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A case of tetralogy of Fallot with no neurological deficit after prolonged hypoxia

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Introduction

Hypoxic attacks in tetralogy of Fallot (TOF) consist of anoxic spells thought to be initiated or exacerbated by infundibular hypercontractility and hypoxia caused by augmentation of right-to-left shunting that results when low right ventricular pressure encounters insurmountable high pulmonary artery pressure during hypovolemia. Since most TOF repairs are performed in children, hypoxic attacks occur less often in older patients [1]. Because characteristic adult-type TOF includes development of pulmonary arterial malformations [2,3] and complications from pulmonary hypertension [4,5], perioperative management differs in the older patient. Although many recent reports have discussed hemodynamic status during anoxic spells, very few have referred to protective mechanisms of the brain during severe systemic hypoxia. We report a case of hypoxic attacks without neurological sequelae wherein attacks were considered a result of massive bleeding in association with adult-type TOF.

Case report

A 48-year-old man with a previous diagnosis of TOF presented with dyspnea and chest pain occurring postprandially, after alcohol ingestion and after mild exercise for the past 6 months. He was admitted to our hospital due to increase of repeated episodes for the previous 1 month and was scheduled for surgical repair of the TOF. These attacks continued after admission, and his last attack occurred 1 week before operation. Clinical examination showed erythrocytosis (hemoglobin concentration, 17.5 g·dl^{-1}; hematocrit, 51.6%), slight coagulopathy (thrombo test, 72%), and slight hypofibrinogenemia (fibrinogen, 187 mg·dl^{-1}). Electrocardiography showed subendocardial ischemia and right ventricular hypertrophy. Angiography revealed severe infundibular stenosis and mild valvular stenosis without coronary disease. Preoperative catheterization measurements were as follows: right ventricular pressure similar to left ventricular pressure, mean pulmonary artery pressure 30 mmHg, left to right shunt ratio 59%, Qp/Qs 2.3, aortic O_2 saturation 88%. Chest X-ray showed right aortic arch and no increase in density in the entire lung field.

The patient received routine premedication with 0.4 mg scopolamine hydrobromide and 50 mg pethidine intramuscularly 30 min prior to induction of anesthesia. He was sedated and hemodynamically stable; blood pressure (BP) was 120/70 mmHg. Appropriate monitors were attached, and a left radial artery cannula was inserted for continuous BP monitoring. General anesthesia was induced with 0.5 mg fentanyl and 0.1 mg·kg^{-1} midazolam intravenously. Intubation was performed after giving 0.2 mg·kg^{-1} vecuronium intravenously with no remarkable change in vital signs or ECG. Anesthesia was maintained with 50% nitrous oxide in 50% oxygen and 40 μg·kg^{-1} fentanyl as required until sternotomy was performed. A pulmonary catheter was inserted via the right internal jugular vein, and the following initial mean pressures were obtained: right ventricle, 90 mmHg; pulmonary artery, 15 mmHg; pulmonary capillary wedge, 9 mmHg; and central venous pressure, 17 mmHg. SEP (somatosensory evoked potential) was monitored continuously to evaluate cerebral oxygenation and blood perfusion. Arterial BP and heart rate

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were maintained at about 120/70 mmHg and 60 bpm, respectively, after intubation. Routine blood gas and cell count studies were normal (pH, 7.42; $PaCO_2$, 31.7 mmHg; PaO_2, 153.8 mmHg; HCO_3^-, 20.8 mmol·l^{-1}; SaO_2, 99.4%; hemoglobin concentration, 15.3 g·dl^{-1}; hematocrit, 45.5%). Nitroglycerin was started for hypertension occurring after the initial skin incision. Sudden massive bleeding occurred immediately after sternotomy, with an estimated blood loss of 1300 ml. Central venous pressure fell from 14 to 10 mmHg. Simultaneously, SpO_2 decreased to 35%, BP decreased to 72/54 mmHg, and heart rate increased to 108 bpm. $S\bar{v}O_2$ was 33%, and mean pulmonary artery pressure decreased from 30 to 10 mmHg. We considered that this hypoxic attack was induced by sudden blood loss. Upon termination of the nitroglycerin, 250 μg of phenylephrine and 0.2 mg of propranolol were administered intravenously shortly after the start of symptoms. A 750-ml autologous transfusion and 850 ml of Ringer's lactate solution were given simultaneously. Despite these treatments, this first attack persisted for about 25 min. Blood gas analysis during the hypoxic attack showed severe hypoxia and anemia (pH, 7.328; $PaCO_2$, 47.2 mmHg; PaO_2, 16.9 mmHg; HCO_3^-, 24.5 mmol·l^{-1}; SaO_2, 22.5%; hemoglobin concentration, 7.1 g·dl^{-1}; hematocrit, 20.3%; 36.3°C). After an additional injection of 0.2 mg of propranolol, SpO_2 rose from 49% to 72%, heart rate and BP returned to within normal range (heart rate, 120 to 89 bpm; BP, 70 to 95 mmHg), and a continuous dopamine drip at 5 μg·kg^{-1}·min^{-1} was started to maintain vital organ perfusion. Shortly after dopamine administration, another hypoxic attack, in which systolic BP decreased to 68 mmHg at nadir, occurred and persisted for 30 min. Blood gas analysis showed PaO_2 was also very low (19.3 mmHg) at this time. Cardiopulmonary bypass (CPB) was begun 55 min after the start of the first attack. During CPB, the patient was stable, and CPB weaning was successful. Red-cell 2,3-DPG (2,3-diphosphoglycerate) values measured during the second spell and on the first postoperative day were very high (10.3 and 8.9 μmol·l^{-1}, respectively). The SEP N2 wave was slightly prolonged during the attacks but returned to normal after initiation of CPB. The patient awoke 2 h after surgery and was extubated the following day. No neurological deficit was observed postoperatively. The subsequent postoperative course was uneventful, and the patient was discharged home 21 days later.

