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A CASE OF TOXIC METHEMOGLOBINEMIA FOLLOWING LIDOCAINE APPLICATION FOR CIRCUMCISION

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ABSTRACT:
Toxic methemoglobinemia is a potentially life-threatening condition. It develops generally as a complication of the use of local anesthetics. Prompt recognition and quick institution of therapy is of utmost importance. In this paper, a case of methemoglobinemia that occurred after lidocaine application for circumcision is presented in order to increase awareness among clinicians about this condition. The case was treated successfully with intravenous methylene blue.
Key words: Methemoglobinemia, Lidocaine, Methylene Blue

SÜNNET İÇİN KULLANILAN LİDOKAİN SONRASI GELİŞMİŞ TOKSİK METHEMOGLOBİNEMİ
ÖZ:
Toksik methemoglobinemi yaşamı tehdit edebilen bir durumdur. Genellikle lokal anesteziklerin kullanımına bağlı yan etki olarak gelişir. Erken tanı ve tedavi önemlidir. Bu yazıda, klinisyenlerin farkındalığını artırmak amacıyla, sünnet için kullanılmış lidokaine bağlı gelişen methemoglobinemi olgusu sunulmaktadır. Olgu intravenöz metilen mavisiyle başarıyla tedavi edilmistir.
Anahtar Kelimeler Methemoglobinemi, Lidokain, Metilen Mavisi

INTRODUCTION

Methemoglobinemia is a hematological emergency characterized by increased amounts of methemoglobin, hemoglobin in which the iron of heme is oxidized to the ferric form.[1] Methemoglobin is not able to carry oxygen and causes cyanosis. Under physiological state, it is rapidly converted back to hemoglobin by a reduction system (NADH-dependent methemoglobin reductase, NADH-cb5r) in erythrocyte and remains below 2%. When the stability between oxidation and reduction is disrupted due to increased oxidants, decreased capacity of reduction, or presence of an abnormal hemoglobin variant, methemoglobinemia occurs. Young infants have lower erythrocyte levels of NADH-cb5r [2,3] and may develop methemoglobinemia after exposure to drugs. Local anesthetics are well-known causes of toxic methemoglobinemia. [3-10] Rapid diagnosis and treatment of this serious condition can be life-saving. In this paper, we describe a typical presentation of toxic methemoglobinemia secondary to lidocaine application in order to increase awareness among clinicians about this potentially lethal but easily treatable condition.

CASE REPORT

A 41-day-old male infant was admitted to our Pediatric Emergency Room for cyanosis. A circumcision had been performed 1 h prior, and soon after the procedure he developed cyanosis. Lidocaine was injected locally during the procedure. His background and family history were unremarkable. On admission he was restless. Vital signs were within normal limits. No respiratory distress was present and cardiopulmonary auscultation was normal. The cyanosis persisted and oxygen saturation was 86% by pulse oximetry under oxygen supplementation. Arterial blood gas analysis revealed a pH of 7.38, pCO_2 of 35.7 mmHg, and pO_2 of 67.4 mmHg. His complete blood count and biochemical parameters were normal. Toxic methemoglobinemia was suggested and blood methemoglobin concentration was measured at 43.6%. The diagnosis was correct but, unfortunately, we lacked the antidote for methemoglobinemia in the emergency room. We immediately communicated with other medical centers nearby and acquired methylene blue with great difficulty within 60 minutes. Soon after a single dose (1 mg/kg) of intravenous methylene blue administration his cyanosis began to disappear. Consequent measurements of blood methemoglobin concentration revealed a gradual decrease. Methemoglobin level was 3.4% at 1 h, 2.8% at 8 h, and only 0.2% at 24 h. The patient remained in the observation room for 36 h and thereafter he was discharged without any complication. His glucose-6-phosphate-dehydrogenase (G6PD) level at 44 days of age was normal and he remained well at follow-up evaluations.

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DISCUSSION

Methemoglobinemia is a clinical disorder characterized by cyanosis, caused by environmental toxicity, deficiency of physiologically active NADH-cb5r or a hemoglobin variant (HbM).[1,2] Environmental toxicity is the only acquired form and develops after exposure to oxidant agents. Unlike the recessive forms, it may be life-threatening because it develops abruptly. Patients that abruptly develop high levels of methemoglobinemia may be severely symptomatic and should be treated quickly.

Clinical symptoms are related to the level of methemoglobin. Cyanosis becomes apparent at levels of 10%. High levels of methemoglobin cause serious tissue hypoxia leading to dispnea, tachycardia, arrhythmia, convulsion, stupor, or coma. Levels above 70% are lethal. Symptoms also depend on the rapidity of methemoglobin formation. After acute exposure to an oxidant agent, treatment should be initiated urgently even if the patient is asymptomatic. The present patient was a symptomatic young infant with a critical level of methemoglobin induced by an oxidant agent and he was treated immediately.

Circumcision is a painful cutaneous procedure performed under local anesthesia. A review of the literature on methemoglobinemia secondary to local anesthetics indicates that lidocaine is a causative agent generally in association with other anesthetics. [3, 7-9] Papers presenting lidocaine as a single causative agent are very few. [10] In the present case, a lidocaine injection was applied before circumcision, and subsequently cyanosis developed. Therefore, we conclude that lidocaine *per se* is responsible for the development of toxic methemoglobinemia.

Methylene blue is the antidote for methemoglobinemia. Administration of methylene blue at an initial dose of 1 to 2 mg/kg over 5 minutes has a dramatic effect. However, there are limitations in its usage. Methylene blue stimulates the production of the reduced NADPH substrate of NADH-cb5r via the pentose phosphate pathway of red cells. [11] It can result in acute hemolysis in G6PD deficient individuals, as G6PD deficiency causes an ineffective pentose phosphate pathway. Therefore, before administration of methylene blue the absence of combined G6PD deficiency should be confirmed. However, there is no easily accessible laboratory test for G6PD deficiency and the family should be directly asked about this condition. In the present case, methylene blue was administered before the result of the enzymatic activity test was obtained, based on the negative family history. Fortunately, no hemolysis was observed and thereafter his G6PD level was normal. Ascorbic acid infusion is an alternate treatment for toxic methemoglobinemia when methylene blue is unavailable or in G6PD deficient individuals. [12] Delay in acquiring and consequently in administration of either of these two drugs may cause critical situations. For this reason, methylene blue and/or ascorbic acid should be present as antidotes immediately available in the emergency room.

In conclusion, via the present case we would like to emphasize that cyanosis developing after local anesthesia should alert clinicians to toxic methemoglobinemia and the presence of methemoglobinemia must be promptly treated. It is important for clinicians to be aware of this serious condition. The first treatment modality is methylene blue infusion and this agent should be present as an antidote immediately available in the emergency room.

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