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NEONATAL HEMOLYTIC ANEMIA DUE TO GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY: A CASE REPORT

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ABSTRACT

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most common hereditary enzymatic disorders affecting red blood cells worldwide and is a significant cause of neonatal hyperbilirubinemia and hemolytic anemia. Clinical manifestations in neonates are variable and may present atypically, leading to delayed diagnosis and management. We report a case of a term male neonate delivered via cesarean section who developed progressive respiratory distress shortly after birth. The infant had Apgar scores of 7 and 8 at 1 and 5 minutes, respectively, and required continuous positive airway pressure (CPAP) due to worsening respiratory distress. Laboratory evaluation revealed metabolic acidosis, electrolyte imbalance, anemia (hemoglobin 11.4 g/dL), and coagulopathy. Subsequent findings showed fluctuating hemoglobin levels, suggesting ongoing hemolysis. Screening for G6PD deficiency demonstrated reduced enzyme activity (1.2 U/g Hb), which was later confirmed by quantitative assay (2.8 U/g Hb; reference 10.0–14.2), consistent with G6PD deficiency. The patient was diagnosed with neonatal pneumonia and hemolytic anemia secondary to G6PD deficiency. Clinical condition improved with supportive management, including respiratory support and antibiotic therapy. This case represents an atypical presentation of G6PD deficiency, where respiratory distress and systemic involvement preceded classical features such as jaundice. The patient's enzyme activity corresponds to Class III (moderate deficiency) based on WHO classification, in which hemolysis is often triggered by oxidative stress, particularly infection. Neonatal pneumonia likely acted as the precipitating factor in this case. The variability in clinical presentation highlights the diagnostic challenges of G6PD deficiency in neonates. G6PD deficiency should be considered in neonates with unexplained anemia or clinical deterioration, even in the absence of overt jaundice. Early recognition and appropriate management are essential to prevent severe complications, including acute hemolysis and bilirubin-induced neurologic dysfunction.

Keywords: Neonatal, Hemolytic Anemia.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most common hereditary enzymatic disorders affecting red blood cells worldwide, with an estimated prevalence of more than 400 million individuals. This condition is inherited in an X-linked

recessive pattern and results in impaired protection of erythrocytes against oxidative stress, predisposing affected individuals to hemolysis (Lee HY, Ithnin A, Azma RZ, Othman A, 2022).

G6PD plays a critical role in the pentose phosphate pathway by generating nicotinamide adenine dinucleotide phosphate (NADPH), which is essential for maintaining reduced glutathione and protecting red blood cells from oxidative damage. In the absence of sufficient G6PD activity, erythrocytes become highly susceptible to oxidative injury, leading to hemoglobin denaturation, membrane instability, and ultimately hemolytic anemia (Mak GK, Shah M, 2026).

In neonates, G6PD deficiency is an important cause of indirect hyperbilirubinemia and hemolytic anemia. Clinical manifestations may vary, ranging from asymptomatic conditions to severe jaundice and life-threatening hemolysis. Notably, neonatal presentations often differ from those in older children, as hemolysis may occur even in the absence of identifiable triggers such as infection, drugs, or fava bean exposure. Furthermore, G6PD deficiency is a well-recognized risk factor for severe neonatal hyperbilirubinemia, which can progress to bilirubin-induced neurologic dysfunction or kernicterus if not promptly recognized and managed (Orman B, Çetinkaya S, Öner N, Akçaboy M, Fettah A, Lafcı NG, 2023).

In Southeast Asia, including Indonesia, G6PD deficiency remains a significant public health concern, with reported prevalence ranging from 1% to 14%. Despite its clinical importance, routine neonatal screening is not universally implemented, leading to potential delays in diagnosis and management. Early recognition is therefore essential, particularly in neonates presenting with unexplained jaundice or anemia (Tsuzuki S, Akahira-azuma M, Kaneshige M, Shoya K, Hosokawa S, 2026).

We report a case of a term male neonate born via cesarean section who developed progressive respiratory distress and was found to have hemolytic anemia associated with confirmed G6PD deficiency (enzyme level 2.8 U/g Hb). The infant initially presented with poor respiratory adaptation at birth (Apgar score 7/8) and subsequently developed worsening respiratory distress requiring continuous positive airway pressure (CPAP) support. This case highlights the importance of considering G6PD deficiency as a differential diagnosis in neonates with clinical deterioration, anemia, and possible hyperbilirubinemia, even in the early neonatal period.

LITERATURE REVIEW

G6PD is a critical enzyme in the pentose phosphate pathway, responsible for generating nicotinamide adenine dinucleotide phosphate (NADPH), which plays an essential role in maintaining red blood cell integrity against oxidative stress. In G6PD-deficient individuals, reduced NADPH production impairs the regeneration of reduced glutathione and other antioxidant systems, leading to accumulation of reactive oxygen species and subsequent oxidative damage to erythrocyte membranes and hemoglobin. This process ultimately results in hemolysis, which may present as acute or chronic hemolytic anemia depending on the severity of enzyme deficiency and the presence of triggering factors

(Cappellini, M. D., & Fiorelli, G. E. M. I. N. O, 2008).

