Case report: Successful pregnancy and delivery after myocardial infarction and essential thrombocythemia treated with clopidrogel

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Summary

We describe a case of a woman with essential thrombocythemia (ET) who had a subsequent successful pregnancy after a myocardial infarction and aortocoronary bypass grafting. We report the therapeutic management with clopidogrel and low molecular weight heparin. A healthy child was born spontaneously after 41 weeks of pregnancy. The placenta was morphologically normal. No maternal cardiac problems occurred.

Key words: Clopidrogel; Thrombocythemia; Pregnancy; Myocardial infarction.

Introduction

Essential thrombocythemia is a chronic myeloproliferative disease of unknown origin. Disturbances of proliferation and differentiation of the hematopoietic stem clone induce a hyperplasia of myelotic cells. Megakaryocytes and thrombocytes are the most frequently involved [1]. The clinical consequences of this disease implicate disturbed microcirculation and functional complaints such as paresthesias, dizziness, headache, visual problems, venous and arterial thrombosis, including myocardial and cerebral infarctions. During pregnancy the risk of abortion, retardation and intrauterine death of fetuses is elevated. The reasons are placental thrombi and bleeding [2-4].

Unfortunately, a causal therapy is not known, but a cytoreductive therapy with hydroxy urea, interferon-α, anagrelids or inhibitors of thrombocyte aggregation [1] is usual. Clopidrogel is a relatively new inhibitor of platelet aggregation, which selectively inhibits the binding of ADP with the receptor on thrombocytes. Until now, the efficacy of this medication during pregnancy and the breast feeding period has been investigated only in animal experiments, but clinical data are not yet available [5].

We report here on a patient with essential thrombocythemia and anamnestic myocardial infarction treated with clopidrogel having a normal pregnancy without any complications.

Case Report

Clinical history

A 24-year-old woman at 38 weeks' gestation (2 gravida, 0 para) was admitted to our department.

The family history was free of major diseases. In April 1998, the patient suffered from an acute anterior wall myocardial infarction with a complete thrombotic obstruction of the descending anterior ramus. After observing a paraclinically imposing high thrombocyte number, an essential thrombocythemia was diagnosed. After normalization of the thrombocyte count following chemotherapy, a bypass operation was performed in June 1998. Postoperative medication included 300 mg acetylesaliscyle acide and 500 mg tiklopidin daily. When taking these medications, the patient subsequently became pregnant but then had a spontaneous abortion during the second trimester in December of 1998. After that, the medication was changed to clopidogrel orally (2 x 75 mg daily).

Pregnancy

Therapy with clopidogrel was maintained during the entire pregnancy until ten days before delivery because of high thrombosis and embolic risks. Additionally, the patient received subcutaneously, intermittently low molecular heparin (5,000 IU dalteparin sc.) depending on thrombocyte counts (threshold 500 Gpt/l). The patient also received folic acide until week 37 of gestation. Controls of thrombocyte levels were performed regularly and electrocardiograms every three months. Further diagnostics were not necessary because of normal pregnancy and fetal development.

Despite the previous infarction the transthoracic echocardiogram was normal. In coagulation diagnostics only increased thrombocyte counts ranging from 470 to 620 Gpt/l were remarkable.

Delivery

Ten days before delivery clopidrogel therapy was stopped and a therapy of 2 x daily 2500 IE low molecular weight heparin (dalteparin) was continued subcutaneously. The day of delivery itself 3 x 5,000 IE heparin s.c. was applied.

Induction of delivery was performed in week 41+3 of pregnancy via oxytocin infusion. ECG was normal during the entire delivery period. Regular contractions started after six hours. The maximal dose of continuous oxytocin infusion was 0.7 IE/h. After a total length of labor of 11 h 36 min, the fetus was born spontaneously from 1. occipito-anterior position.

The newborn was a vital mature girl of 3,170 g and 48 cm with a cord blood pH of 7.39 and APGAR of 9/10/10/10 (after 1/5/10/60 min.). The placenta followed, spontaneously and completely, after 5 min. The placenta was morphologically normal without any infarcts or areas of fibrin deposition. The mediolateral episiotomia was sutured under local anesthesia. There was no unusual or excessive bleeding at the time of delivery.

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Puerperium

The puerperium passed without complications and was afebrile. Breast feeding of the newborn was not desired because of the cardiac disease and the medication of the mother.

The episiotomia was cured per primam. The postpartum (p.p.) ECG was free of pathological signs and the cardiac situation was completely compensated.

Until day 21 p.p., the patient received 2,500 IE fragmin daily, and from day 3 p.p. additionally clopidogrel orally. The mother was discharged five days after delivery together with her daughter with a platelet count of 490 Gpt/l, both in good health condition.

Discussion

The diagnosis of essential thrombocythemia (ET) occurs occasionally. Therapy is necessary when thrombocytosis is > 1,000 x 10^9/l or when additional symptoms appear, such as disturbed blood circulation, emboli, thrombosis or infarctions, as happened in our case. Because this disease is rarely seen in younger individuals, there are only a few reports about it in pregnancy. In most cases increased abortion rates, fetus mortalis, preterm deliveries or growth retardation have been described as possible complications for the fetus [6-9]. Abortions occur most frequently during the first trimester in association with histologically confirmed placental infarctions [10]. Maternal complications are less frequent and include thromboembolias, thrombophlebitides, and thrombosis during or shortly after pregnancy [6, 10, 11].

Therapy during pregnancy usually consists of three medications: interferon-α, acetylsalicyle acid, and heparin. The success of interferon therapy is controversial. Some authors report the successful application of interferon-α during pregnancy against ET [9-12]. Dosage and time of beginning of therapy are also controversial. In any case, the dose should be reduced when thrombocyte counts decrease [9, 10].

However, two authors have reported on unsuccessful interferon-α therapy [13, 14]. In one case only a passing success of therapy was reported [14]. Another paper communicates the failure of therapy because of an abortion at the eighth week of pregnancy [13].

Most frequently acetylsalicyl acid is applied. This inhibitor of platelet aggregation was investigated in several studies during pregnancy and the breast feeding period [13]. An increased risk of fetal malformations was not described. In animal experiments, prolonged delivery times, preterm closure of the ductus arteriosus and increased blood losses were observed. In newborns, intracranial bleeding may occur. During breast feeding, a low dose therapy does not seem to harm the child [5].

Acetylsalycile acid was used either as a single medication or in combination together with heparin s.c., interferon-α or after application of chemotherapy such as melphalan [10, 13]. Although retrospective studies with high numbers of patients are lacking, generally, the success of pregnancy seems to be better in patients who received acetylsalycile acid therapy than in non-treated patients. Both, fetal and maternal complications, occurred notably less frequently in patients receiving acetylsalycile acid.

Because of the special risk profile of our patient (myocardial infarction) the platelet aggregation inhibitor clopidogrel was chosen.

Experiments on rats and rabbits did not show disorders of fetal development [5]. In animal experiments, clopidogrel was found in milk, but until now, secretion in human milk has not been reported. Clinical experience with the application of clopidrogel during pregnancy and breast feeding period does not yet exist.

Our patient had no thrombophlebitides or thromboembolic complications. During the above described management of delivery prolonged or stronger bleeding did not occur.

The placenta had no infarctions or microthrombi. The child was normotrophic and did not show any signs of retardation. As clopidogrel might pass into milk – as known from animal experiments – breast feeding was avoided and the woman was ablated because clopidogrel should be resumed during puerperium.

Further clinical studies are necessary for definitive evaluation of the therapy chosen in our case.

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