CASE REPORT

Immune thrombocytopenic purpura presenting with spontaneous gingival haemorrhage in pregnancy

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SUMMARY

Gingival bleeding is a common intraoral finding, typically associated with inflamed tissues and periodontal disease. It is easily provoked by periodontal probing or toothbrushing. Spontaneous gingival bleeding rarely occurs and may be the only sign of systemic bleeding problems such as thrombocytopenia, leukaemia or coagulopathy. In pregnancy, acute onset of thrombocytopenia may occur in systemic disorders such as severe pre-eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes, low platelets) or the acute fatty liver of pregnancy. The diagnosis and management of such conditions may challenge physicians. It requires a systematic approach with a comprehensive history to exclude causes of gingival haemorrhage such as periodontal disease, anticoagulant therapy, maxillofacial trauma, haematological disorders or a bacterial infection. The authors describe a case of immune thrombocytopenic purpura presenting with spontaneous gingival haemorrhage in pregnancy. This case highlights the fact that medical intervention to correct the underlying aberration of haemostasis is necessary for local measures to stop the gingival bleeding successfully.

BACKGROUND

Immune thrombocytopenic purpura, previously known as idiopathic thrombocytopenic purpura is an autoimmune, haematological condition diagnosed by a markedly decreased number of circulating blood platelets of $<100 \times 10^9/L$, in the absence of any other cause of thrombocytopenia.¹ It results from the production of autoantibodies against one's own platelets and impaired platelet production, thereby reducing the total platelet blood count.² It is classified into acute (usually occurs in children) and chronic (usually occurs in adults) if the platelet count has not stabilised within 6 months. It accounts for 5% of cases of pregnancy-associated thrombocytopenia and is thought to result in complications in 1-2/10 000 pregnancies.³ Clinical features become evident when the platelet count falls below $50\,000/mm^3$. Bleeding gums is an oral manifestation of this condition and physicians should be educated as to the implications of a patient with persistent and continuous bleeding from the gingivae in the absence of any other medical condition.

CASE PRESENTATION

A 28-year-old woman presented to the Emergency Department complaining of spontaneous

and persistent gingival bleeding not precipitated by trauma. The patient was a primigravida in her second month of pregnancy. Her medical history was unremarkable and there was no family history of clotting disorders. She was not taking any medication. She had no known medication allergies. She was a non-smoker and did not consume alcohol. The gingival bleeding started spontaneously the previous evening. She attended her dentist the following morning. On examination, her gingivae were erythematous, swollen and hyperplastic. Supragingival calculus deposits were noted. She had no history of periodontal disease. The clinical impression was of pregnancy-induced gingivitis. A scale and polish was performed.

Following this, she was unable to achieve haemostasis and she attended the Emergency Department. She reported a history of gingivitis but had never experienced an episode of gingival bleeding of this nature. Her observations were stable. The patient was examined by a member of the maxillofacial team. There was no palpable lymphadenopathy. Clinical examination revealed a petechial rash on her extremities and torso. Abdominal examination revealed no hepatosplenomegaly. Intraorally, profuse gingival bleeding was observed at the lower incisors and from the upper left quadrant. Mucocutaneous petechiae, ecchymosis and haemorrhagic blisters with spontaneous bleeding on her lower lip were observed. Oropharyngeal petechiae and ecchymosis were noted (figure 1). Local measures were employed to achieve intraoral haemostasis which included pressure with adrenaline-soaked gauze and tranexamic mouth-rinse.

INVESTIGATIONS

Her venous blood gas confirmed normal physiology. Urinalysis was negative. A full blood count was carried out including an international normalised ratio (INR) and clotting screen. Her INR, fibrinogen and partial thromboplastin time values were within the normal range. Her kidney and liver function tests were within normal limits. True, severe thrombocytopenia was reported in the presence of a normal white blood cell and red blood cell morphology with a platelet count of $2 \times 10^9/L$ (table 1). No blasts or immature forms were observed. An urgent referral was made to the haematology registrar who admitted the patient for further investigations. An autoimmune screen was carried out which revealed the presence of non-specific enzyme reactive antibodies. All other causes of thrombocytopenia were excluded to confirm

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Figure 1 Mucocutaneous petechiae, ecchymosis and haemorrhagic blisters with spontaneous bleeding on her lower lip were observed. Oropharyngeal petechiae and ecchymosis were noted.

the diagnosis of idiopathic thrombocytopenic purpura (ITP) in pregnancy.

TREATMENT

She was treated with intravenous tranexamic acid 1 g acutely in the Emergency Department.

She remained an inpatient in the Haematology Ward for 7 days. She was reviewed by the Obstetrics Registrar. She was treated with intravenous tranexamic acid 1 g three times per day, oral prednisolone (1 mg/kg) and she received two doses of intravenous immunoglobulin (Ig). Her platelets responded from 2 to $41 \times 10^9/L$ at discharge. A once daily 40 mg dose of prednisolone was prescribed on discharge for 20 days.

