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Case Report

A report of two cases of polycythemia in patients with Tetralogy of Fallot (TOF) in heart failure and the dilemma of management in a resource poor setting

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Abstract

Congenital heart diseases are commonly seen in resource poor settings, like in Sub-Saharan Africa. Tetralogy of Fallot (TOF) is one of the cyanotic congenital heart diseases, and is a known cause of polycythemia. Congestive heart failure, however, is an unusual finding in TOF. The recommended management of polycythemia is treatment of underlying cause (in this case, surgical repair of TOF) or partial exchange blood transfusion (PEBT) when surgery is delayed. The former option is usually not possible in our setting due to poverty. Two cases of TOF with polycythemia and heart failure were seen in our clinic, from ages 3 and 7 years. They were managed conservatively with PEBT and anti-failure regimen because of lack of funds for corrective repair overseas. They survived on this therapy for 14 years and 6 months respectively. This paper aims to draw attention to the challenges encountered, and hence a call for caution, in managing polycythemia in patients with TOF in heart failure using PEBT, with special focus on the immediate or short-term post procedure outcome.

Keywords: Tetralogy of Fallot, Polycythemia, Heart failure, Partial exchange blood transfusion

Introduction

Congenital heart disease (CHD) is an enormous problem in low middle income countries, particularly in Sub-Saharan Africa, where majority of the estimated 500,000 children born yearly with CHD reside [1]. These children with heart diseases are mostly managed conservatively due to the families' inability to finance definitive surgery [2]. TOF comprise four cardiac abnormalities: right ventricular outflow tract obstruction (RVOTO), ventricular septal defect (VSD), overriding aorta and right ventricular hypertrophy (RVH) [3]. There are other anatomical variants and cardiac anomalies that may be associated with TOF [4,5]. It is the commonest cause of cyanotic congenital heart disease beyond the neonatal age and accounts for 7-10 % of all congenital cardiac malformations, globally [3]. TOF constitutes 10–26.2% of all congenital cardiac diseases in Nigerian children [6-8]. Congestive heart failure is an unusual manifestation of classic TOF but some infants with mild RVOTO may have heart failure due to a large ventricular left to right shunt before development of severe RVOTO later in life [9,10]. This is seen in pink or acyanotic TOF [9.10]. Other causes of heart failure in TOF include myocardial infarction, infective endocarditis, cardiomyopathy, severe hypoxia, anaemia, or systemic hypertension [10,11]. Uncommon anatomical variants such as aortic insufficiency, absence of the pulmonary valve or one pulmonary artery, or functional obstruction of the ventricular septal defect by the tricuspid valve may also predispose to heart failure [4,5].

More commonly, TOF is a cause of secondary polycythemia. Polycythemia is defined as red blood cell (RBC) count, hemoglobin level, and total RBC volume above the upper limits of normal for age and gender [12]. In post pubertal individuals, an RBC mass >25% above the mean normal value (based on body surface area) or a hemoglobin level >18.5 g/dL (in males) or >16.5 g/dL (in females) indicate polycythemia [13] while in infants a hematocrit of greater or equal to 65% is considered polycytemia [14]. Polycythemia increases blood viscosity and

decreases tissue perfusion. This can result in headaches, lethargy, confusion, anorexia, dyspnea, irritability and seizures. It can also cause thrombosis with lesions in the lungs and kidneys [15,16]. Patients with heart failure and polycythemia are at risk of stroke and myocardial ischemia, as high hemoglobin level can promote systemic vasoconstriction by trapping nitric oxide and by generation of oxygen-derived free radicals [16]. The recommended treatment of polycythemia caused by TOF is surgical repair of the abnormality or partial exchange blood transfusion (PEBT) and low-dose iron therapy when surgery is delayed [16-19]. Partial exchange blood transfusion is known to reduce hematocrit, blood viscosity and reverse the pathologic effects of polycythemia]20]. It is also documented to improve myocardial relaxation and contractility, and restore cerebral blood flow velocity [20]. Other documented effects of PEBT include normal cardiac output and stroke volume as early as five hours after the procedure and constant right and left ventricular filling pressures [20,21]. Increased mean arterial and pulmonary arterial pressures by up to 40% and decreased oxygen carrying capacity by about 33% were also reported [21]. Deaths that occur within 7 days of PEBT are considered PEBT related deaths [22]].

The presence of polycythemia in a heart failure patient poses a therapeutic challenge [16]. It is hoped that the report of these cases would alert physicians on the possible outcome of PEBT in this category of patients some days after the procedure and a call for caution in the use of PEBT in patients with TOF, polycythemia and heart failure.

