Vedolizumab and chickenpox in immune patient during pregnancy

Silvia Bonassisa[1*], Carmen Imma Aquino[1, 2], Alessandro Libretti[1], Roberta Amadori[1], Valentino Remorgida[1] and Daniela Surico[1]

[1] Department of Gynaecology and Obstetrics, University of Piemonte Orientale, AOU Maggiore della Carità, Via Mazzini 28, 28100, Novara, Italy

[2] Department of Translational Medicine, University of Piemonte Orientale, AOU Maggiore della Carità, Via Mazzini 28, 28100, Novara, Italy

Correspondence Author: Silvia Bonassisa

Received 7 Dec 2022; Accepted 14 Jan 2023; Published 23 Jan 2023

Abstract

Vedolizumab (VDZ) is a humanized immunoglobulin G1 monoclonal antibody approved for use in adults affected by moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC). In accordance with the Food and Drug Administration (FDA), VDZ is safe during pregnancy. Immunosuppressive drugs increase the risk of infections especially when used in combination, but some treatments may also expose the patients to the reactivation of latent infections. A 39-years old pregnant woman G1 P0 started immunosuppressive therapy with Vedolizumab, after the failure of previous treatments. She had already been tested for HBV, EBV and VZV, in addition to previous serology, resulting in immunity. At the 12 weeks of pregnancy, a first suspicious symptomatology for VZV began to appear and chickenpox caused by Varicella-Zoster virus was suspected. Blood tests showed a strong positivization of viral DNA in the blood. The patient decided to terminate the pregnancy for the fear of congenital chickenpox syndrome. In this case we observed an unexpected viral reactivation to an extent like a first infection although the patient was immune. It is therefore essential to carefully evaluate the administration of Vedolizumab in the first trimester, underlining that a reactivation of the VZV and the manifestation of chickenpox is possible even if the women was cataloged as immune.

Keywords: pregnancy, obstetrics, abortion, complications

Introduction

Inflammatory bowel diseases (IBD) are diseases of yet unknown etiology characterized by chronic inflammation of the gastrointestinal tract [1, 2]. Active IBD could be associated with poor pregnancy outcomes [3]. Vedolizumab (VDZ) is a humanized immunoglobulin G1 monoclonal antibody approved for use in adults with moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC) [4]. VDZ blocks the interaction between an integrin on the surface of gut-specific lymphocytes and a receptor on the vascular endothelium of the intestinal tract (α4β7 and MAdCAM-1, respectively) [5]. In accordance with the Food and Drug Administration (FDA), VDZ can be used during pregnancy, but studies on human fetotoxicity are few and no long-term data is available [6, 7]. Immunosuppressive drugs increase the risk of infections especially when used as combination [8, 9], but some treatments may also expose the patients to the reactivation of latent infections such as tuberculosis (TBC), hepatitis B (HBV) and C (HCV), Varicella Zoster Virus (VZV), Cytomegalovirus (CMV), and Epstein Barr Virus (EBV) [10-12].

Case report

A 39-years old pregnant woman G1 P0 was followed by our department's high risk pregnancy clinic as she suffered from ulcerative colitis (UC). She started immunosuppressive therapy with Vedolizumab in 2017, after the failure of previous treatments with Mesalazine, Thiopurines and Anti TNF. She stopped therapy in May 2019 after obtaining mucosal healing, but due to a new relapse, she restarted VDZ in November 2019 with clinical and endoscopic remission. She became pregnant in September 2020. In case of severe disease progression and lacking of alternative therapy options, use of VDZ is acceptable during pregnancy and breastfeeding, so after a consultation between a gastroenterologist and gynaecologist, therapy was continued [13]. According to the ECCO guidelines, it was decided to continue the treatment until 24 weeks of gestation considering the risk of preterm labour and small for gestational age (SGA) newborns.

Except for a surgery of pancreas divisum correction, the patient had a silent anamnestic history. Maternal serology resulted negative for HIV, HCV, LuE, HbSAg. She was susceptible to Toxoplasmosis, had suffered a CMV infection and had relapsed a HSV1 infection. She had already been tested for HBV, EBV and VZV, in addition to previous serology, resulting in immunity and Quantiferon test was negative before starting biologic therapy with VDZ.

At the 12 weeks of pregnancy, a first symptomatology suspicious for VZV began to appear, with fever and an itchy rash with small, fluid-filled blisters. Chickenpox caused by VZV was suspected. At the beginning of pregnancy, the Immunoglobulin G were 722 mUI/ml and IgM were 0,93 mUI/ml, showing an immunity. Acyclovir therapy was started to treat the reactivation of the disease. The ultrasound exam during the 12 weeks and 3 days of gestation showed a nuchal translucency of 1,60 mm and normal fetal biometry. After the symptoms worsened, the patient was referred to Tertiary

Referral Hospital where the diagnosis was confirmed and the patient was hospitalized. Blood tests showed a strong positivization of viral DNA in the blood (VZV DNA PCR= 18.180 copy/ml) and on vesiculo-cutaneous swab (VZV DNA PCR= 431100000 copy/ml). After a consultation about the possible effects on the fetus, the patient decided to terminate the pregnancy for the fear of congenital chickenpox syndrome, possible with a probability of 0.59% and 0.84% for women infected with VZV during the entire pregnancy and for those infected within the first 20 weeks of pregnancy, respectively [14].

