CASE REPORT

Baby boy blue … and mommy too! A rare case of methaemoglobinaemia presenting simultaneously in a mother-neonate pair

Siew Cheng Foong, MRCP (UK)[1], Yee Chern Hwang, MRCP(UK)[2], Wai Cheng Foong, MRCPCH (UK)[1], May Loong Tan, MRCPCH (UK)[1]

[1]RCSI & UCD Malaysia Campus, Malaysia, [2]Island Hospital, Malaysia

SUMMARY

Methaemoglobinaemia occurs when there is >1% methaemoglobin in erythrocytes. In an infant, they can present either congenitally or in an acquired form. We present a rare case of methaemoglobinaemia presenting simultaneously in a mother and infant pair. The mother and infant were discharged well on Day-4 post-delivery with both mother and baby recording oxygen saturation levels of 100%. On Day-7, during a routine clinic visit, they were incidentally found to be centrally cyanosed. There were no other abnormalities. On investigation, the methaemoglobin levels were elevated in the infant (23.9%) and mother (14.3%). Treatment with ascorbic acid normalised mother's methaemoglobin levels; but baby's levels remained high until the administration of oral methylene blue. Both baby and mother remained well and pink at last follow-up at 2 years 8 months of age. This case illustrates difficulties in ascertaining the cause of methaemoglobinaemia. Post-delivery, the mother-neonate pair were pink, and their haemoglobin electrophoresis were normal, hence it was unlikely to be congenital methaemoglobinaemia. The team could not identify any triggering factors for acquired methaemoglobinaemia. There was also the uncertainty of the necessity to treat the baby. This is because treatment is not without harmful effects and despite the high methaemoglobin levels, the infant was otherwise well. Only a single published paper recommended that high methaemoglobin levels must be treated, and the recommendation was not supported by evidence. Lessons learnt from our case are that neonates with methaemoglobinaemia can be safely treated with oral methylene blue, but more research is needed on the benefit-risk profile of treatment.

INTRODUCTION

While case reports of methaemoglobinaemia is not uncommon, there are no reports of methaemoglobinaemia presenting simultaneously in a previously well mother and her newborn baby boy a few days after delivery. We present this case to illustrate the difficulties in ascertaining the cause of methaemoglobinaemia in both mother and baby; and also the management dilemma in this otherwise well newborn.

Methaemoglobinaemia occurs when erythrocytes contain >1% methaemoglobin (metHb). This increases oxygen affinity of haemoglobin and shifts the oxygen dissociation curve to the left;[1] which reduces oxygen availability to tissues resulting in tissue hypoxia.[2]

Congenital methaemoglobinaemia is rare. It is commonly due to cytochrome-b5-reductase deficiency (Type I methaemoglobinaemia), sometimes due to Haemoglobin M disease and rarely due to cytochrome-b5 deficiency (Type II methaemoglobinaemia). Both Type I and Type II methaemoglobinaemia are autosomal recessive while Haemoglobin M disease is autosomal dominant. Type 1 methaemoglobinaemia is generally asymptomatic but Type II methaemoglobinaemia is associated with early infancy death or severe neurological impairment later in life.[3]

Acquired methaemoglobinaemia is more common but often under-reported.[4] Anaesthetic agents such as lidocaine and prilocaine (in topical creams) and benzocaine (in topical sprays) are the known metHb inducers.[1] These agents oxidize haemoglobin to metHb and are themselves metabolised into reactive metabolites that further oxidize haemoglobin to metHb. In individuals with high levels of gut coliforms, food and water with high nitrate levels can cause methaemoglobinaemia because coliforms convert nitrate to nitrite; and nitrite is a potent metHb inducer. Symptoms of methaemoglobinaemia range from mild cyanosis to life-threatening events such as renal failure, shock, seizures and death.[1]

Ascorbic acid and methylene blue are commonly used treatment modalities.[5] Ascorbic acid scavenges free radicals, thus decreases metHb formation[6] while methylene blue reduces metHb back to haemoglobin. Ascorbic acid may take more than 24 hours before its effect is seen, and several doses may be needed. There are concerns about kidney stone formation if high doses are used.[7] Conversely, methylene blue shows maximal effect within 30 minutes. However, it can cause hypotension, a paradoxical rise in metHb and in neonates it can also cause haemolytic anaemia and respiratory distress.[8]

CASE REPORT

A primigravida mother with uncontrolled hypertension, underwent emergency lower segment caesarean section at 37 weeks gestation. Bupivacaine was given for spinal anaesthesia and magnesium sulphate for her hypertension.

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Corresponding Author: Siew Cheng Foong
Email: scfoong@rcsiucd.edu.my

Fig. 1: Pink at birth (left), cyanosed on Day 7 (top right), chocolate- brown coloured arterial blood (bottom right).

The delivery was uneventful. The baby boy weighed 2.5kg at birth and was pink. Throughout the surgery and post-operative period, the pulse oximetry saturation of the mother was 100% breathing room air.

