CASE REPORT

May-Hegglin Anomaly: A Rare Cause of Thrombocytopenia and Potentially Overlooked

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ABSTRACT

May-Hegglin Anomaly is a rare congenital platelet disorder with macrothrombocytopenia and leucocytes inclusions. We report a 25-year-old primigravida Malay woman with asymptomatic severe thrombocytopenia and strong family history of thrombocytopenia. Blood film showed the presence of many giant platelets with inclusion bodies in the neutrophils. Initially, she was treated as immune-mediated thrombocytopenia. However, the platelet count was not responding to corticosteroid therapy. This case report highlighted the rare cause of thrombocytopenia due to congenital cause in a young Malay ethnic primigravida woman who was asymptomatic for bleeding manifestation. This case also emphasized the importance of detailed family history and a proper evaluation of peripheral blood smear as a key for establishing the diagnosis as well as multidisciplinary approaches in treating the patient. Hence, this rare cause of thrombocytopenia would not be overlooked.
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INTRODUCTION

Thrombocytopenia is a common problem in pregnancy and is usually due to acquired causes, mainly gestational and immune-mediated (1). Congenital thrombocytopenia is very rare, especially in the Malaysian population. The diagnosis of congenital thrombocytopenia may be overlooked if the family history and peripheral blood smear morphology are not adequately evaluated.

May-Hegglin Anomaly (MHA) is a group of an autosomal dominant disease characterized by giant platelets with thrombocytopenia and basophilic inclusions (Döhle's bodies) within granulocytes. MHA is due to *MYH9* gene mutation. *MYH9* gene is a gene that encodes for the non-muscle myosin heavy chain IIA (NMMHC-IIA). Besides MHA, *MYH9* gene mutation was also found in Sebastian platelet syndrome (SPS), Fechtner syndrome (FS), and Epstein syndrome (EPS). These disorders are autosomal dominant genetic disorders. All of these are manifested by macrothrombocytopenia as well as leucocyte inclusions (2). The diagnosis of MHA is suspected when there is a presence of characteristic blood film findings with a strong history of thrombocytopenia in her family.

CASE REPORT

A 25-year-old Malay primigravida at 39 weeks of gestation presented with signs and symptoms of labour. Since the first trimester, she was noted to have severe thrombocytopenia and had an uneventful regular antenatal checkup at a primary health care centre. There was no history of bleeding manifestation throughout the pregnancy. Physical examination was unremarkable with no bruises or petechiae. She had a strong family history of severe thrombocytopenia, but no proper diagnosis had been made (Figure 1). Peripheral blood count showed haemoglobin of 11 g/dL, white blood cells of 8 x 10^9/L and platelet count of 3 x 10^9/L. Her peripheral blood smear showed many giant platelets with normal granules and neutrophils with Döhle's bodies (Figure 2). This blood film was also not examined using electron microscope due to unavailability in our laboratory.

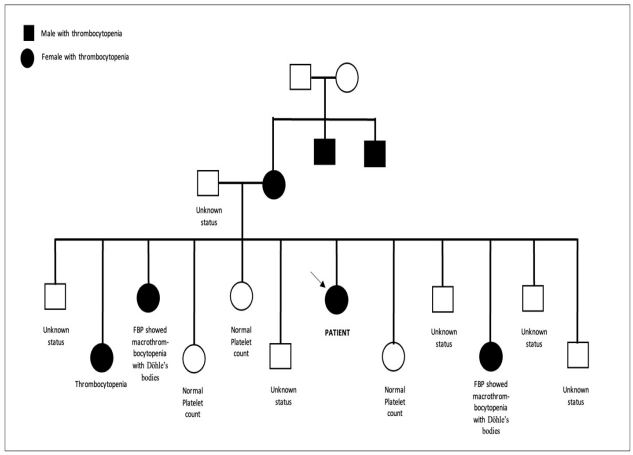

Figure 1: Family pedigree. Her mother and three of her sisters noted to have severe thrombocytopenia during pregnancy. Two of her sister had similar FBP findings as patient which were macrothrombocytopenia and Döhle's bodies.

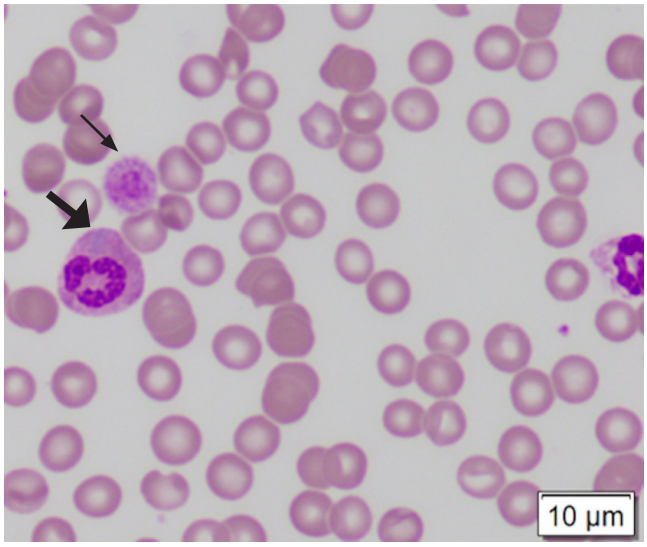

Figure 2 : Peripheral blood film showed giant platelet (small arrow) and Döhle's bodies (large arrow) in the neutrophils. (Stain: Wright Giemsa Stain, under 40x magnification).

