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Idiopathic thrombocytopenic purpura inregnancy

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Introduction

Idiopathic thrombocytopenic purpura (ITP), also known as autoimmune thrombocytopenic purpura (AITP) is an acquired disease of adults and children, characterized by transient, self-limited (acute form) or persistent (chronic form) decrease of the peripheral blood platelet count ($<150 \times 10^9/L$), due to a premature destruction by the reticuloendothelial system.¹ Adult chronic ITP has an incidence of 58–66 new cases per million population per year² affecting mainly women of childbearing age (female: male, 3:1).³ Consequently, haematologists often manage pregnant women with a previous or *de novo* diagnosis of ITP. The unique and particular characteristic of ITP in pregnancy is that the physicians must treat, at the same time, both the mother (differential diagnosis with other causes of thrombocytopenia; effects of pregnancy on ITP; need of therapy) and the fetus (assessment of the risk of neonatal thrombocytopenia; the mode of delivery to minimize the hemorrhagic risk; need of a specific treatment after partum).

The aim of this section is a brief review of the clinical aspects of ITP in pregnancy.

Differential diagnosis and frequency of pregnancy-related thrombocytopenias

A mild decrease in the platelet count is commonly observed, with a reduction of 10% of mean and of 2.5th, mainly in the third trimester, without relationship with initial platelet count;⁴ thus, a separate normal range should be calculated for pregnant and non-pregnant women.

Thrombocytopenia in pregnancy may occur as an isolated abnormality, such as a) gestational thrombocytopenia (a benign disorder characterized by a mild decrease of platelet count, occurring most commonly in the third trimester of pregnancy in

healthy women, with normal platelet values before and after pregnancy, no maternal hemorrhage or neonatal thrombocytopenia); b) ITP; c) drug-induced thrombocytopenia; d) type IIB von Willebrand disease or e) one of the many congenital thrombocytopenias. Furthermore, the decrease of platelet count may be due to pregnancy-specific syndromes (such as pre-eclampsia, HELLP syndrome or acute fatty liver) or to non-pregnancy-specific syndromes (such as thrombotic microangiopathies, systemic lupus erythematosus, intravascular disseminated coagulation, viral infections, primary and secondary bone marrow dysfunctions).

An accurate estimate of the frequency of these causes was calculated by Burrows and Kelton, in a very large, prospective, cross-sectional study.⁵ A total of 1.027 thrombocytopenic mothers (platelet count $150 \times 10^9/L$) among 15.471 (platelet count performed before delivery), was found, giving an incidence of 6.6% (CI 95%: 6.2–7). The most common cause was gestational thrombocytopenia (756 mothers, relative frequency: 73%, absolute frequency: 4.8%), followed by the thrombocytopenia associated to the hypertensive disorders (216 mothers, relative frequency: 21%, absolute frequency: 1.4%). ITP mothers were 31 (relative frequency: 3%, absolute frequency: 0.25%), whereas 13 cases were associated to other hematological and medical diseases, such as aplastic anemia or acute leukemia. Table 1 summarizes some clinical characteristics, useful for differential diagnosis at *bed-side* of the patient.

Clinical picture

A physician managing a pregnant woman with thrombocytopenia will have to deal with two main clinical pictures. In the first, the patient has a prior history of ITP and she is either in stable, chronic phase, in which no diagnostic investigation is needed, or she is reporting a previous diagnosis of ITP, despite having a normal platelet

Table 1. Differential diagnosis of thrombocytopenias in pregnancy.

<i>Cause of thrombocytopenia</i>	<i>Time of onset</i>	<i>Grade of thrombocytopenia</i>	<i>Biochemical abnormalities</i>	<i>Clinical symptoms</i>
Gestational	III trimester	mild	no	no
ITP	I-II trimester	mild to severe	no	bleeding in severe cases
Eclampsia	III trimester	mild to severe	DIC ⁽⁴⁾ proteinuria	hypertension
HELLP ⁽¹⁾	III trimester	mild to severe	DIC, hemolytic anemia ↑ AST/ALT	no or complex presentation
TTP ⁽²⁾	II trimester	mild	hemolytic anemia	fever, CNS ⁽⁵⁾
HUS ⁽³⁾	post-partum	mild	hemolytic anemia	fever, renal failure
AFL ⁽⁶⁾	III trimester	mild	DIC, hemolytic anemia, hypoglycemia	complex presentation

⁽¹⁾= Hemolytic anemia, elevated liver enzyme, low platelet; ⁽²⁾= Thrombotic thrombocytopenic purpura; ⁽³⁾= Hemolytic uremic syndrome; ⁽⁴⁾= Disseminated intravascular coagulation; ⁽⁵⁾= Involvement of central nervous system; ⁽⁶⁾= Acute fatty liver.