RESEARCH METHODS

Case Presentation

A male neonate was admitted to the neonatal intensive care unit (NICU) shortly after birth due to progressive respiratory distress. The infant was delivered via cesarean section at term gestation with a birth weight of approximately 2600 grams. At birth, the baby did not cry immediately but had good muscle tone, with Apgar scores of 7 and 8 at 1 and 5 minutes, respectively. Within the first hours of life, the neonate developed worsening respiratory distress. Initial vital signs showed a heart rate of 130 beats per minute, respiratory rate of 63 breaths per minute, and oxygen saturation of 94% on room air. Physical examination revealed chest retractions, positive nasal flaring, and bilateral rhonchi. These findings indicated significant respiratory compromise, and continuous positive airway pressure (CPAP) was initiated. The Downes score was 6, indicating moderate to severe respiratory distress. Chest examination showed deep retractions with vesicular breath sounds present bilaterally without rhonchi or wheezing.

Despite escalation of CPAP support up to a setting of 8/40, the infant remained in significant distress, with persistent tachypnea (RR 62 breaths per minute), increased work of breathing, retractions, and a rising heart rate of 140 beats per minute. This clinical deterioration indicated failure of CPAP, and the patient subsequently required endotracheal intubation. Mechanical ventilation was initiated using pressure control mode (PC 30, PEEP 6, rate 35, FiO_2 12). Supportive management included orogastric tube placement and intravenous fluid therapy (D5 with KCl and calcium supplementation at 80 mL/kg/day). Empirical antibiotic therapy was initiated due to suspected neonatal sepsis and congenital pneumonia. Arterial blood gas analysis demonstrated metabolic acidosis, with pH of 7.28, low bicarbonate level (12 mmol/L), base excess of −15, and a decreased PCO_2 of 26 mmHg, suggesting partial respiratory compensation. Electrolyte disturbances were also observed, including hyponatremia (Na 121 mmol/L) and severely decreased ionized calcium (<0.25 mmol/L).

Hematological examination initially showed anemia with hemoglobin of 11.4 g/dL, elevated leukocyte count (16,940/mm^3), and hematocrit of 32.2%. Red blood cell count was 3.05 $\times 10^6$/µL, with macrocytic indices (MCV 105 fL, MCH 37 pg), while platelet count was within normal limits. During hospitalization, the patient developed severe anemia, with hemoglobin dropping to 5.3 g/dL, hematocrit to 14.7%, and erythrocyte count to 1.48 $\times 10^6$/µL, accompanied by marked leukocytosis (24,880/mm^3) and elevated inflammatory markers (CRP 38.57 mg/L). These findings indicate ongoing hemolysis with superimposed infection or inflammatory response. Arterial blood gas analysis further revealed metabolic acidosis, with pH of 7.28, low bicarbonate (12 mmol/L), and base excess of −15. Electrolyte imbalance was also present, including hyponatremia (Na 121 mmol/L) and severely decreased ionized calcium (<0.25 mmol/L). On subsequent evaluation, hemoglobin level increased markedly to 20.9 g/dL, with hematocrit rising to 58.9%

and erythrocyte count to 6.63 $\times 10^6$/µL. This fluctuation in hemoglobin levels reflects severe hemolytic episodes followed by compensatory erythropoiesis and/or hemoconcentration during clinical recovery, consistent with hemolytic anemia secondary to G6PD deficiency.Coagulation profile showed prolonged prothrombin time (22.3 seconds) and elevated INR (1.99).

Importantly, screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency revealed decreased enzyme activity. Initial testing showed a G6PD level of 1.2 U/g Hb (reference >2.2 U/g Hb), indicating suspected deficiency. This finding was later confirmed by a quantitative assay demonstrating markedly reduced G6PD activity of 2.8 U/g Hb (reference 10.0–14.2 U/g Hb), confirming the diagnosis of G6PD deficiency. During hospitalization, the patient required ventilatory support with synchronized intermittent mandatory ventilation (SIMV) before gradual improvement allowed for extubation and transition to CPAP, followed by nasal cannula oxygen. Clinical condition progressively improved, with resolution of respiratory distress and stabilization of hemodynamic status. The diagnosis was established as neonatal pneumonia with hemolytic anemia secondary to G6PD deficiency.

At the end of hospitalization, the infant showed good clinical improvement, with stable vital signs, adequate oral intake, and resolution of respiratory symptoms. The patient was discharged with parental education regarding G6PD deficiency, including avoidance of oxidative stressors and the importance of follow-up monitoring.

