

VITAMIN K DEFICIENCY BLEEDING: A CASE SERIES

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ABSTRACT

Vitamin K deficiency bleeding (formerly known as hemorrhagic disease of newborn) is a rare condition where infant developed a bleeding disorder due to inadequate level of vitamin K in their body. This condition is rarely encountered nowadays given the fact that prophylactic vitamin K would be given to all the newborns in all hospital deliveries of Malaysia. According to the Malaysia guideline, vitamin K injection is required to be administered at birth. However, there are still occurrence of such cases especially in the rural area of East Malaysia where unregistered, home delivery is common. On top of that, other factors such as geography, social and financial status also play a role in contributing to the occurrence. Vitamin K deficiency bleeding in infant can be divided into early, classical, and late depending on the time of presentation. Medical officers working in this area of the country should be aware of this condition at the back of their mind if a bleeding infant is brought to them. Education should also be given to parents-to-be regarding the importance of hospital delivery and vitamin K injection to prevent this disastrous condition and hence the neonatal mortality rate in the country.

Keywords: *Vitamin K, infant, bleeding*

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INTRODUCTION

Vitamin K deficiency bleeding, previously known as hemorrhagic disease of newborn is a condition caused by deficiency in vitamin K in the newborn baby. The common features are usually unexpected bleeding from multiple sites and it can be from the skin, umbilicus, gastrointestinal tract and sometimes intracranial hemorrhage. This condition can usually be treated by administration of vitamin K parenterally, which also confirms the disease. A newborn has a low level of vitamin K in the body at birth as compared to the mother because vitamin K does not cross the placental barrier well. Hence, the source of vitamin K is usually from the milk and prophylactic injection of vitamin K given at birth. Breast milk has a lower level of vitamin K as compared to formula milk. Nevertheless, the level of vitamin K in this 2 group will reach adult values by the age of six weeks. It is very rare nowadays due to prophylactic vitamin K injection to all the hospital-delivered newborn. However, we still see these cases especially in the rural area of the country in East Malaysia, and we thought this could be multifactorial. Here, we present a case series of hemorrhagic disease of newborn that we encountered in the emergency department of our hospital for year 2015.

CASE 1

A 13-day-old baby boy, non-Malaysian, unbooked pregnancy, delivered at home, was brought in by his mother, with active bleeding from the umbilicus half an hour prior to arrival to hospital. Otherwise, child does not have any other symptoms. He breastfed well, no fever, normal bowel habit and urinating normally.

Upon examination, child was active on handling, with good pulse volume and capillary refill time less than 2 seconds. His BP was 84/49, heart rate 166 bpm, random blood sugar 4.2 mmol/L, and afebrile. He weighed 3.5 kg. His abdomen was soft with no organomegaly detected. However, his umbilical stump has

already detached and there was active bleeding seen from there.

IM vitamin K 1mg was given immediately and intravenous line was set up and blood investigations taken. His haemoglobin level was 13.5 g/dL, platelet was $721 \times 10^3 /\mu\text{L}$. Child was referred to paediatric team and admission was granted. However, parents took risk to bring back the child because of financial problem and they worry that they are unable to pay for the admission.

CASE 2

A 9-day-old baby girl who was delivered at home, unbooked pregnancy, not immunized, non-Malaysian brought to emergency department by the mother complaining of bleeding from the umbilical stump and gum about one hour prior to arrival to emergency department. Child was delivered at home by midwife, and cord was cut under non-sterile technique. Subsequently, child able to breastfeed well and active at home. She had no fever, no URTI symptoms and normal bowel habit. Mother was a 17-year-old, para 2 lady. She has never had any screening or booking done during her current and previous pregnancies. After the child was delivered, no vaccination was given and child was never brought to seek any medical care.

