CASE REPORT

Use of ticagrelor in human pregnancy, the first experience

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SUMMARY

Ticagrelor was daily administered throughout pregnancy to a 37-year-old pregnant woman until 36 weeks of gestation. The patient, with Behçet disease, suffered from a non-ST elevation myocardial infarction 4 months before conception, possibly related to hypertension and tobacco abuse. Pregnancy and postpartum periods were uneventful. She delivered a healthy but small-for-gestational-age term neonate.

BACKGROUND

We report the first case of use of ticagrelor during pregnancy. Ticagrelor is a new class of antiplatelet agent used as secondary prevention in combination with acetylsalicylic acid after an acute coronary syndrome. Class C was assigned to this new drug by the US Food and Drug administration. Data of use in human pregnancy are non-existent.

CASE PRESENTATION

A 37-year-old woman with Behçet disease suffered from a non-ST elevation myocardial infarction (NSTEMI). Mild stenosis of the left anterior descending coronary artery was treated with implantation of a drug-eluting stent through percutaneous coronary intervention. Following the hospital guidelines, ticagrelor 90 mg two times a day for 1 year in combination with acetylsalicylic acid 80 mg once daily (life time) was initiated for secondary prevention, as was atorvastatin 40 mg daily.

Other cardiac risk factors included hypertension and smoking (30 cigarettes/day). Antihypertensive treatment included perindopril 5 mg and bisoprolol 5 mg daily. Behçet disease was treated at the same time with cyclosporine 50 mg two times a day, and prednisolone 8 mg and colchicine 1 mg daily. The patient's obstetric history included caesarean section for breech position and a subsequent uneventful term vaginal delivery.

The patient was counselled to not become pregnant after this recent acute coronary syndrome and daily treatment with cyclosporine, however, she stopped her oral contraception and presented with a spontaneous singleton pregnancy 4 months after the NSTEMI.

TREATMENT

At the first prenatal visit at 6 weeks of gestation, cyclosporine, atorvastatin and colchicine were discontinued. Perindopril was replaced by amlodipine 5 mg daily and, after multidisciplinary counselling between obstetricians, cardiologists and neonatologists, it was advised to continue the treatment with

ticagrelor for 8 months, until 7 days before a planned delivery.

Acetylsalicylic acid 80 mg once daily, prednisolone 8 mg once daily and bisoprolol 5 mg once daily were continued throughout the entire pregnancy.

Regular prenatal follow-up was provided (1 visit/3 weeks) with Doppler examination of the uterine artery at 12, 18 and 22 weeks of gestation.

Cardiac check-ups with clinical examination, ECG and cardiac ultrasound, were planned. Ophthalmological examination was conducted at 28 weeks of gestation.

OUTCOME AND FOLLOW-UP

The pregnancy was uneventful. The patient did not suffer from flare-ups of Behçet disease during pregnancy. Prenatal ultrasound examinations, and cardiac and ophthalmological check-ups did not show any abnormalities.

Ticagrelor was stopped at 36 weeks of gestation because the patient reported episodes of painful contractions; endovaginal measurement of cervical length was 10 mm. Actual labour did not start and induction was performed at 38 weeks with intracervical dinoprost gel (Prepidil, Ferring, Belgium). During labour, amniotomy was performed and intravenous oxytocin was given according to local protocol. The patient received epidural anaesthesia (puncture with 17 gauge Tuohy needle, epidural catheter and continuous administration of a mixture of hyperbaric bupivacaine and sufentanil). She delivered, without any problems, a healthy baby boy of 2645 g (5th centile for our local population), Apgar scores 8/9/10 after 1, 5 and 10 min, respectively, and umbilical artery pH 7.24; 5 IU oxytocin was given intravenously after delivery, as is routinely carried out in our hospital.

No significant events occurred in the postpartum period. At writing, the patient was continuing breast feeding her baby. Cyclosporine, colchicine and atorvastatin will be administered again after the lactation period.

Histopathological examination of the placenta demonstrated no specific lesions, but did show iron-loaded macrophages in the deciduas, suggesting antenatal bleeding, although this was never noted clinically.

DISCUSSION

To the best of our knowledge this is the first report on the use of ticagrelor in pregnancy. Ticagrelor is a new and powerful antiplatelet agent. Ticagrelor is a nucleoside analogue and reversibly blocks the

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P2Y₁₂ receptor.¹ P2Y₁₂ inhibitors increase the risk of bleeding. Potential complications in pregnancy could include: antenatal vaginal bleeding, placental abruption, postpartum haemorrhage, placental transmission resulting in fetal/neonatal bleeding and eventual problems due to haemorrhage during neuraxial anaesthesia. Clopidogrel is the most widely used P2Y₁₂R antagonist.² Several recently reviewed reports on the use of clopidogrel in pregnancy have been published. Based on the limited available data, clopidogrel in pregnancy has not been linked to maternal or fetal/neonatal complications.

The association of ticagrelor with acetylsalicylic acid was reportedly superior in prevention of a new thromboembolic event after an acute coronary syndrome, compared with the association of clopidogrel and acetylsalicylic acid.³ The advised period of administration is 12 months. This new drug is a class C drug in pregnancy because no controlled data of use in human pregnancy exist and animal studies showed fetal mortality and/or abnormalities at doses greater than the maximum administered to humans. In our case, a multidisciplinary board decided that the benefits of administration of ticagrelor during pregnancy in this patient with multiple cardiac risk factors, outweighed the possible risks. When used in pregnancy, we advise stopping ticagrelor 7 days before planned delivery so as to know that normal coagulation has resumed.

The limited fetal growth in this case can be linked to several factors including the use of ticagrelor and/or the patient's vascular status, and the use of polymedication (especially bisoprolol). Hypertension and smoking are important confounding factors as causes for the limited fetal growth. It is possible that some subclinical bleeding, resulting in iron-loaded decidual macrophages, is related to the use of either acetylsalicylic acid or ticagrelor.

Learning points

- ▶ Ticagrelor is a new and effective drug for use in secondary prevention of thromboembolic events after an acute coronary syndrome.
- ▶ This is the first reported case of ticagrelor being given during human pregnancy.
- ▶ A small-for-gestational-age fetus and subclinical decidual haemorrhage were noted.

Contributors MV drafted the article. YJ revised it critically and gave his final approval of the version to be published. DM collected the data and obtained the informed consent. JM collected data and was responsible for the follow-up of this pregnancy.

Competing interests None declared.

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