OUTCOME AND FOLLOW-UP

Her pregnancy remained uneventful, with no abnormal peripartum or postpartum bleeding observed and she delivered a

healthy baby vaginally at 40 weeks. Four weeks post partum, no abnormal bleeding was reported on 5 mg of prednisolone daily. Consequently, her prednisolone was reduced further to 2.5 mg on alternate days. Her platelet count was $126 \times 10^9/L$ and she remains under 4 weekly review at the Haematology Clinic.

DISCUSSION

Immune thrombocytopenic purpura, previously referred to as ITP, is an auto-immune disorder characterised by autoantibody-induced platelet destruction and reduced platelet production leading to a low peripheral blood platelet count. It has a female predilection. The International Working Group has defined thrombocytopenia as a platelet count $<100 \times 10^9/L$ and it is observed in only 1% of pregnant women. Thrombocytopenia is second to anaemia as the most common haematological abnormality encountered during pregnancy. Pregnancy is associated with a physiological decrease in the platelet count, which mainly occurs in the third trimester and is known as gestational thrombocytopenia. It accounts for 75% of cases during pregnancy and is typically characterised by a platelet count $>70 \times 10^9/L$. The platelet count returns to normal within 6 weeks of delivery. Reese *et al* showed that among the women who had uncomplicated pregnancies, the decline in platelet counts began in the first trimester and continued throughout pregnancy, with the nadir occurring at the time of delivery when 9.9% of the women had platelet counts $<150\,000/mm^3$.^{3 4} The mechanism remains unknown, but haemodilution has been suggested as well as the increase in spleen size that occurs in pregnancy. Acute thrombocytopenic purpura is most commonly seen in young children, with a sudden onset, following a viral illness, vaccination or an insect bite. Only 15%–30% develop the chronic form.

Patients may complain of easy bruising, epistaxis, menorrhagia or bloody stools. Haematuria and gastrointestinal bleeding may also occur. Although rare, an intracranial haemorrhage may occur. Oral manifestations include petechiae, ecchymosis or haematomas. Spontaneous bleeding rarely occurs until platelet numbers fall below $30 \times 10^6/L$ as in our case. Many haematological conditions may present with oral manifestations like ITP, for example, aplastic anaemia, hyperglobulinaemia and Von Willebrand disease.⁴ Drug-induced thrombocytopenia can also occur. Secondary ITP includes isolated thrombocytopenia secondary to some infections such as HIV, hepatitis or *Helicobacter pylori* and autoimmune disorders such as systemic lupus erythematosus. Leukaemia, aplastic anaemia, haemolytic uraemic syndrome and congenital thrombocytopenia should be considered in the differential diagnosis.

The basic evaluation of thrombocytopenia in pregnancy includes a complete blood count, reticulocyte count, a peripheral blood smear, liver function tests and a viral screen for HIV and hepatitis. If clinically indicated, other tests to consider include antiphospholipid antibodies, antinuclear antibodies, thyroid function tests, DIC testing (prothrombin time, partial thromboplastin time, fibrinogen and fibrin split products) and the Coombs test. A bone marrow biopsy would show an increased number of immature megakaryocytes. The foetus and neonate may also develop thrombocytopenia due to the placental passage of maternal IgG. It is diagnosed and managed post partum. Foetal scalp blood sampling or percutaneous umbilical blood sampling is not advised. Table 2 describes the therapeutic options for the management of ITP during pregnancy.⁵

Women with no bleeding manifestations and a platelet count $>30 \times 10^9/L$ do not require any treatment until 36 weeks gestation or sooner if delivery is imminent. If platelet counts

Table 1 Haematological investigations confirmed thrombocytopenia

Complete blood count

WCC $7.50 \times 10^9/L$

Differential count

Neutrophils 4.19%

Lymphocytes 0.63%

Haemoglobin 139 g/L

MCV 97.8 fL

Renal

Sodium 137 mmol/L

Potassium 4.3 mmol/L

Urea 6.1 mmol/L

Creatinine 110 $\mu\text{mol/L}$

Liver function

ALT 23 IU/L

Globulins 2.65 g/dL

Bilirubin 4 $\mu\text{mol/L}$

Total protein 6 g/L

CRP 2 mg/L

Clotting

INR 1.0

APTT 30 s

PT 11 s

Fibrinogen 200 mg/dL

Platelets $2 \times 10^9/L$

ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; CRP, C reactive protein; MCV, mean corpuscular volume; PT, prothrombin time; WCC, white cell count.