Upon arrival, child looks lethargic, tachypnoeic, pale, capillary refill time more than 2 seconds with cold peripheries. Blood pressure was 40/20mmHg, heart rate was 136 bpm, and respiratory rate 56 bpm. There was active bleeding seen from the umbilical stump area. IM vitamin K 1 mg was immediately given. We face difficulty in setting up the intravenous line, most probably due to hypovolemia. Multiple attempts done and subsequently we proceed with intra-osseous line which also failed. Paediatric team was then called up to assist us in the intravenous line setting.

Child was then intubated by the paediatric team in view of respiratory distress.

She was then given 40ml/kg of normal saline bolus while awaiting for the crossmatch blood. However, she developed bradycardia and CPR was commenced for 8 minutes and patient revived. Blood transfusion was started after the crossmatch blood obtained and completed within 20 minutes. After transfusion, child became bradycardic again and CPR commenced for the second time. Child was pronounced death after 20 minutes of no ROSC. Her blood result showed haemoglobin level of 4.49 g/dL and platelet $26.1 \times 10^3/\mu\text{L}$.

CASE 3

A day 1 and 12 hours of life baby girl who was delivered at home, non-Malaysian, not immunized, booked pregnancy, was brought in to emergency department by her aunt, referred from a private GP for umbilical cord infection. Further history from the aunt revealed that the child has been having bleeding from the umbilicus started from last night and it has been persistent until the day of presentation. No other bleeding elsewhere was seen. Child was delivered at home by a midwife and cord was cut under non-sterile technique. We were not able to get other history as the mother did not come together with the baby and all the history was obtained from the aunt.

Upon arrival, patient looks active, not tachypnoeic, good pulse volume. Heart rate was 131 bpm, afebrile, respiratory rate 30, and saturation was 95%. Bleeding was seen from umbilicus. Child was pink. There was no organomegaly and no murmur could be appreciated. The lungs were clear with equal breath sounds. IV line was set up and blood taken for investigations. A diagnosis of hemorrhagic disease of newborn was made. IM vitamin K was given. Patient was put on maintenance drip and referred to paediatric team. We were unable to do a cross-matching of blood for transfusion purpose because the patient's mother were not there for blood taking.

Patient's blood result revealed a haemoglobin level of 23.7 g/dL, haematocrit 72.1

and platelet $242 \times 10^3/\mu\text{L}$. We were unsure of why is this child polycythaemic, but it was presumed that most probably it is due to delayed cord cut during delivery. After admission, a partial exchange transfusion was done for the polycythaemia and her haemoglobin came down to 21.8 g/dL. She was started on IV ampicillin and gentamicin and transfuse with fresh frozen plasma. On day 2 of admission, her serum bilirubin was taken and it was 317. She was then put under phototherapy.

She was discharged well after completed 5 days of antibiotic in ward. Blood culture was negative.

CASE 4

A day 7 of life baby boy, home delivery, non-Malaysian, not immunized, was brought in by mother referred from private GP for umbilical bleeding on the day of presentation, sudden onset. Baby was delivered at home by midwife and cord was cut under non-sterile method. After delivery, child able to breastfeed, active, no fever, no rapid breathing and generally well until the day of presentation.

Upon arrival, BP 96/40 mmHg, heart rate 142bpm, respiratory rate 58 bpm, saturation 99% on air. He was active, crying, moving all 4 limbs and pink. Pulse volume was good and CRT less than 2 seconds. IM vitamin K 1 mg was immediately given to the child and maintenance drip was started. Blood investigations showed haemoglobin level of 20g /dL, haematocrit 62.7 and platelet $204 \times 10^3/\mu\text{L}$. Patient was referred for admission.

In ward, patient was started on IV ampicillin and gentamicin and also IV vitamin K for 3 days. No blood products were transfused in view that the bleeding has already stopped. Patient also developed neonatal jaundice during admission secondary to polycythaemia and was under phototherapy. He was discharged well after 4 days and the blood culture came back negative.