The baby was exclusively breastfed from birth. While still in the hospital on Day-3 of life, phototherapy was started for neonatal jaundice. He did not have glucose-6-phosphate dehydrogenase (G6PD) deficiency. Before discharge on Day-5, his pulse oximetry saturation (SpO_2) breathing room air was 97%. On Day-7 of life, the baby's parents brought him to the paediatric clinic to review his bilirubin level. The paediatrician attending to the baby noticed that the mother and infant were centrally cyanosed. The mother and father had not realised this until it was pointed out by the attending paediatrician. The mother and baby's SpO_2 on air were 85% and 88% respectively and did not improve with a trial of supplemental oxygen. However, both mother and infant were otherwise well and did not look or feel sick.

Physical examination of mother and infant did not reveal any abnormal findings apart from the central cyanosis. The infant's echocardiogram and chest X-ray were also normal. Methaemoglobinaemia was suspected when the infant's arterial blood was found to be chocolate brown in colour and his arterial blood gasses were normal (pH 7.43, pO_2 83mmHg, pCO_2 36mmHg, HCO_2 23.6mmol/L) despite the low SpO_2. Further investigation confirmed elevated metHb levels in both mother (14.3%) and baby (23.9%). Haemoglobin electrophoresis of both mother and baby excluded Haemoglobin M.

Breastfeeding was temporarily stopped as we explored extensively for methaemoglobinaemia triggering substances, but none were found.

Mother was prescribed one dose of ascorbic acid orally and her metHb levels normalised (1.6%) after three days. The infant received three doses of ascorbic acid orally eight hours apart but metHb levels remained high (24.2%). Methylene blue (0.6mg/kg) was administered via a nasogastric tube and five hours later, metHb levels normalised (3%). Sixteen hours later, it rebound and a second dose (0.8mg/kg) was given. Over the next three days, metHb levels fluctuated between 2.9% and 6.9% before maintaining below 3%. Throughout this period, the infant was clinically well and had resumed breastfeeding four days later.

At six weeks of age, the infant underwent bilateral herniotomy under general anaesthesia uneventfully. His growth and development were normal at his last clinic visit at the age of two years eight months. Neither mother nor baby had recurrence of methaemoglobinaemia.

DISCUSSION

Our case illustrated an unusual simultaneous presentation of metHb in both mother and baby. Determining if this was congenital or acquired methaemoglobinaemia would be useful in the management of the case. Congenital methaemoglobinaemia would require genetic counselling as well as explanation of the long- term prognosis to the parents. On the other hand, acquired methaemoglobinaemia would require advice on avoidance of triggering factors. However, determining the cause proved to be very difficult in this case. We did not manage to test for cytochrome-b5-reductase levels because the parents did not consent for the test to be done. However, congenital methaemoglobinaemia was unlikely because both mother and baby had recorded normal oxygen saturations before discharge from hospital; their haemoglobin electrophoresis results were normal thus excluding Haemoglobin M disease; and there was no family

history of cyanosis. However, we could not be certain that this was acquired methaemoglobinaemia either because we could not identify any possible triggering agent apart from bupivacaine, the spinal anaesthesia administered to the mother before delivery. Bupivacaine has a half-life of three hours,[9] hence there should not be a lag time of seven days before symptoms manifested. Furthermore, its availability in breast milk is low[2] and the trial of breastfeeding cessation did not help improve the baby's condition. Detailed history taken from the mother also did not reveal any other possible sources of triggers. The mother was not on any medication after delivery and was staying in a house with many other people after discharge. None of them developed methaemoglobinaemia hence it was unlikely due to the environment, food or water she had consumed.

Extensive literature search did not come up with evidence on whether or not asymptomatic methaemoglobinaemia should be treated. The only information available was that metHb levels above 25% should be reversed[2] but there was no available research to support this recommendation. We were therefore faced with a dilemma on the justification to offer treatment as the neonate was otherwise not ill and had arterial blood gasses that were within normal limits. As stated earlier, treatment is not without risks. At the same time, we also did not know if there would be health consequences if the metHb levels were not brought down as literature on this was sparse. Therefore, a decision was made to treat the methaemoglobinaemia. Although reports suggested that methylene blue was first line treatment[10] given its faster mode of action, the doctors chose to have a trial with ascorbic acid first because it was thought to be relatively safer compared to methylene blue. However, although ascorbic acid had successfully normalised the mother's metHb levels, it failed to work for the baby. As the parents had been worried about the possible adverse effects with the use of intravenous methylene blue in their otherwise well child, the doctor gave the neonate a trial of oral methylene blue which successfully normalised the metHb level without any adverse effects. A nasogastric tube was used to administer the methylene blue to avoid discoloration to the tongue and the possibility of mucosal burns as per the warning in the medication leaflet.

LESSONS LEARNT

Methaemoglobinaemia can occur simultaneously in both mother and baby. Determining the cause is an important part of the management but it can be difficult. Oral methylene blue was used safely and effectively to reverse methaemoglobinaemia in this neonate. However, there is a lack of evidence to support treatment in asymptomatic patients. Therefore, research is needed to determine the benefit-risk profile of treatment for asymptomatic methaemoglobinaemia.

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