The immature platelet fraction was very high (72.7%). Coagulation screening tests were normal. C-reactive protein was negative. The molecular study for the *MYH9* gene mutation was not performed because it is not available in Malaysia. At first, the patient was suspected of having immune-mediated thrombocytopenia and she was started on intravenous methylprednisolone for three days and platelet count increased to 43 x 10^9/L as shown in Table I. Based on clinical manifestation and laboratory findings, it is most likely May-Hegglin anomaly. The patient underwent an emergency caesarean-section due to poor progress and four units of random platelet concentrates were transfused as prophylaxis before the procedure. There was no excessive bleeding noted during and after the caesarean section. She was discharged well with a platelet of 19 x 10^9/L. The platelet count was between 10-19 x 10^9/L after 3 weeks postpartum with no significant bleeding.

DISCUSSION

About 75% of thrombocytopenia in pregnancy is due to a benign process of gestational thrombocytopenia and only 1-2% are made up of rare causes of thrombocytopenia (3). For this case, gestational thrombocytopenia (GT) is excluded because in GT, a patient usually presents with mild thrombocytopenia (> 70 x 10^9/L) and it occurs during the third trimester in contrast to this patient who had severe thrombocytopenia and detected since the first trimester of pregnancy. Furthermore, she had a strong family history with a similar presentation and GT was also excluded (1)(3). MHA can also be misdiagnosed as immune-mediated thrombocytopenia (ITP) if a thorough evaluation of peripheral blood smear and detailed bleeding history, including family history are not properly taken.

MHA is a rare autosomal dominant disorder due to *MYH9* gene mutation characterized by neutrophils with abnormal inclusion in the cytoplasm, large platelet and variable degree of thrombocytopenia. It is part of the myosin heavy chain (MHC) single gene defect group, which includes Fechtner syndrome (FS), Sebastian syndrome (SPS) and Epstein syndrome (EPS). These disorders exhibit diverse clinical manisfestations, including bleeding tendency, renal impairment, cataracts or hearing loss. FS usually presents with macrothrombocytopenia, inclusion bodies, nephritis, hearing loss and cataract. In contrast, EPS may have all except no inclusion bodies or cataract. SPS may have all the features except for nephritis. In order to differentiate MHA from ITP, it is important to note that MHA does not respond to intravenous immunoglobulin. Platelet counts in MHA patients may not significantly increase, although a mild transient increase in platelet count between 20-30 x 10^9/L may occur if high dose corticosteroid is added. In comparison with immune causes, MHA did not have specific autoantibodies whereas these autoantibodies are detectable in about 50% of ITP patients (2).

In peripheral smear of MHA, the platelet count ranges from 40–80 x 10^9/L to normal values. Cytoplasmic inclusions resembling Döhle's bodies are seen in neutrophils which identical in this case and it can also be seen in monocytes, eosinophils and basophils. The inclusions appear pale blue, large and spindle-shaped. The inclusion bodies are not seen in platelets. Large and giant forms of platelets are more uniform than ITP, which are irregular in size with few giant platelets present. In some patients, the presence of macro thrombocytes can often lead to underestimation of platelet count by automated

Table I : Summary of serial of full blood count on daily monitoring

Day of hospitalization (Day)	1	2	3	4	5	6	7
Platelet count (x 10^9/L)	3	6	15	43	22	17	19
Hemoglobin (g/dL)	11.7	11.1	11.9	9.9	8.8	8.4	8.3
White blood cell count (x 10^9/L)	8.01	8.16	8.88	14.9	13.4	13.9	14
Name of medication or blood product therapy received	Nil	IV methylprednisolone 500mg OD	IV methylprednisolone 500mg OD	IV methylpredniso-lone 500mg OD 4 units of random platelets		Nil	Nil

IV= intravenous, OD= once daily, FBC=full blood count

analyzers. In such cases, the platelet count can be better estimated based on a careful morphologic evaluation of the peripheral blood smear (4). Electron microscopy examination will show platelets with abnormal lentiform shape (5).

One systematic review of MHA during pregnancy involved 75 pregnancies, showed that 11 out of 40 women had incidental thrombocytopenia during the antenatal check-up and five women were misdiagnosed as ITP, including three who underwent splenectomy for resistant ITP. Postpartum haemorrhage was reported in four pregnancies of which one had packed cell transfusion, one had platelet and cryoprecipitate transfusion and another two were managed conservatively (5). This showed that only small percentage presented with severe bleeding. To our knowledge, there was a case reported by Chin H.H et al.,2017 which highlighted the MHA in Chinese family in East Malaysia.

Bleeding manifestation in MHA is usually mild and depends on the platelet count. As for this case, four units of platelets were given before caesarean section and no excessive bleeding was noted during and after the delivery. However, MHA may present challenges during pregnancy and be associated with adverse maternal outcome because of bleeding complications. Joint management by haematologists and obstetrician is mandatory to plan an appropriate management of delivery. Genetic counselling should include a discussion of the inheritance pattern and investigations required for the patient and the baby.

CONCLUSION

MHA is frequently misdiagnosed as immune thrombocytopenia or gestational thrombocytopenia if it occurs during pregnancy. A proper assessment of peripheral blood smear with the presence of the triad (thrombocytopenia, giant platelets and Döhle's bodies inclusions) and family history is very important for the correct diagnosis as the detection of *MYH9* mutation is limited in certain countries.

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