DISCUSSION

Abnormal bleeding in newborn can be due to multiple causes. The main cause is vitamin K deficiency. Previously known as hemorrhagic disease of newborn, vitamin K deficiency bleeding (VKDB) is a condition in which a newborn experience unexpected bleeding due to deficiency of vitamin K in their body. According

to American Academy of Paediatric in 2003, a single, intramuscular dose of vitamin K 0.5 - 1mg should be given to all newborns to prevent such condition from happening¹.

This condition can be classified by 3 distinct periods of time after birth, namely the early-onset, late-onset and classic².

VKDB syndrome	Time of presentation	Common bleeding sites	Etiological factors
Early	First 24 hours	Scalp, subperiosteal or skin, intracranial, intrathoracic, intra-abdominal	Maternal drugs (e.g. warfarin, anticonvulsants)
Classical	Days 1-7	Gastrointestinal, umbilical, skin nose, circumcision	Mainly idiopathic, breast feeding (low-milk intakes)
Late	Days 8 onwards (peak 3-8 weeks)	Intracranial, skin, gastrointestinal	Idiopathic or secondary, breast feeding, undiagnosed cholestasis often present. Secondary cases from malabsorption due to underlying disease (e.g. biliary atresia, α -1 antitrypsin deficiency, cystic fibrosis) or to chronic diarrhea. Antibiotic therapy sometimes implicated.

(adapted from Shearer MJ, 2009)

Early VKDB usually happens when the mothers take anticonvulsant or antituberculosis medication. The mechanism of how this could cause early VKDB is unclear. However, prevention can be done by administering vitamin K to the mother during their last 2-4 weeks of pregnancy. If this is not done, vitamin K supplementation given after the birth might be too late to prevent this condition.

Classic VKDB commonly occurs in the umbilicus, GI tract (ie, melena), skin, nose, surgical sites (ie, circumcision), and, uncommonly, in the brain³. Late onset vitamin K deficiency bleeding occurs between age 2-12

weeks, but can be seen up to 6 months after birth, and more commonly seen in exclusively-breastfed infants⁴. Intestinal malabsorption defects (cholestatic jaundice, cystic fibrosis, α -1 antitrypsin deficiency etc.) are also the causes of late VKDB⁵. In this case series, there are two cases that fall in the category of classic vitamin K deficiency and another two fall in the category of late-onset vitamin K deficiency.

According to IJland et al, diagnosis of VKDB can be made when the prothrombin assay results were grossly abnormal compared with the standards for age: international normalized ratio (INR) >4 control value, prothrombin time (PT) $\geq$

4 control value and at least one of the following was present⁴:

1. Normal platelet count or raised and normal fibrinogen
2. Prothrombin assay returned to normal after vitamin K administration
3. Concentration of proteins induced by vitamin K absence (PIVKA) exceeded normal controls

According to Malaysia Ministry of Health report on routine neonatal vitamin K administration at birth, the incidence of classical VKDB has been reported to vary between 0.4% to 1.7% in the absence of vitamin K prophylaxis. When routine administration of parenteral vitamin K was introduced to newborns, VKDB cases ceased. However, we still encounter few cases in Sandakan. All the 4 cases presented here are all delivered at home. Hence, there is a failure in administering vitamin K, when the child is delivered by non-medical personnel. Also, all the 4 cases involved non-Malaysian and there are few reasons that can be proposed by such observation.

Firstly, geographical factor. Sandakan is situated at the east coast of Sabah facing Sulu Sea and this form an easy access for people from the neighbouring countries, namely Philippines and Indonesia. These migrants would usually be charged higher if they present themselves to seek for medical attention in hospital in Malaysia and it creates a financial burden to them. Some of them are illegal immigrants with no proper documents and no legal job, and some are even unemployed. This further contributes to their financial instability. Hence, they usually opt for home delivery assisted by midwife or other family members who are not trained to perform such procedure. When a child is delivered at home and no medical personnel were informed regarding the delivery, it leads to prophylaxis failure.

