THROMBOCYTOPENIA

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NORMAL changes haematological parameters in pregnancy

- Red cell : inc. plasma vol.(50%) , inc. red cell mass (25%) =dec. hb and hct. And increase MCV (immature cells)
- WBC :inc. WBC count : inc. neutrophils , monocytes , decrease in lymphocyte
- Platelets : reduce count in around 6% (dilution)

Platelet disorder in pregnancy

- Platelets are formed from megakaryocytes which are large multinucleate cells found in the bone marrow .
- Their differentiation and proliferation is under the control of thrombopoietin .
- Each megakaryocytes can generate 2000-3000 platelets .

Thrombocytopenia in pregnancy

- Thrombocytopenia affect 6-10% of all pregnant women and after anemia is the most frequent haematological disorder in pregnancy
- The normal serum level of platelets in pregnancy is 150–400 *10^9 /L.

- Reduction of serum platelet counts is considered mild if the count is <100,moderate at 50–100 and severe at <50.
- Common signs of thrombocytopenia include petechiae, nose bleeding and, more rarely, haematuria and gastrointestinal bleeding

Causes of thrombocytopenia in pregnancy

- Gestational thrombocytopenia (75%)
- Iso-immune (idiopathic) thrombocytopenia purpura (ITP)
- Pre-eclampsia & HELLP SYNDROME (15-20%)
- Disseminated intravascular coagulation (DIC)
- Thrombotic thrombocytopenic purpura (TTP)
- Haemolytic uraemic syndrome
- Anti-phospholipid syndrome & sle .

Causative diagnosis	Mechanism	Diagnostic features
Gestational thrombocytopenia	Physiological dilution, accelerated destruction	Third trimester, platelets >70 × 10^9/l; incidental finding
Immune thrombocytopenic purpura	Immune destruction, suppressed production	Diagnosis of exclusion
Thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome	Peripheral consumption, microthrombi	Unwell, fever, neurological and renal dysfunction
Haemolysis, elevated liver enzymes and low platelet count syndrome (HELLP syndrome)	Peripheral consumption, microthrombi	Raised LDH, ALT and bilirubin, haemolytic anaemia +/− pre-eclampsia, DIC
Hereditary thrombocytopenia	Bone marrow underproduction	Family history, abnormal platelets
Pseudothrombocytopenia	Laboratory artefact	Platelet clumps on blood film
Viral infection/drugs	Multifactorial	Viral illness, drugs taken, risk factors
Leukaemia/lymphoma	Bone marrow infiltration	Abnormal blood film; enlarged liver/spleen/nodes

ALT = alanine aminotransferase; DIC = disseminated intravascular coagulation; LDH = lactate dehydrogenase

Investigation of thrombocytopenia in pregnancy

- Full history & examination
- Blood film & reticulocyte count
- Pt & ptt , fibrinogen , LDH
- LFT
- Consider SLE serology
- Consider APLS screen

Gestational Thrombocytopenia

- Is the most common cause of Thrombocytopenia and accounts for 75 % of the cases .
- The fall in platelet count is secondary to haemodilution and increase platelet activation and clearance .
- How patient presents ?

- platelet count outside pregnancy is normal

-it usually resolve 1-2 months post-natally .

-platelet count usually remains above 70*10^9/L

- diagnosed after other DDX have been considered .

-there is no associated morbidity in the fetus and the risk of neonatal Thrombocytopenia is NOT increase .

- usually present late in pregnancy .

-platelet count should monitored 4 weekly .

Features of Gestational Thrombocytopenia:

1. Diagnosis of exclusion; no tests are available to distinguish from immune thrombocytopenic purpura
2. Mild thrombocytopenia, platelet count usually $>70 \times 10^9/l$
3. No associated maternal bleeding
4. No past history of thrombocytopenia outside pregnancy
5. Occurrence in third trimester
6. No associated fetal thrombocytopenia
7. Spontaneous resolution after delivery
8. May recur in subsequent pregnancies

Iso-immune (idiopathic) thrombocytopenia purpura (ITP)

- Is an autoimmune disease with antibodies detectable against several platelet surface structures .
- Affects 1 in 1000-10,000 pregnancies .
- It occurs as a first presentation in a 1/3 of cases and as a relapse in women with pre-existing disease in 2/3 .
- UNLIKE GT , the platelet count can fall SIGNIFICANTLY .
- These women may suffer associated symptoms of mucosal bleeding
- UNLIKE GT , it may present at any point in pregnancy (1st trimester)

Iso-immune (idiopathic) thrombocytopenia purpura (ITP)

- Transplacental transfer of maternal antiplatelet antibodies may cause thrombocytopenia in the infant .
- **The incidence of thrombocytopenia in the infant is around 25% .**
- **The incidence of neonatal ICH is less than 1% .**

- **Risk factors :**

-occurrence in an older sibling .