Discussion

VZV, the virus known for causing chickenpox in children and Herpes Zoster in adults, is particularly insidious in patients with IBD due to risk of developing into a Varicella Virus infection specifically in immunosuppressed patients. In fact, fatal cases of varicella in IBD patients have been reported [15]. A recent review of literature about 213 VDZ-exposed documented pregnancies in IBD patients, reported no evidence for safety concerns regarding pregnancy outcomes associated with VDZ therapy. Due to the limited scope of available records, research is needed to understand the safety profile regarding the use of anti-integrin therapy during pregnancy [16]. Our patient was immunized against the virus by vaccination. Nonetheless, during pregnancy the patient still had clinical manifestation of chickenpox. Chickenpox in the first or second trimester is related to a risk of congenital fetal infection syndrome, although in the third trimester it may lead to severe neonatal varicella or maternal pneumonia with very poor outcomes. In our case we observed an inexplicable and unexpected viral reactivation similar to a 'first infection' even if the patient was immune.

Conclusions

The voluntary interruption pregnancy was devastating for the woman and for the equipe who attended her. Thus, we would invite to use Vedolizumab with extreme caution in the first trimester, underlining that reactivation of a previous VZV infection and the onset of chickenpox is possible even if the woman is immune.

Acknowledgements

No acknowledgements

Ethics

This paper is a case report and not a research study. Therefore, ethical approval was not necessary.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest statement

No potential conflict of interest was reported by the authors.

Funding

No funding

Author contributions statement

All authors contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

Data statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

References

1. Baumgart DC, Sandborn WJ. "Crohn's disease," 2012, doi: 10.1016/S0140-6736(12)60026-9.
2. Ordás I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. "Ulcerative colitis," 2012, doi: 10.1016/S0140-6736(12)60150-0.
3. Van Der Woude CJ, *et al*. "The second European evidenced-based consensus on reproduction and pregnancy in inflammatory bowel disease," J. Crohn's Colitis, 2015. doi: 10.1093/ecco-jcc/jju006.
4. BB *et al*. "Vedolizumab outcomes in real-world bio-naive ulcerative colitis and crohn's disease patients (evolve) in Canada: Treatment patterns, clinical effectiveness and safety," United Eur. Gastroenterol. J., 2018.
5. Gisbert JP, Domènech E. "Vedolizumab en el tratamiento de la enfermedad de Crohn," Gastroenterol. Hepatol., 2015. doi: 10.1016/j.gastrohep.2014.12.003.
6. Mahadevan U, Matro R. "Care of the Pregnant Patient with Inflammatory Bowel Disease," Obstet. Gynecol., 2015. doi: 10.1097/AOG.0000000000000978.
7. "Vedolizumab (Entyvio) for inflammatory bowel disease," Med. Lett. Drugs Ther., 2014.
8. Toruner M, *et al*. "Risk Factors for Opportunistic Infections in Patients with Inflammatory Bowel Disease," Gastroenterology, 2008. doi: 10.1053/j.gastro.2008.01.012.
9. Fries W, Cottone M, Cascio A. "Systematic review: Macrophage activation syndrome in inflammatory bowel disease," Alimentary Pharmacology and Therapeutics, 2013. doi: 10.1111/apt.12305.
10. Cascio A, Iaria C, Ruggeri P, Fries W. "Cytomegalovirus pneumonia in patients with inflammatory bowel disease: A systematic review," International Journal of Infectious Diseases, 2012. doi: 10.1016/j.ijid.2012.03.008.
11. Beaugerie L, *et al*. "Lymphoproliferative disorders in patients receiving thiopurines for inflammatory bowel disease: a prospective observational cohort study," Lancet, 2009. doi: 10.1016/S0140-6736(09)61302-7.
12. Shale MJ, Seow CH, Coffin CS, Kaplan GG, Panaccione R, Ghosh S. "Review article: Chronic viral infection in the anti-tumour necrosis factor therapy era in inflammatory bowel disease," Alimentary Pharmacology and Therapeutics, 2010, doi: 10.1111/j.1365-2036.2009.04112.x.
13. Puchner A, Gröchenig HP, Sautner J, Helmy-Bader Y, Juch H, Reinisch S, *et al*. Immunosuppressives and biologics during pregnancy and lactation: A consensus report issued by the Austrian Societies of Gastroenterology and Hepatology and Rheumatology and Rehabilitation. Wien Klin Wochenschr. 2019;131(1-2):29-44. doi: 10.1007/s00508-019-1448-y. Epub 2019 Jan 14. PMID: 30643992; PMCID: PMC6342891.
14. Ahn KH, Park YJ, Hong SC, Lee EH, Lee JS, Oh MJ, *et al*. Congenital varicella syndrome: A systematic review. J

Obstet Gynaecol. 2016;36(5):563-6. doi: 10.3109/01443615.2015.1127905. Epub 2016 Mar 10. PMID: 26965725.

15. Cullen G, Baden RP, Cheifetz AS. Varicella zoster virus infection in inflammatory bowel disease. Inflamm Bowel Dis. 2012;18(12):2392-403. doi: 10.1002/ibd.22950. Epub 2012 Mar 20. PMID: 22434654.
16. Terjung B, Schmelz R, Ehehalt R, *et al*. Safety of vedolizumab in the treatment of pregnant women with inflammatory bowel disease: a targeted literature review Therap Adv Gastroenterol. 2020;13 PMID:33149762.