Secondly, transport problem. Majority of immigrants work in estate and stay there with the

whole family. Those without legal documents will stay in the inner part, mainly to prevent themselves from getting caught by the authority. This become a problem when there is emergency such as delivery where it will take them a long duration to come to hospital, provided if they have transport at that time. However, most of these people are poor and could not afford own transport and hence the delay in reaching hospital. All these factors contribute to these people choosing home delivery than hospital delivery.

Some parents were interviewed and asked regarding the reason of not bringing their child for vaccination after delivery and their answer is related to the well-being of previous children. When there is an elder child who was also delivered at home without any complication and is now healthy, this would strengthen the parents' belief of children do not need vaccination after birth. As a result, parents do not know the importance of vitamin K until their child starts to bleed abnormally.

Malaysia guidelines recommends an intramuscular dose of vitamin K 1mg to be given to all newborns at birth as prophylaxis to prevent VKDB. However, it is also found that there are other countries choose oral vitamin K than parenteral vitamin K. For example, in Netherlands, a daily low oral dose of vitamin K₁ after an initial dose of 1mg vitamin K₁ directly after birth for exclusively breastfed infants seemed to be as effective as parenteral vitamin K₁ prophylaxis⁴.

In 1990, a study conducted by Golding and colleagues reported an approximate doubling of the risk of leukaemia in children who had been given intramuscular vitamin K at birth but no increased risk when given by the oral route⁶. However, in 1999, a working group of the WHO International Agency for Research on Cancer (IARC) concluded that there was "inadequate evidence in humans and experimental animals for the carcinogenicity of vitamin K substances". In the USA, a position paper concluded that the

confirmed benefits of vitamin K far outweigh the hypothetical association with childhood cancer⁷ (Ross et al, 2000). The American Academy of Pediatrics also issued a policy statement discounting any association with cancer and reaffirmed that 0.5 or 1 mg of phyloquinone should be given as a single IM injection.

This case series has some limitations. First, cases included are those who presented to emergency department and this does not include patient presented to private or public clinic or directly to the ward. Furthermore, there are district hospitals in Sandakan area which also encounter similar case. There are also parents who deliver their child at home and never bring to hospital even the child was bleeding. Hence, the cases presented here do not reflect all cases in Sandakan or Sabah state. It is believed that the cases encountered here are only the tip of iceberg, and there are more cases that went unreported, especially when it involves non-Malaysian.

Second, there are only 4 cases in the year 2015 that presented to emergency department which is a small sample size. If more cases could be obtained, further analysis of patient's socio-economic background and other details could be performed. Third, the diagnosis of vitamin K deficiency bleed was not really made in the above cases. Reason being no prothrombin assay was repeated after the administration of vitamin K and there are also coagulation study which was initially sent was being rejected due to improper collection of sample, for example, inadequate sample, clotted specimen or wrong collecting tube. Fourth, there are two cases of late vitamin K deficiency bleeding in this case series but whether they belong to idiopathic or secondary

cause is not known. This is because no liver function test was taken and hence there was no evidence to prove the presence of cholestasis. Another problem encountered is no machine is available in our hospital setting to measure the concentration of PIVKA and hence the third criteria could not be established.

We suggest that a larger scale observational study to be carried out in the future with more sample size which involve a bigger area of Sabah state so that more analysis could be carried out with regards to their socio-economic background in relation to vitamin K deficiency bleeding.

CONCLUSION

In conclusion, Vitamin K deficiency bleeding in newborn can be prevented by simply giving vitamin K to the newborn, parenteral or enteral. This can prevent the disastrous and unexpected abnormal bleeding. Indirectly, it can reduce the neonatal mortality rate and reflect a better health care system in our country. Adequate education need to be given to the parents-to-be so that they understand the importance of vitamin K in the prevention of VKDB and when to bring the child to hospital if there is an abnormal bleeding detected. Medical officers working in this part of the country also need to be well aware of this condition which is no longer prevalent in West Malaysia, so that appropriate treatment can be given.

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