-history of splenectomy and severe and/or refractory ITP .

Iso-immune (idiopathic) thrombocytopenia purpura (ITP)

- The aim of management in ITP in pregnancy is to control bleeding symptoms and to allow for safe delivery .
- **in the 1st & 2nd trimester**

Bleeding symptoms rarely occur with plt. Count more than 20*10^9 , and therefore Asymptomatic women with plt. Count above this threshold are unlikely to require treatment in the 1st & 2nd trimester .

Treatment should be intiated if BLEEDING or excessive bruising occurs OR plt. Count falls less than 20*10^9/L

Iso-immune (idiopathic) thrombocytopenia purpura (ITP)

- **Around the time of delivery :**

The platelet count need to be raised to a threshold to ensure minimal haemorrhagic complication .

There should be close collaboration of the obstetrician ,haematologist and anaesthetist .

A platelet count of more than 50*10^9/L is acceptable for vaginal or caesarean section .

It is recommended that platelet count should be more than 75*10^9/L for spinal anesthesia .

Treatment

- **First line treatment of ITP in pregnancy is corticosteroid** , which achieve **good response in 70-80 % of women** .
- Possible S/E : GDM , HTN
- Steroids are not teratogenic but may be associated with PROM and placental abruption
- To avoid unnecessary S/E , the minimal therapeutic dose should be used , with dose escalation if poor response .
- An appropriate starting dose of prednisolone is 20 mg daily .

Treatment

- For refractory cases , or where a rapid increase in platelet count is required , intravenous immunoglobulin (IVIG) can be given (1 g/kg)
- Possible S/E :headache , aseptic meningitis and renal impairment .

- Other tx : high dose anti-d , azathioprine

- For EMERGENCY BLEEDING OR DELIVERY WITH LESS THAN 50*10^9 : PLATELET TRANSFUSION +IVIG+ IV METHYLPREDNISOLONE

Treatment

- Routine Cordocentesis is not recommended as the risk outweigh the benefits ,given that the random platelet transfused will be rapidly destroyed .
- The mood of delivery should be determined by obstetric indication , however to minimize trauma , fetal scalp electrodes , blood sampling and use of vaccum or rotational forceps should be avoided . (lift-out forceps can be used)
- A cord platelet count should be taken .
- IM vit. K withheld until the count is known

- a count less than 70*10^9 : repeat sample at day 5 (nadir reached due to splenic development)

-if count less than 30*10^9 : platelet transfusion & intracranial US

Pre-eclampsia & HELLP

- Consumptive thrombocytopenia occurs in around 30% of women with pre-eclampsia .
- HELLP (HEMOLYTIC ANEMIA M ELEVATED LIVER ENZYME AND LOW PLATELET)

- THESE TOPICS WILL BE DISCUSSED LATER , but you should always keep them in mind when dealing with thrombocytopenia in pregnancy .

Pre-eclampsia & HELLP

- Diagnostic criteria for pre-eclampsia include new onset, hypertension and proteinuria (>300 mg/ 24 hours) at >20 weeks of gestation.
- The estimated incidence is 5–10% of all pregnancies worldwide with increased incidence among primigravidae or multigravidae with new partners.
- The aetiology is not fully understood, but there is an association with the presence of laboratory thrombophilia and a known genetic predisposition. There is increased endothelial cell activation leading to the activation of platelets and the coagulation cascade.
- In general, women with pre-eclampsia have lower platelet counts than normal: approximately 15% within the thrombocytopenic range.
- The condition resolves quickly after delivery, therefore conservative management is appropriate for mild or moderate pre-eclampsia.
- Severe thrombocytopenia occurs among <5% of women with pre-eclampsia, but it can be associated with DIC. This requires aggressive management and correction of the coagulopathy with fresh frozen plasma, cryoprecipitate and platelet transfusions.

HELLP syndrome

- This is a combination of haemolysis, elevated liver enzyme levels and low platelet counts.
- It can complicate severe pre-eclampsia in about 10% of cases.
- It occurs most frequently in the third trimester, but it can get worse initially postpartum or, occasionally, present at this time.
- The syndrome can occur without hypertension or proteinuria and the diagnosis may be missed in these circumstances.
- The presenting symptoms can be very vague, with nausea, malaise and epigastric or right upper quadrant pain. Staff should have a high level of suspicion and check the full blood count and liver function.
- The pathophysiology of this condition involves endothelial damage with release of tissue factor and coagulation activation.