count (e.g. after splenectomy). Also in this case, no diagnostic investigation is needed, but neonatal thrombocytopenia is still possible in both cases, because of the presence of maternal anti-platelet antibodies that can cross the placental barrier and enter the fetal circulation. In the second clinical picture, the mother does not refer any previous history of ITP. If her platelet count is substantially decreased (<70–80×10⁹/L) a diagnostic investigation is needed, to differentiate ITP from the other causes of pregnancy-related thrombocytopenias (see table 1). If the reduction of the platelet value is mild (>80–100×10⁹/L), gestational thrombocytopenia cannot be excluded with certainty and neonatal thrombocytopenia might occur, so that the newborns should be treated as if born by a mother with ITP (see Table 2 for a summary).

Among laboratory investigations, there is a general agreement that blood film examination (to exclude spurious thrombocytopenia and morphological abnormalities of platelets, leukocytes and red blood cells), coagulation screening, liver function test, antiphospholipid antibodies assay are all recommended, whereas measurement of platelet antibodies is not appropriate and the bone marrow evaluation is recommended only if leukemia or lymphoma or bone marrow failure are suspected.⁶⁻⁸

Prognosis and clinical outcome

In the pregnant ITP patient, the fetus as well as the mother may be affected by thrombocytopenia, thus it is important to evaluate the prognosis (morbidity and mortality) of both of them.

Unfortunately, few studies have addressed the clinical outcomes, in term of hemostatic complications, in

ITP obstetric patients. Very recently, a retrospective review based on clinical records of 92 women with ITP (123 children delivered in 119 pregnancy) was published by Mc Master University group,⁹ aiming at collecting information on symptoms and need of treatment during pregnancy and at delivery. Information was available for 116 pregnancies, showing that in 76 women (65.5%) hemorrhage was not present; in 15 (12.9%) and 21 (18.1%) cases the women had mild and moderate bleeding symptoms; only in 4 pregnancies a severe bleeding was observed (2 hematuria, 1 hematoma, 1 gastrointestinal hemorrhage). In 37 out of 119 pregnancies (31.1%) women required treatment (steroids and/or immune globulins) to raise their platelet counts. A total of 98 (82.4%) deliveries were vaginal and 21 (17.6%) were by cesarian section (the mean platelet count was not statistically significant between the two groups). Hemorrhagic complications were uncommon (4 women with a blood loss of at least 1 L) without need of red blood cells transfusion. In the post-partum, 2 women experienced prolonged bleeding, but they did not require blood products. With the caveat of a probable referral bias, one could conclude that maternal bleeding can occur in ITP, but it is uncommon and the pregnancy do not have an unfavourable impact on mother's disease.

As to the neonatal outcome, the high perinatal mortality (12%–21%) reported in older studies¹⁰ was not confirmed and there is now a general agreement that the frequency of intracranial hemorrhage is very rare, around 0–1%.^{5,13} However, severe thrombocytopenia (<20×10⁹/L) in the newborns of ITP mothers is found in 3 to 5% of cases.¹¹⁻¹² Several studies have attempted to define some maternal characteristics predicting the platelet level of the newborns, but no correlation was found with maternal platelet count, a history of

Table 2. Different clinical pictures and diagnostic work-up of ITP in pregnancy.

History	Clinical picture	Diagnostic work-up	Neonatal thrombocytopenia
PREVIOUS THROMBOCYTOPENIA	remission →	not need →	possible
	chronic →	not need →	possible
DE NOVO THROMBOCYTOPENIA	acute →	differential diagnosis (Table 1) →	possible
	mild →	distinction from gestational thrombocytopenia very difficult →	possible

prior splenectomy and with the maternal platelet antibody;¹⁴ the unique, reliable predictor of neonatal thrombocytopenia is a history of previous neonatal thrombocytopenia¹⁵ and, perhaps, the severity of the disease in the mother.¹⁶

