TOXIC METHEMOGLOBINEMIA AFTER INJECTION OF PRILOCAINE IN A NEWBORN*

A Case Report

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SUMMARY: Kara A, Yiğit Ş, Aygün C, Oran O. (Neonatology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Toxic methemoglobinemia after injection of prilocaine in a newborn: a case report. Turk J Pediatr 1998; 40: 589-592.

The acute onset of cyanosis in an infant is an alarming development. We report an infant who became cyanotic after injection of prilocaine. Prilocaine is a local anesthetic that is widely used in clinical practice, but usage in infancy easily causes methemoglobinemia. Acquired methemoglobinemia occurs in individuals exposed to an increased amount of agents that oxidize hemoglobin iron. *Key words: toxic methemoglobinemia, newborn, cyanosis, prilocaine.*

The acute onset of cyanosis in an infant is an alarming development, usually suggesting hypoxia. In an infant, cyanosis resulting from lung diseases, air leak syndrome, diaphragmatic hernia, hypoplastic lungs, cardiac diseases, persistent pulmonary hypertension, central nervous system diseases, polycythemia, choanal atresia, hypothermia, hypoglycemia, sepsis or methemoglobinemia is the chief consideration in the differential diagnosis. In the case of methemoglobinemia, the cause of cyanosis is oxidation of heme iron to the ferric state, making it less able to bind with oxygen[1]. Methemoglobinemia may be hereditary or acquired. There are reports of methemoglobinemia secondary to drug exposure[2-7]. We present a case of methemoglobinemia that occurred after the use of a local anesthetic, prilocaine.

Case Report

A full-term male infant was referred to Hacettepe University İhsan Doğramacı Children's Hospital at 25 days of life because of prenatally diagnosed right hydronephrosis. He was born to a 29-year-old woman, gravida 2, para 1, after an uneventful cesarean section, performed on request of mother. Hydronephrosis was diagnosed on routine ultrasonographic examination during prenatal period

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at sixth month. Postnatal abdominal ultrasonography showed ureteropelvic stenosis, so urinary diversion by 7F pigtail catheter was performed with ultrasonography guide on the 25th day of life. At that time, 4.5 to 5 ml (4 mg/kg) prilocaine hydrochloride (Citanest® 0.5%) was injected as local anesthesia. Within 90 minutes the infant had become dusky and by two hours he was quite blue. There were no murmurs and his pulse was normal. Blood gases done while the infant received oxygen nasally revealed normal pH, partial arterial pressure of CO_2 levels, partial pressure of O_2 155 mmHg, and arterial O_2 saturation of 99 percent. Chest radiogram and electrocardiogram were normal, hemoglobin was 12.3 g/dl and results of blood chemistry were within normal limits, including renal function test. Since the infant remained blue despite oxygen therapy and because a blood spot on filter paper took a brown color, methemoglobinemia was considered. Blood methemoglobin was determined as described in literature[8] and found to be 2.52 g/dl (20.4%) confirming a diagnosis of methemoglobinemia. Four mg (1 mg/kg) of methylene blune in 50 ml of saline was given intravenously over half an hour and a dramatic resolution of the cyanosis was seen within another half an hour. On the following day the methemoglobin level was 0.03 g/dl (5%).

Discussion

Hemoglobin is unique for its vital function of oxygen transport. Its ability to reversibly bind to oxygen depends on the heme iron being maintained in the ferrous (Fe^{2+}) state. Oxyhemoglobin, when incubated under physiologic conditions, slowly autooxidizes to methemoglobin. During the journey of red blood cells in the circulation, hemoglobin is exposed to a variety of oxidants that enhance methemoglobin formation at a rate of two to three percent per day[9]. The reduction of methemoglobin in red blood cells to ferrous form depends on electron carriers, cytochrome b_5, nicotinamide adenine dinucleotide and enzyme cytochrome b_5 reductase.

Methemoglobinemia may be hereditary (defect in the reduction of methemoglobin or in the structure of hemoglobin such as hemoglobin M) or acquired. Acquired methemoglobinemia occurs in normal individuals exposed to increased amounts of agents that oxidize hemoglobin iron. Newborns and infants appear to be unusually susceptible to the development of this form of methemoglobinemia. This increased risk is due to decreased amounts of cytochrome b_5 and cytochrome b_5 reductase in erythrocytes of newborns[1] and to easier oxidation of fetal hemoglobin to the ferric state than hemoglobin A[10]. Methemoglobinemia can be induced by a wide range of drugs and toxins. Aniline dyes, nitrates, nitrites, sulfones, acetaminophen, benzocaine, dapsone, nitroglycerin, nitroprusside, sulfanilamide and prilocaine have been described as causing

methemoglobinemia[11]. Prilocaine is a widely used local anesthetic and two of its metabolites, 4 hydroxy-2-methylaniline and O-toluidine, have been implicated in this condition[2].

Blood appears dark in color, but in contrast to deoxygenated blood, it does not change color to bright red when mixed with air in methemoglobinemia. This is the basis of a simple screening test for detection of methemoglobin[12]. A drop of blood is placed on filter paper and then allowed to dry while the filter paper is waved in the air. Blood that is not saturated with oxygen turns red, whereas methemoglobin remains brown. This test detects levels of ferrihemoglobin greater than ten percent of total hemoglobin.

Adult patients whose methemoglobin levels are above 40 percent or who appear to be symptomatic should be treated with intravenous methylene blue at a dose of one to two mg/kg as in the form of a one percent solution[1]. The level of methemoglobin should fall to normal within an hour after treatment but if not, a second dose can be administered[1,11]. In the newborn period methemoglobin levels greater than 15 to 20 percent are treated with methylene blue[10]. Ascorbic acid may be given either orally or parenterally to reduce the level of methemoglobin, but it acts much slower than methylene blue[13]. Failure to note improvements after methylene blue is administered in acquired methemoglobinemia suggests G6PD deficiency.

Acquired methemoglobinemia is a potentially harmful, even lethal process, especially in the newborn period, that may result from application of a local anesthetic, prilocaine[3-7]. It is the intent of this report to make pediatricians aware of the potential of this adverse effect of prilocaine. If methemoglobinemia is quickly diagnosed and treated, the outcome can be excellent.

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