Discussion

Perioperative hypoxic attacks in TOF patients generally occur less often in older patients than in children because the adult pulmonary artery and left ventricle are better developed [1,5]. Some investigators feel, however, that development of valvular and infundibular stenosis resulting from prolonged right ventricular stress is responsible for complications that include cardiac muscle weakness and hypoxic attacks. Low cardiac function is found more often in older patients, and mortality among them remains high [5].

It is well known that severe hypoxia in which PaO2 is less than 20 mmHg generally causes low cerebral and cardiac function and, if it is prolonged, causes irreversible damage [6,7]. Based on increases in hematocrit [8] and 2,3-DPG [9,10] in chronic hypoxia, it is thought that in cyanotic congenital heart disease, including TOF, oxygen delivery to the tissue during hypotension or hypoxia differs from that in noncyanotic heart disease. We found no marked prolongation or low amplitude of SEP, despite marked hypoxia of over 1 h, and no neurological deficit was seen postoperatively. These observations suggest that no serious cerebral hypoxia occurred during the attacks. Kamide et al. [11] reported a similar TOF case, with no neurological deficit seen after 30 min of hypoxia. We think that the lack of neurological deficit in their case might have been due to maintenance of adequate mean blood pressure and to improvement in oxygen delivery due to the low hematocrit resulting from fluid replacement with Ringer's lactate. Rosenthal et al. [8] showed that an excessive hematocrit might impair tissue oxygen delivery because of increased blood viscosity and that hemodilution might improve tissue oxygen delivery and peripheral blood microcirculation. Kiyohara et al. [12] reported that cerebral ischemia following carotid ligation in rats, indicated by low ATP and changes in lactate/pyruvate levels, is more severe in the presence of low hematocrit. We measured hematocrits of 20.3% to 24.6%; it is not likely that these low hematocrit levels offered any brain protection during our patient's attacks. Out patient's red blood cell 2,3-DPG was supranormal during surgery and on the first postoperative day. Increase in 2,3-DPG plays an important role in oxygen release to the tissues and in hemoglobin oxygen affinity [9]. It is well known that the oxygen dissociation curve for red blood cells containing high levels of 2,3-DPG shifts to the right at a normal P50 level. At a low P50 level, however, when the oxygen dissociation curve is displaced to the right, the oxygen affinity of hemoglobin at the low P50 level is stronger than at the normal level, and oxygen release to the tissue may diminish. It is unlikely that 2,3-DPG was the chief mechanism of brain protection, and it is unclear how the high level of 2,3-DPG in this patient participated in brain protection, although others have reported that the oxygen dissociation curve in patients with cyanotic heart disease also shifts slightly to the right [1,10,13]. Regarding hypothermia-related brain protection, our patient's temperature was normal

during the hypoxic attacks, so there is no evidence that progressive hypothermia was involved in the improvement in his outcome. Oxygen consumption has been shown to decrease linearly at systemic oxygen transport levels below $400\,ml \cdot min^{-1} \cdot m^{-2}$, and fractional oxygen extraction from arterial blood increases as systemic oxygen transport falls as a function of reduced mixed venous oxygen consumption at low levels of systemic oxygen transport in patients with congenital heart disease [10]. Because oxygen transport is associated with cardiac index, and a small difference between SaO_2 and $S\bar{v}O_2$ indicates proximity, it appears that our patient's systemic oxygen transport and consumption may have been low, whereas oxygen extraction from arterial blood to tissue may have been high during the hypoxic attacks. Another theory to explain the protective effect is that of preconditioning caused by the repetitive preoperative hypoxia. In hypoxic preconditioning, sublethal anoxia protects against damage from subsequent hypoxic insult. Some investigators have reported that nitric oxide release caused by hypoxic preconditioning in rats offers some protection from brain injury [14,15]. Other reports have indicated that in myocardial cells, nitroglycerin, existing as exogenous nitric oxide, induces preconditioning [16,17], but it is not clear whether this occurs in the brain. In our case, administration of nitroglycerin was terminated after the first hypoxic attacks occurred. It is unclear whether nitroglycerin exerts a protective neurological effect as a preconditioning substance in sublethal hypoxic conditions; further studies of this phenomenon are needed.

We conclude that although the etiology of neurological preservation was not clear in our case, various factors, such as low tissue oxygen consumption, high fractional oxygen extraction, and preconditioning, may have participated in the satisfactory outcome. We should eliminate all situations that cause low pulmonary blood flow and should manage anesthesia with the goal of providing adequate monitoring and oxygen delivery in patients with TOF.

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