DISCUSSION

This case illustrates a complex and atypical presentation of neonatal hemolytic anemia associated with glucose-6-phosphate dehydrogenase (G6PD) deficiency, accompanied by respiratory distress, metabolic acidosis, and systemic involvement. G6PD deficiency is one of the most common enzymatic disorders worldwide, affecting approximately 400–500 million individuals, with higher prevalence in malaria-endemic regions such as Southeast Asia, including Indonesia. Despite its high prevalence, the clinical manifestations are highly variable, particularly in the neonatal period (Hassan MK, Saha AK, Kundu LC, Begum P, Yousuf A, 2017). The clinical presentation of G6PD deficiency is heterogeneous. While many affected individuals remain asymptomatic, exposure to oxidative stressors such as infection, certain medications, or fava bean ingestion can precipitate hemolytic episodes . In neonates, infection is one of the most important triggers. In the present case, the coexistence of neonatal pneumonia likely acted as a significant oxidative stressor, triggering hemolysis. This is consistent with existing literature, which identifies infection as a major precipitating factor of hemolytic crises in G6PD-deficient patients (Tsuzuki S, Akahira-azuma M, Kaneshige M, Shoya K, Hosokawa S, 2026).

Unlike the classical presentation of G6PD deficiency in neonates, which is predominantly characterized by hyperbilirubinemia and jaundice, this patient initially presented with progressive respiratory distress and metabolic

acidosis. Such atypical presentations have been reported, although they are less common. Previous case reports have demonstrated that neonatal G6PD deficiency may present with severe hemolytic anemia and hyperbilirubinemia even in the absence of identifiable triggers, reflecting the wide clinical variability of this condition. This variability is influenced by genetic heterogeneity, residual enzyme activity, and environmental factors. Furthermore, recent evidence suggests that neonatal hyperbilirubinemia in G6PD deficiency may not always be solely due to overt hemolysis. Impairment in antioxidant defense systems, including disruption of peroxiredoxin pathways and imbalance between oxidant and antioxidant mechanisms, may contribute to bilirubin accumulation even without massive red blood cell destruction. This may explain why some neonates exhibit significant clinical manifestations despite relatively subtle early hematologic abnormalities (Mak GK, Shah M, 2026).

Laboratory findings in this case support the diagnosis of G6PD deficiency, with a confirmed low enzyme level of 2.8 U/g Hb (reference 10.0–14.2), indicating significant enzymatic deficiency . According to WHO classification, the severity of G6PD deficiency correlates with residual enzyme activity, with lower levels associated with higher risk of hemolysis. However, it is important to recognize that enzyme activity does not always directly correlate with clinical severity due to interindividual variability and differences in genetic variants. This explains why some patients with moderate deficiency may still develop severe clinical manifestations (Lee HY, Ithnin A, Azma RZ, Othman A, 2022).

Based on the WHO classification of G6PD deficiency, the patient's enzyme activity (2.8 U/g Hb, approximately 20–30% of normal) is consistent with Class III deficiency, which is categorized as moderate deficiency associated with intermittent hemolysis. This classification aligns with the clinical presentation in this case, where hemolysis was likely triggered by infection, a well-known oxidative stressor in G6PD-deficient individuals. In addition to hemolytic anemia, this patient demonstrated multisystem involvement, including metabolic acidosis and coagulopathy. These findings are likely secondary to systemic inflammation, hypoxia, and infection, rather than G6PD deficiency alone. Similar findings have been reported in neonatal cases where G6PD deficiency coexists with infection, emphasizing that the clinical picture may be complex and multifactorial (Kwaifa, I. K., Erhabor, O., Yakubu, A., Bagudo, A. I., Ali, B. H., Uchechukwu, O. F., ... & Moses, S, 2025).

Another important aspect highlighted by this case is the challenge of diagnosing G6PD deficiency during acute illness. Enzyme activity levels may be influenced by reticulocytosis or ongoing hemolysis, potentially leading to variability in results. Therefore, clinical correlation remains essential in establishing the diagnosis. Management in this case was primarily supportive, including respiratory support, treatment of infection, and careful monitoring of hematologic parameters. This approach aligns with current recommendations, which emphasize supportive care, avoidance of

oxidative triggers, and management of complications such as anemia and hyperbilirubinemia to prevent severe outcomes, including kernicterus (Hassan MK, Saha AK, Kundu LC, Begum P, Yousuf A, 2017).

In conclusion, this case highlights that G6PD deficiency in neonates may present with atypical and severe clinical manifestations beyond isolated jaundice. Infection plays a critical role as a trigger for hemolysis, and the clinical severity is not solely determined by enzyme activity levels. Early recognition, appropriate diagnostic evaluation, and comprehensive management are essential to prevent life-threatening complications in affected neonates.

CONCLUSION

This case highlights an atypical presentation of neonatal hemolytic anemia due to glucose-6-phosphate dehydrogenase (G6PD) deficiency in a term neonate with concurrent infection. Unlike the classical presentation dominated by neonatal jaundice, this patient initially manifested with progressive respiratory distress and systemic involvement, emphasizing the heterogeneity of clinical manifestations in G6PD deficiency. This case underscores the importance of considering G6PD deficiency in neonates with unexplained anemia or clinical deterioration, even in the absence of overt jaundice. Early recognition, appropriate diagnostic evaluation, and prompt supportive management are essential to prevent severe complications, including acute hemolysis and bilirubin-induced neurological dysfunction. Additionally, this case highlights the need for increased awareness and consideration of neonatal screening in high-prevalence regions.

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