

## Case report

### Acute Haemolysis Precipitating Rhabdomyolysis and Acute Kidney Injury in a Newly Diagnosed G6PD Deficiency: A Case Report

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#### Abstract

Glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common X-linked genetic condition among Malaysians that have largely caused acute intravascular haemolysis. In G6PD deficient children, the phenomenon of rhabdomyolysis and myoglobinuria is a rare complication as muscle has more resistant to undergo acute myolysis. A 22-month-old Malay child was presented with severe anaemia following with ingestion of large amount of fava beans. He then developed into acute kidney injury together with the laboratory findings of intravascular haemolysis, rhabdomyolysis, and the presence of multi-systems bloods derangement. He showed positive response to hyperhydration, haemodialysis and blood transfusions.

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#### Introduction

Glucose-6-Phosphate Dehydrogenase deficiency (G6PD) is an enzymopathy which is commonly diagnosed predominantly in Malay and Chinese ethnics, and has the overall incidence of 3.1% among the Malaysian<sup>1</sup>. There is dearth of case reports regarding the presence of rhabdomyolysis in children following with acute intravascular haemolysis by G6PD deficiency leading to Acute Kidney Injury (AKI)<sup>2,3,4,5</sup>. G6PD works by catalysing the reaction in the pentose phosphate pathway by reducing nicotinamide adenine dinucleotide phosphate (NADPH) and protecting the cells against oxidative stress. In the blood, erythrocytes are susceptible to free radical damage especially in G6PD deficient children, due to lack of mitochondria. Our case report illustrated on the youngest case reported in an undiagnosed G6PD presenting with AKI following haemolysis and rhabdomyolysis episodes.

#### Case

A previously healthy child 22-month-old boy presented to the Emergency Department with a short history of rapid breathing and being unwell. His parents noticed his gradual pallor of his skin colour, yellowish sclera and dark urine. Significantly, he had been eating a large portion of fava beans 2 days prior to the admission. There was no family history of blood disorder and G6PD deficiency. The patient also did not have any history of intermittent pallor or being jaundice in neonatal period. Both parents are non-consanguineous.

Physical examination revealed a pale, lethargic and mildly jaundice boy with body temperature 37.8 °C, heart rate 180 beats/min, respiratory rate 54 breaths/min and blood pressure 90/40 mmHg. He required intubation, boluses of normal saline (40mls/kg) and inotropic support due to the severe decompensated hypovolemic shock. There was liver palpable 4cm below the right subcostal margin.

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Initial venous blood gas showed severe metabolic acidosis with pH 7.09, pCO<sub>2</sub> 20.7mmHg, HCO<sub>3</sub> 7.3 mmol/L, BE -21.8, lactate of 15mmol/L and plasma haemoglobin level of 2.5g/dL. Results of

other laboratory investigations are listed in Table 1. Urinalysis showed the presence of both bilirubin and haemoglobin.

**Table 1:** Blood chemical and enzyme values during admission and hospital course

Day of admission	1	2	3	6	7	8	9	10	16
Haemoglobin, g/dL	2.5	4.7	9.6	9.1	8.2	7.7	10.4	11.8	13.7
Reticulocyte	4.8	4.45	6.21	-	-	-	-	-	-
Total bilirubin, umol/L	134	109	-	13	11	13	15	17	14
Conjugated bilirubin	17	33	-	-	-	-	-	-	-
Lactate dehydrogenase, U/L	2829	2905	13771	2026	-	-	2042	-	-
Uric acid, umol/L	609	1070	1139	864	582	592	571	378	345
Aspartate aminotransferase, U/L	76	190	4086	1074	162	68	71	58	42
Alanine aminotransferase, U/L	18	91	2274	1411	542	243	239	190	165
Creatinine, umol/L	56	66	171	201	244	283	174	134	114
Creatinine kinase, U/L	-	-	8450	-	-	-	-	-	-
Direct coombs test	-ve								
Urine Haemoglobin		+ve							

He was diagnosed as severe acute haemolytic anaemia and was transfused slowly up to 10mls/kg of packed red cell on day 1 of admission, with the aim haemoglobin level of more than 8g/dL. He gradually developed into acute kidney injury (AKI) with creatinine of 283umol/L. Hyperhydration and urine alkalinisation were commenced due to the reduction of renal functions from acute tubular necrosis (ATN). This was evident from the increase in urea, creatinine and the presence of high uric acids. Intravenous frusemide infusion was commenced to ensure good urine output and fluid balance. These measures were unsuccessful and with persistent myoglobinuria, elevated serum Creatinine Kinase (CK) and uric acids, urgent haemodialysis was commenced on day 8 in view of progressive renal failure. Post haemodialysis, his renal function started to improve and normal diuresis returned.

