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PROPOFOL-RELATED INFUSION SYNDROME

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Clinical Case Report

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Abstract

Propofol is a drug that is used for induction of anaesthesia at surgery. Its use is sometimes associated with sudden hemodynamic instability, which may be life-threatening. To report the occurrence of the propofol-related infusion syndrome in a child. **A** 13 year- old girl who received a bolus dose of propofol for induction of anaesthesia at surgery developed sudden hemodynamic instability. Investigations suggested that the child had developed propofol- related infusion syndrome. Close monitoring and supportive management eventually enabled the patient to recover from this dreaded complication. It was not possible to determine the exact reason why the child developed this syndrome. An accurate specific diagnosis of this condition and prompt institution of appropriate therapy aid recovery from this syndrome.

Keywords: Propofol-related infusion syndrome; induced Brugada syndrome; anaesthesia

Introduction

There are many complications which arise out of anaesthesia that would require immediate medical attention. We recently encountered an uncommon, yet life- threatening complication, when using propofol for induction of anaesthesia in a child, namely the propofol-related infusion syndrome (PRIS). Close monitoring and supportive management eventually enabled the patient to recover from this dreaded complication.

Case Report

A 13 year- old girl was posted for dacryocystorhinostomy on 8th October, 2009; pre-anaesthetic evaluation did not reveal any abnormal findings. On the table, she received propofol (90 mg) for induction of anaesthesia along with succinylcholine (2mg/kg), and was maintained with propofol infusion (100 mg/kg/min). She developed bradycardia, which was not responsive to atropine . She was immediately shifted to the intensive medical care unit. On examination, she was found to have developed bradycardia, tachypnea and hypotension. An electrocardiogram (ECG) revealed a ST elevation in leads v1-v3 with a right bundle branch block (Fig. 1); these changes were not present in a ECG that had been taken before surgery. Serum levels of triglycerides, potassium, creatinine phosphokinase(CPK) and CPK-MB were found to be elevated. Arterial blood gas analysis revealed metabolic acidosis. Myoglobin was detected in the urine.

The child was suspected to have toxic myocarditis and her vital parameters were maintained with ionotropic support. An ultrasound of the abdomen revealed a fatty liver. Her blood pressure returned to normal after five days, whereupon she was weaned off ionotropes. At the end of one week, her ECG , blood and arterial blood gas parameters were found to have returned to normal. A review of the literature suggested that the child had developed PRIS. Cytochrome oxidase c level in the blood was tested for and was found to be low .The child received carnitine and trimetazidine for two weeks, after which she was discharged for further follow up.

Discussion

PRIS occurs more commonly in children than adults who are anaesthetised with propofol, possibly due to differences in pharmacodynamic and pharmacokinetic properties[1-5]. Early metabolic acidosis, refractory bradycardia, hemodynamic instability, multiorgan failure, hepatomegaly, serum lipemia, rhabdomyolysis and induced Brugada are components of this syndrome[1]. PRIS has been defined as arrhythmia during propofol infusion with one or more of the following: a) lipemic plasma; b)metabolic acidosis with or without increased serum lactate; c) rhabdomyolysis with myoglobinuria[2].

The actual mechanism underlying PRIS has yet to be ascertained. Possible mechanisms include inhibition of enzymes in the mitochondrial respiratory chain, impaired fatty-acid oxidation and/or presence of unidentified toxic metabolites[4]. In the 1990's, a few children were reported to have died following use of propofol[2]. Most of the deaths were attributed to viral myocarditis; however, postmortem examination did not reveal any signs of myocarditis.

An interesting finding in patients who have developed PRIS, as in our patient, is a low level of cytochrome oxidase c[1,4,5]. Whether this mitochondrial defect represents the cause of the condition, or occurs as a side-effect, is yet to be ascertained. It is postulated that there is a failure of the mitochondrial electron transport chain resulting from impaired fatty-acid oxidation, secondary to reduced mitochondrial entry of long chain acylcarnitine ester, due to inhibition of the transport protein (carnityl palmityl transferase (CPT)-1 .Increased levels of malonyl carnitine and 3- acylcarnitine have been found in these patients.

Free fatty acids (FFA) are free energy substrates for the heart muscle, particularly at times of stress in children. In patients with PRIS, the heart muscle is deprived of FFA due to mitochondrial inhibition. The stress of surgery leads to release of catecholamines and steroids, which adds to the insult. Impairment in fatty acid metabolism in the liver leads to lipemia and fatty liver changes . These acute changes persist for a week. Supportive care should be provided during this period to maintain vital parameters. Although carnitine and trimetazidine, which shift the cardiac fuel from FFA to carbohydrate, are theoretically beneficial, this benefit has not been proven.

All cases reported previously have had prolonged exposure to propofol (at least for more than 48 hours) before they developed PRIS, and the children had all succumbed to PRIS. However, in our patient, PRIS manifested within that few minutes of exposure to the drug. We believe that the short duration of exposure to propofol, early recognition of the complication and intensive care helped us to save the patient . The Food and Drug Administration of the USA has warned against the use of propofol in children, especially in doses exceeding 4 mg/kg/hr or as an infusion for more than 48 hours[3].

Many questions remain unanswered regarding PRIS and its idiosyncrasies. The high mortality rate and the relative youth of the affected individuals have raised concerns about clinical outcomes when using propofol. Further case studies and thorough investigations are needed to unravel the details regarding the mechanisms underlying this uncommon syndrome.

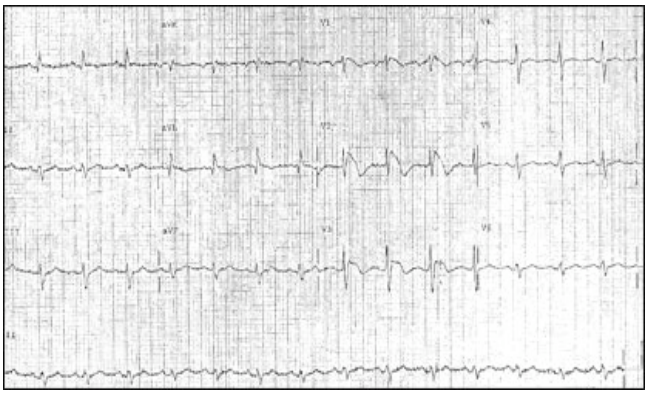

Figure 1: An electrocardiogram of the child showing an induced Brugada syndrome, with a ST elevation in leads v1-v3 with a right bundle branch block.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests