pulmonary thromboembolism.
Bronchoscopy	No structural abnormalities or microbiological growth were detected, including in bronchoalveolar lavage samples.