## Discussion

Most G6PD deficient children live their lives without symptoms. The commonest clinical presentation in these children are neonatal jaundice and acute haemolysis secondary to exogenous agents trigger. The history of large consumption of fava bean in our patient is a common trigger for acute haemolysis episode. Other potential triggers in our context are drugs, henna, naphthalene balls and mosquito coils. Severe anaemia in this case possibly as a result from

large fava beans consumption by the patient.

Our patient has been a healthy child with no significant neonatal jaundice or positive history of G6PD deficiency in the family. His previous G6PD cord blood screening was negative. It is known that cord blood screening for G6PD was 98.6% sensitive with negative predictive value of 99.5%<sup>6</sup>. The initial full blood picture showed acute haemolysis due to the oxidative stress changes, suggesting to more common but rarely reported cases of G6PD deficiency.

He subsequently developed rhabdomyolysis with the presence of myoglobinuria and AKI. There were several reasons on why our patient developed AKI with severe haemolysis. Rhabdomyolysis is the breakdown of skeletal muscle due to various causes, in this case, ingestion of fava beans has caused toxic intracellular component release, hence presentation of multisystem findings such as metabolic acidosis, hypovolaemia, coagulations derangement and AKI<sup>7</sup>. Severe anaemia, haemoglobinuria and the presence of uric acid causing ATN owing to tissue ischaemia and hypoxia. Deposition of iron and consequently, the toxic effects of haemosiderin on renal tubules and glomeruli, leads to acute kidney injury (AKI)<sup>8</sup>.

The myolysis were documented when high lactate dehydrogenase (LDH) and CK in the blood and crimson red colour urine suggesting myoglobinuria. Myoglobinuria in haemolytic crisis in G6PD deficient

individuals is often not investigated. Muscular manifestation is not a well-recognized complication from a G6PD deficient and only a few cases have been described<sup>1</sup>. Skeletal muscles are much more resistant to oxidative damage than RBCs in the G6PD-deficient persons because muscle cells possess alternate enzymes, such as catalase and superoxide dismutase, which are absent in erythrocytes. The lower levels of catalase and superoxide dismutase in muscles have some dependency on glutathione to remove reactive oxidative radicals<sup>3</sup>. It has been suggested that for muscle damage to occur due to glutathione and the alternative pathways being overwhelmed, it would take a very large oxidative stress burden<sup>3</sup>. This probably explains the rarity of severe muscle manifestations in G6PD-deficient patients leading to rhabdomyolysis.

Severe haemolysis in G6PD-deficient individuals is recognised but is not a common presentation<sup>4,8,9</sup>. One study on G6PD activity of quadriceps muscle biopsy specimens concluded that in all three subsets of deficiency reported all patients studied had symptoms of cramps, myalgia and fatigability<sup>9</sup>. Mangat et al. reported a case of a 2-year-old African American child with sickle cell trait, who was later found to be G6PD deficient after ingesting naphthalene balls and developing red coloured urine associated with pallor<sup>4</sup>. His urine showed the presence of haemoglobin as well as myoglobin.

In contrast with all these cases reported, our patient developed severe AKI and acute liver injury which has not been reported previously. Since rhabdomyolysis and myoglobinuria are well documented causes of

AKI, it is logical to deduce that the former might have played a major role in intravascular haemolysis-induced AKI<sup>10</sup>. Myoglobinuria should be sought in children presenting with severe intravascular haemolysis especially those who are suspecting or undiagnosed with G6PD deficiency. The presence of myoglobinuria on top of haemoglobinuria might lead to a more severe degree of AKI in this situation, and detecting it could help the clinicians to predict severe impairment of renal function.

In conclusion, we described a rare sequelae of G6PD deficiency in undiagnosed 22-month-old Malay boy who developed rhabdomyolysis and AKI, following acute haemolytic crisis after the exposure to a large amount of fava bean. The current literatures indicate that severe manifestations of muscle damage in G6PD deficient individuals are still rare but need to be excluded as part of comprehensive medical management.

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