Hemophilia during pregnancy

ABSTRACT

QUESTION A patient in my clinic, who is 10 weeks into her first pregnancy and is a known carrier of hemophilia B, is considering the advantages and disadvantages of antenatal tests and is especially worried about a vaginal delivery that might cause bleeding. How should I manage her pregnancy?

ANSWER Many female carriers of hemophilia were found to have lower-than-expected levels of plasma factors, which are thought to be due to X chromosome inactivation. Chorionic villous sampling is the preferred test to determine the sex of the fetus and whether a male infant is affected with hemophilia. Vaginal delivery is not contraindicated and has been proven during the last two decades to be as safe as cesarean section. Vacuum extraction should be avoided to minimize risk of intracranial hemolysis and severe cephalhematoma.

RÉSUMÉ

QUESTION Une patiente de ma clinique, qui en est à sa dixième semaine d’une première grossesse, est atteinte d’hémophilie B. Elle tente d’évaluer les avantages et les inconvénients de subir des épreuves prénatales et s’inquiète particulièrement d’un accouchement par voie vaginale, qui pourrait causer une hémorragie. Comment devrais-je prendre en charge sa grossesse?

RÉPONSE On a constaté chez plusieurs femmes hémophiles des niveaux de facteurs plasmatiques plus bas que la normale qui seraient attribuables à l’inactivation du chromosome X. Le prélèvement des villosités choriales est le test privilégié pour déterminer le sexe du fœtus et savoir si un enfant mâle est atteint d’hémophilie. L’accouchement par voie vaginale n’est pas contre-indiqué et s’est révélé, au cours des deux dernières décennies, comme étant aussi sûr que la césarienne. L’extraction à vide devrait être évitée pour minimiser le risque d’hémolyse intracrânienne et un céphalhématome grave.

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hemophiliac women at a centre in the United Kingdom to consciously decide against having any, or any more, children. A report from Sweden comparing hemophiliac carriers with a control group\(^7\) found that carriers who did not choose prenatal diagnosis often refrained from further pregnancies after the birth of a hemophiliac child and had fewer children than other carriers. Logistic regression analysis showed that choosing to have prenatal diagnosis correlated with family history of hemophilia and a positive attitude toward abortion.

**Procedures during pregnancy**

Ethical issues around prenatal sex determination of fetuses have been raised ever since procedures, such as amniocentesis and chorionic villous sampling, became available. A survey of obstetricians\(^4\) found that 75% said they would obtain prenatal ultrasound to determine fetal sex in families with a history of bleeding disorders and 48% said they would use ultrasound to check for intracranial hemorrhage in male fetuses. If family history was negative for bleeding disorders, less than 10% of respondents would screen for bleeding diathesis in mothers or obtain ultrasound scans of fetuses. The response rate in this study was low (23%), and more than half the respondents had had no cases of known hemophilia in the 5 years before the survey.

Fewer than half of women opt for sex determination when it is offered in the context of possible pregnancy termination.\(^5,7\) In one study,\(^6\) half of the women said they would choose termination, even as late as 16 to 20 weeks’ gestation. Of 41 pregnancy terminations reported in one study,\(^2\) only 27% of women mentioned hemophilia as a direct reason for it.

Any invasive antenatal procedure, such as chorion villous sampling or direct fetal sampling, subjects mothers and hemophiliac (male) fetuses to risk of bleeding. In early pregnancy, when most such procedures are carried out, factor VIII might not yet have risen to a high level. Physicians should check for factor level before any invasive procedure, and anti-D immunoglobulin should be administered to Rh D-negative mothers.\(^8\)

Prenatal diagnosis and counseling is important for known hemophilia carriers. As many as 50% of hemophilia cases, however, are the result of sporadic mutations with no previous known cases in the family.\(^9\) Family physicians and obstetricians should be aware of signs suggesting coagulation deficiencies and test to rule out hemophilia.

Until preimplantation determination of sex (based on genetically testing one of eight blast cells in an embryo) is widely available, and hemophiliac carriers can be offered the possibility of implantation of only female embryos, prenatal diagnosis using DNA obtained during chorion villous sampling at 11 to 12 weeks’ gestation is the preferred method.\(^9\)

**Use of coagulation factors**

Levels of factor VIII rise as pregnancy progresses, but levels of factor IX do not. One way of preventing massive bleeding during and following labour is prophylactic administration of the appropriate factors. In 1983, Seeds et al\(^10\) reported a successful predelivery automated plasma exchange in a severely affected hemophilia B carrier.\(^10\)

A technique was recently introduced to correct the hemostatic defect in fetuses with proven hemophilia.\(^11\) An intrauterine infusion of recombinant factor VIII was given during early labour; although the neonatal course was normal, the child developed an inhibitor to the recombinant factor given as treatment at the early age of 1 year.

**Mode of delivery**

In the past, vaginal delivery was contraindicated for hemophiliac carriers due to the possibility of uncontrolled bleeding, the need for invasive procedures under anesthesia (eg, epidural analgesia), and intrauterine hemorrhage if vacuum or forceps extraction became necessary during labour. Cesarean section gave obstetricians more control over delivery and was frequently used for hemophilia carriers.

During the last two decades, reports have shown that pregnancy outcome of carriers can be good, even with vaginal delivery. Ljung et al\(^12\) reported good outcome of 104 vaginal deliveries out of 117 deliveries in Sweden. They concluded that risk of serious bleeding with vaginal delivery was small, and cesarean section should not be the rule.\(^12\)

In another retrospective review, Kadir et al\(^1\) reported on 82 pregnancies of hemophilia carriers. Among the 50 that proceeded to delivery, use of fetal scalp electrodes\(^8\) and fetal blood sampling\(^4\) had no adverse consequences, even in affected male infants. One of two deliveries using vacuum extraction resulted in a large cephalhematoma requiring transfusion. Incidence of postnatal bleeding was reported to be higher than usual (22% primary bleeding, 11% secondary bleeding).

In one survey,\(^4\) 57% of obstetricians said they frequently delivered known hemophilia carriers by the vaginal route, and 11% said they preferred cesarean section; 85% said they rarely used vacuum extraction, and 74% said they rarely used forceps delivery for hemophilia carriers.

Intracranial hemorrhage has been reported in 1% to 4% of hemophiliac
newborns. In one retrospective report, four infants (out of 117 deliveries) with intracranial hemorrhage were all sporadic hemophilia patients and had encouraging outcomes. Delivery by vacuum extraction is still not recommended due to the risk of intrauterine hemorrhage and severe cephalhematoma. Of 17 deliveries by vacuum extraction, 12 infants were reported to have subgaleal or cephalic hematoma, and four had intracranial hemorrhage.

Much time has elapsed since hemophilia was associated with early death due to bleeding, disabling arthropathy, and risk of blood-borne infections. Nevertheless, the cost of treating hemophiliac patients as well as the complications of treatment (eg, inhibitors against factor concentrate) makes this unique disease a challenge to prospective parents, family physicians, and obstetricians. The availability of recombinant factor and introducing prophylaxis at an early age, albeit costly, have dramatically changed the outcomes of hemophiliac fetuses and children.

References