Therapy

A more extensive review on the management of ITP in pregnant women can be found in selected references.⁶⁻⁸ Very briefly, no specific treatment is appropriate for asymptomatic patients with platelet count $>20-30 \times 10^9/L$. If a therapy is required, the first choice is the steroid treatment, 1 mg/kg/day, tapering to the minimum effective dose after 2-3 weeks. In case of no response, or significant side-effects (such as hypertension, diabetes, excessive weight gain) or an unacceptably high dose required for maintenance, intravenous administration of immune globulins, at dosage of 0.4 g/Kg/days for 5 day is the second choice. A platelet count $>80 \times 10^9/L$ seems safe for spinal anaesthesia,¹⁷ but no anticoagulant or aspirin should be administered concomitantly. For the very rare cases of ITP refractory to steroids and immune globulins, splenectomy can be carried out preferably in the second trimester. Concerning the mode of the delivery,

several aspects should be taken into account. First, the inability to predict the fetal platelet count, indirectly and directly (cordocentesis and fetal scalp blood sampling have now been abandoned, because of their technical difficulties, the possibility of inaccurate platelet count and the risk of fetal mortality). Second, the lack of data from prospective randomized trials showing that the cesarian section could be more safe than the vaginal route. Finally, the possibility that intracranial hemorrhage can occur also during the gestation or only 3-5 days after partum. Thus, the management of delivery should be decided almost entirely on obstetrics considerations. A platelet count $>30 \times 10^9/L$ is safe for vaginal delivery, while a platelet level $>50-80 \times 10^9/L$ is usually considered sufficient for a surgical partum. At time of delivery from the cord, and 3-5 days thereafter (preferably every day for the first 7-10 days), a platelet count must be obtained on all newborns from mothers with present or previous ITP without regard to their current platelet count. In case of thrombocytopenic newborns, a specific treatment (steroids or immune globulins) might be necessary in presence of bleeding symptoms or in case of severe thrombocytopenia ($<20 \times 10^9/L$). Intracranial ultrasonography is recommended in all newborns with reduced platelet count.

References

1. Woods VL, Kurata Y, Montgomery RR, Tani P, Mason D, Oh EH, McMillan R. Autoantibodies against platelet glycoprotein Ib in patients with chronic immune thrombocytopenic purpura. *Blood* 1984; 64: 156-60.
2. Mc Millan R. Therapy for adults with refractory chronic immune thrombocytopenic purpura. *Ann Internal Med* 1997; 126: 307-14.
3. Waters AH. Autoimmune thrombocytopenia: clinical aspects. *Sem Hematol* 1992; 29: 18-25.
4. Sill PR, Lind T, Walker W. Platelet values during normal pregnancy. *Br J Obstet Gynecol* 1985; 92: 480-3.
5. Burrows RF, Kelton JG. Fetal thrombocytopenia and its relation to maternal thrombocytopenia. *N Engl J Med* 1993; 329: 1463-6.
6. George JN, Woolf SH, Raskob GE et al. Idiopathic thrombocytopenic purpura. A practice guideline developed by explicit methods for the American Society of Hematology. *Blood* 1996; 88: 3-40.
7. British Committee for standard in Hematology General Haematology task force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. *Br J Haematol* 2003; 120: 574-96.
8. Cines DB, Bussel JB. How I treat idiopathic thrombocytopenic purpura (ITP). *Blood* 2005; 106: 2244-51.
9. Webert KE, Mittal R, Sigouin C, Heddle NM, Kelton JG. A retrospective 11-year analysis of obstetric patients with idiopathic thrombocytopenic purpura. *Blood* 2003; 102: 4306-11.
10. Murray JM, Harris RE. The management of pregnant patient with idiopathic thrombocytopenic purpura. *Am J Obstet Gynecol* 1976; 126: 449-51.
11. Burrows RF, Kelton JG. Pregnancy in patients with idiopathic thrombocytopenic purpura: assessing the risk for the infant at delivery. *Obstet Gynecol Surv* 1003; 48: 781-8.
12. Sainio S, Joutsu L, Jarvenpaa AL et al. Idiopathic thrombocytopenic purpura in pregnancy. *Acta Obstet Gynecol Scand* 1998; 77: 272-7.
13. Bussel JB, Druzin ML, Cines DB, Samuels P. Thrombocytopenia in pregnancy. *Lancet* 1991; 337: 251.
14. Samuels P, Bussel JB, Braitman LE et al. Estimation of the risk of thrombocytopenia in the offspring of pregnant women with presumed immune thrombocytopenic purpura. *N Engl J Med* 1990; 323: 229-35.
15. Valat AS, Caulier MT, Devos P et al. Relationships between severe neonatal thrombocytopenia and maternal characteristics in pregnancies associated with autoimmune thrombocytopenia. *Br J Haematol* 1998; 103: 397-400.
16. Godelieve C, Christiansen ML, Nieuwenhuis HK, Bussel JB. Comparison of platelet count in first and second newborns of mothers with immune thrombocytopenic purpura. *Obstet Gynecol* 1997; 90:546-9.
17. Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm⁻³. *Anesth Analg* 1997; 85: 385-8.