HELLP SYNDROME

- A full blood count shows anaemia and thrombocytopenia, with fragments present on the blood film (microangiopathic haemolytic anaemia).
- Liver function tests show a raised lactate dehydrogenase, increased bilirubin and abnormal liver enzymes.
- Disseminated intravascular coagulation may be present in approximately 20% of cases and abruption occurs in approximately 16%.
- The central nervous and renal systems are usually unaffected by this condition, in contrast to TTP .
- The neonatal outcome depends on the duration of gestation at delivery: neonatal mortality rates consequent on the necessity of very early delivery are 10–20% and fetal growth restriction is common.

HELLP SYNDROME

- As delivery is the mainstay of treatment for the mother, steroids should be given (to help mature the baby's lungs) and supportive care with fresh frozen plasma with or without cryoprecipitate if disseminated intravascular coagulation is present.
- The platelet count should be maintained at >50.
- The condition usually improves quite quickly after delivery, although it may worsen during the first 24–48 hours postpartum.
- Depending on the clinical scenario, e.g. worsening maternal condition or severe fetal growth restriction, delivery may be indicated at any time from 20 weeks of gestation.
- Conservative management for very early HELLP is controversial and a difficult decision sometimes has to be made between gaining extra time for the baby and the maternal risks.

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

- Is caused by reduced levels of ADAMTS-13 (a disintegrin and metalloproteinase with a thrombospondin type 1 , member 13)
- ADAMTS-13 : a metalloprotease required for the cleavage of ultra-large von Willebrand factor multimers , this leads to tissue ischaemia and sometimes infarction .
- This process can affect : lung , renal and cerebral vasculture .
- Most cases are acquired , however some cases are familial and may present for the first time in pregnancy .
- The mortality rate (due to intracerebral and cardiac events)of **untreated TTP is 80%** , which reduces to **10% with plasma exchange** .

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

- Its defined by the combination of microangiopathic haemolytic anaemia and thrombocytopenia , usually accompanied by neurological symptoms , renal impairment and sometimes fever .

- TTP is a **relatively rare** but important cause of thrombocytopenia in pregnancy , it carries a high mortality and morbidity rate which can be avoided if treatment is started early .

- TTP can be difficult to distinguish from sever pet &HELLP , BUT like these disorder , **THE MAIN THERAPEUTIC MANOEUVRE IS DELIVERY**

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

- Clinical :

typical “pentad” (fever ,renal impairment , neurological symptoms ,thrombocytopenia and micro-angiopathic haemolytic)

- Invx :

fbc and film : schistocytes(fragments) , thrombocytopenia

LFT : inc. bilirubin , LDH / RETICULOCYTE , low haptoglopin

Clotting will be normal

ADAMTS-13 level & ADAMTS-13 antibody (may be low in HELLP)

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) MANAGEMENT :

- Contact haematologist
- Start infusion of FFP
- If in 3rd trimester , consider delivery of baby
- Arrange for urgent plasma exchange
- Start iv methylprednisolone (for 3 days then switch to oral)
- **Then what ?**
- Start folic acid 5 mg , start aspirin and lmwh (when plt more than 50
- Continue plasma exchange until platelet count is normal

. . . . .

- If fetus not delivered immediately , serial growth scan with uterine artery Doppler .
- Warn about risk of recurrence in future pregnancies .
- Avoid oral contraception pill .

Haemolytic uraemic syndrome

- This is a similar syndrome, with microangiopathic haemolytic anaemia and thrombocytopenia but **with predominant renal involvement.**
- In childhood the disorder is usually associated with Escherichia coli infection and a good outcome. In adulthood and in pregnancy there is a poor response to plasma exchange.

Other causes of maternal thrombocytopenia:

Antiphospholipid syndrome:

Thrombocytopenia can be associated with antiphospholipid syndrome but this is rarely severe.

- Viral infection:

Almost any virus can cause a reduction in platelet count. This is usually very transient, but there may be a more prolonged reduction for a number of weeks. HIV and CMV infections are particularly associated with thrombocytopenia.

- Medication :

It's a frequent adverse effect of commonly used drugs. Heparin-induced thrombocytopenia can, rarely, occur with the administration of unfractionated heparin in pregnancy, but has not been described with the use of low molecular weight heparin in pregnancy.

- Malignancy.

THANK YOU …

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