Successfully multiple pregnancies in Crohn's disease under long-term treatment with adalimumab

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To the Editor,

It is well known that anti-TNF-α antibodies may be safe for patients suffering from Crohn's disease (CD) and in pregnancy (1,2). Successful pregnancies of women under treatment with adalimumab (ADA) have been reported (3), but no data are available about what may happen when patients under long-term ADA treatment go through multiple pregnancies.

On December 2007, a 32-year-old female patient consulted for her CD recurrence. She has been suffering from CD since 2001. In 2004 she had undergone ileocolonic anastomosis due to acute terminal ileum stenosis, and had been under continuous treatment with mesalazine and azathioprine since 2006. At entry, inflammatory indexes (WBC, ESR, and CRP) were increased, and CT-enterography showed stenosis of the anastomotic loop with thickening and dilation of the ileal loop (20 cm in length) above the anastomosis. A new course of steroids associated with enteral nutrition allowed remission of the disease. ADA was started (induction regimen 160/80 mg, followed by 40 mg every other week as maintenance regimen) due to previous azathioprine failure in maintaining remission (2). She responded very well to ADA, obtaining and maintaining remission without side-effects. In March 2008, she became pregnant. ADA infusion was carried out up until August 2008, when it was interrupted. The patient, under continuous CD remission during pregnancy (assessed by clinical criteria, laboratory and ultrasonography), had a cesarean delivery at 39th week of a healthy baby boy (2950 grams in weight). The baby was not breastfed and the mother went back to ADA infusion at doses of 40 mg every other week. The baby was followed closely by the pediatrician (by laboratory and clinical assessment) every 2 months during his first year and every six months thereafter, and he was always in good health.

In November 2011, the patient became pregnant again while under continuous CD remission (assessed by clinical criteria, laboratory and ultrasonography). We adopted the same strategy of the first pregnancy, and ADA infusions were interrupted in April 2012 at the 6th month of pregnancy. The patient, under continuous CD remission during her pregnancy, had a cesarean delivery at 38th week of a healthy baby girl (2720 grams in weight). Again, the baby was not breastfed and the mother went back to ADA infusion at doses of 40 mg every two weeks. Again, the baby was closely followed by the pediatrician (by laboratory and clinical assessment) every 2 months, and she was always in good health.

At the last examination (September 2012), the patient was still under treatment with ADA 40 mg eow. Both babies are healthy and no sign or symptom of immunosuppression was noted at that time.

Although Infliximab (IFX) and ADA are classified by the FDA as a pregnancy class B drug, the issue whether IFX or ADA can be continued throughout the entire pregnancy is still controversial. Current guidelines advice to avoid IFX and ADA infusion during the last trimester of pregnancy (1,2). This is because IgG1 immunoglobulins pass the placental barrier in the second and third trimester of pregnancy (4,5). However, the significance of these prolonged high levels is not clear (1,2). Eventual flares during the third trimester can be managed with systemic steroids that are safe during pregnancy.

This case is therefore of interest for clinical practice not only because it confirms that ADA may be safe and effective in maintaining CD remission during pregnancy, but also because it suggests an interesting management of these patients : a long-term ADA treatment interrupted at the 6th month of pregnancy and restored after delivery allows to go through multiple pregnancies while maintaining CD remission.

References

1. MOTTET C., VADER J.P., FELLEY C., FROEHLICH F., GONVERS J.J., JUILLERAT P. *et al*. EPACT II Study Group. Appropriate management of special situations in Crohn's disease (upper gastro-intestinal ; extra-intestinal manifestations ; drug safety during pregnancy and breastfeeding) : Results of a multidisciplinary international expert panel-EPACT II. *J. Crohns Colitis*, 2009, **3** : 257-263.
2. ORLANDO A., ARMUZZI A., PAPI C., ANNESE V., ARDIZZONE S., BIANCONE L. *et al*. Italian Society of Gastroenterology, Italian Group for the study of Inflammatory Bowel Disease. The Italian Society of Gastroenterology (SIGE) and the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD) Clinical Practice Guidelines : The use of tumor necrosis factor-alpha

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Submission date : 30/09/2012
Acceptance date : 30/10/2012

antagonist therapy in inflammatory bowel disease. *Dig. Liver Dis.*, 2011, **43** : 1-20.

3. SCHNITZLER F., FIDDER H., FERRANTE M., BALLET V., NOMAN M., VAN ASSCHE G. *et al*. Outcome of pregnancy in women with inflammatory bowel disease treated with antitumor necrosis factor therapy. *Inflamm. Bowel Dis.*, 2011, **17** : 1846-1854.
4. SIMISTER N.E. Placental transport of immunoglobulin G. *Vaccine*, 2003, **21** : 365-369.
5. VASILIAUSKAS E.A., CHURCH J.A., SILVERMANN N., BARRY M., TARGAN S.R., DUBINSKY M.C. Case report : evidence for transplacental transfer of maternally administered infliximab to the newborn. *Clin. Gastroenterol. Hepatol.*, 2006, **4** : 1255-1258.