Table 2 The therapeutic options for the management during pregnancy

First line therapy	Oral corticosteroids: prednisone Starting dose: 0.25–0.5 mg/kg daily Initial response: 2–14 days Intravenous immunoglobulin (intravenous Ig) Starting dose: 1 g/kg Initial response
Second line therapy (for refractory ITP)	Combined corticosteroids and intravenous Ig Splenectomy (2nd trimester)

are $<30 \times 10^9/L$, first-line therapy is with oral corticosteroids or intravenous immunoglobulin, which has low toxicity. Steroids may exacerbate gestational diabetes and increase the incidence of pregnancy-induced hypertension.⁶ High-dose methylprednisolone can be used in individuals non-responsive to conventional dose prednisolone. Current recommendations aim for a platelet count of $>50 \times 10^9/L$ prior to labour to minimise the risk of maternal haemorrhage during childbirth, regardless of the route of delivery.⁷ Caesarean section should be performed for obstetric indications only.⁸ Women with ITP pose an increased risk of venous thromboembolism and some form of postpartum thromboprophylaxis should be considered.⁹ Sun performed a retrospective study of 235 pregnancies in 195 women with ITP exploring the effects of intravenous Ig and corticosteroids on pregnancy outcomes.¹⁰ There was no difference in maternal platelet counts at delivery between both groups. Response to treatment was observed in approximately 40% of patients treated with either intravenous Ig or corticosteroids. A trend toward fewer pregnancies in the corticosteroid group requiring peripartum transfusion of any blood product was also observed. Scully *et al* performed a prospective study of 47 thrombotic thrombocytopenic purpura (TTP) cases from the UK TTP registry with clinical and laboratory data from the largest cohort of pregnancy-associated TTP and described management through pregnancy, averting foetal loss and maternal complications.¹¹ The majority of acute cases were acquired, auto-antibody mediated, characterised by low ADAMTS13 activity [$<10\%$] and the presence of anti-ADAMTS13 IgG antibodies. A small proportion of TTP cases were due to congenital disease. Pregnancy may be the initial, delayed, presentation of congenital disease and there is a risk of relapse during subsequent pregnancies. Care performed a prospective national cohort study of pregnant women with severe thrombocytopenia (platelets $<50 \times 10^9/L$).¹² This study showed that current UK management of severe ITP in pregnancy results in an exceptionally low morbidity and mortality for the neonate. Mothers with ITP remain at increased risk of severe postpartum haemorrhage (21%) and should be delivered at units that have the capacity to manage this complication.

There is a deficit of cases reported in the dental literature with Mehmet reporting the first case of ITP in a 48-year-old woman presenting with spontaneous gingival haemorrhage to her dentist in 2014.¹³ Following minor oral surgical procedures, adequate haemostasis should be achieved with primary mucosal coverage, the use of absorbable gelatine sponges or bone wax. The risk of gingival bleeding is also higher in the presence of plaque-induced gingival inflammation; therefore, optimal oral hygiene in these patients is vital.¹⁴ In pregnancy, hormonal changes with elevated levels of systemic oestradiol and progesterone can significantly potentiate the effects of local irritants on gingival connective tissue. The first cases of exaggerated gingival responses during pregnancy were described by Eiselt (1840) and Pinard (1877).¹⁵ Pregnancy gingivitis is defined as a 'gingival disease induced by plaque and modified

by systemic factors'.¹⁶ It is characterised by red gingiva that easily bleeds, an enlargement of the gingival margin and by hyperplasia of the interdental papilla.¹⁶ Histologically, it is an unspecific, proliferative, vascular inflammation with an extensive cellular inflammatory infiltrate. The response of the periodontium to pregnancy is multifactorial. Gingivitis in pregnancy is caused by bacterial plaque. As pregnancy progresses, a more anaerobic flora with *Prevotella intermedia*, *Bacteroides intermedius* and *Porphyromonas gingivalis* predominates.¹⁷ Oedematous, hyperplastic and erythematous gingiva may develop. Due to the hormonal variations, a pyogenic granuloma, manifesting as a painless, pedunculated, haemorrhagic or ulcerated lesion often appears during the second or third month of pregnancy. However, there is not any specific type of periodontitis related to pregnancy.

This article highlights the need for awareness among dentists and physicians to refer a patient appropriately when there is no explained cause of persistent gingival bleeding.

Patients may present with oral manifestations of systemic disease. A haematologist can determine the aetiology, advise in the management of thrombocytopenia and help estimate the risk to mother and foetus. A diagnostic approach to investigating thrombocytopenia in pregnancy is required together with antenatal, anaesthetic and perinatal management issues for mother and baby. In women with platelet counts $<100\,000/mm^3$ who do not have pre-eclampsia or a pre-existing disorder associated with thrombocytopenia, a cause other than pregnancy or its complications should be considered. Careful diagnosis, monitoring and treatment in congenital and acquired TTP have assisted in excellent pregnancy outcomes.

Learning points

- About 75% of cases are due to gestational thrombocytopenia, which is benign and poses no maternal or foetal risk; 15%–20% of cases are secondary to hypertensive disorders; 3%–4% are due to an immune process and the remaining 1%–2% are made up of rare constitutional thrombocytopenias, infections and malignancies.
- A multidisciplinary approach is essential in the management of maternal idiopathic thrombocytopenic purpura. Adequate dental plaque control techniques to prevent inflammation, potential bleeding and infection in the patient should be emphasised.

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Reminder of important clinical lesson

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