Case 1

UB presented to the children emergency room of Irrua Specialist Teaching Hospital in June 2004 at the age of 3years with cough and fever of one week and one day duration respectively. On examination he was tachypnoeic (72 cpm), febrile (38.6 ^{0}C), cyanosed, and had a grade 4 digital clubbing. His blood pressure was 80/60 mmHg and he had tachycardia (160 bpm), bulging left precordium, grade 3/6 ejection systolic murmur, and a tender hepatomegaly. His packed cell volume (PCV) was 75%. Chest radiograph showed normal cardiothoracic ratio (CTR), boot shaped heart, and perihilar pneumonic infiltrates. At this time, pulse oximeters and an echocardiography machine were not available in the hospital, and the closest hospital with such services was 350 km away. Patient could not travel to access these services due to financial constraints. He was treated as a case of TOF in heart failure and bronchopneumonia with antibiotics and diuretics. He was discharged after five days on admission and was to be seen in clinic in a week but was lost to follow up. In 2013, at age 12, he was rushed into the emergency room unconscious with a Glasgow comma scale (GCS) of 9/15 (eye opening-4, verbal response-1 and motor response -4). He was dyspnoeic with flaring of the alae nasi, intercostal and subcostal recessions. The SPO_2 in room air was 71%. The PCV was 85%. Malaria parasites were numerous on blood film. Urinalysis showed blood (+++) and protein (+). Hemoconcentration precluded serologic investigations like electrolytes, urea and creatinine. The diagnosis of hyper cyanotic spell, severe malaria and sepsis were made and he was managed accordingly. He had a PEBT with normal saline. Immediate post PEBT PCV was 80%. A repeat PEBT was done a day after to bring down the PCV to 76%. He was placed on ferrous sulphate. He developed heart failure a day after the second PEBT. He was dyspnoeic, with inter costal recession (ICR), bounding pulses, HR of 130 bpm, BP of 100/80 mmHg, RR of 38 cpm and a 4cm soft tender hepatomegaly. Diuretics (intravenous furosemide and oral spirinolactone) were added to his treatment and he was discharged after 2 weeks. He was lost again to follow up until 3 years later, at age 15, while in secondary school. He had a history of multiple hypercyanotic spells which his father claimed were managed in private hospitals. He was investigated by a visiting team of cardiac surgeons from the United Kingdom via the help of an NGO. The ECHO confirmed the diagnosis of TOF. He was also said to need more investigations before surgical intervention outside the country when funds were available. He was placed on oral hydrochlorothiazide and spirinolactone. He was on follow up and had two more PEBT due to polycythemia at about one yearly interval without complications. He was compliant with his anti-failure drugs. He presented in April 2018 (at age 17) with PCV of 80%, PEBT was done and post procedure PCV was 60%. He developed heart failure after this procedure and intravenous frusemide was added to his treatment. The heart failure was controlled and he was discharged on his usual oral anti failure regimen. When he was seen in June 2018, he had headache, fever, and inability to stand. He was dypnoeic, tachypnoiec (36 cpm), and cyanosed (64%). Other findings were PR-110bpm, BP-130/70 mmHg, raised JVP, Apex beat-6th LICS MCL (previously normal), grade 4/6 murmur, liver-6cm (tender) and spleen 4cm. Investigation results were: PCV-72%, WBC-3900 /mm^3, N-59%, L-32.3%. Urinalysis-blood (++), protein (+++); HCO3-10mm/l, urea-56mg/dl. He was managed for hypercyanotic spell, polycythemia with hyperviscosity, TOF in heart failure and discharged home.

He had the last PEBT in August 2018 when he came for a follow up visit and his PCV was 80%, and was discharged home after 6 hours of observation on his oral anti heart failure drugs. He missed the appointment for the post PEBT PCV the next day. He was said to have complained of weakness at home but could not be brought to hospital. He died on the way to the hospital two days after.

Case 2

NV presented in May 2019 at the age of 7 years to our clinic with a history of fast breathing and bluish

discoloration of the lips from birth, a five-month history of recurrent periorbital swelling and a day history of cough. She also had easy fatigability relieved by squatting. The periorbital swelling occurred weekly or biweekly at onset but remained a daily occurrence a week before presentation. It was worse in the morning and resolved as the day progressed. Cough was non distressing and productive of thick whitish sputum. She was cyanosed with SPO_2 of 72% in room air, had conjunctival suffusion, periorbital fullness and a grade 4 digital clubbing. She had a raised JVP and raised blood pressure (130/93 mmHg) at presentation. Subsequently, her blood pressure ranged between 90/60mmHg and 130/100 mmHg on medications. She was dypnoeic, tachypnoeic (RR- 36 cpm) and had a tender hepatomegaly which was 4cm below the right costal margin. She had a pulse rate of 122 bpm, left precordial bulge with the apex beat at the 6th left intercostal space, anterior axillary line, and a grade 4/6 ejection systolic murmur in the pulmonary area. Chest radiograph showed a boot-shaped heart and cardiomegaly. ECG showed right atrial enlargement (RAE) and right ventricular hypertrophy (RVH). Echocardiography (ECHO) showed a dilated right atrium, non-restrictive VSD, an overriding aorta and pulmonary stenosis. Her PCV was 76%. A diagnosis of TOF in heart failure with hypertension was made.
She was managed as an outpatient on captopril, spirinolactone and hydrochlorothiazide. On her second visit to the hospital, her PCV was 82%. She had a partial exchange transfusion with normal saline. The post PEBT PCV was 67%. She was placed on enalapril, spirinolactone and hydrochlorothiazide and discharged home 6 hours after. She was regular on her monthly follow up and anti-failure drugs. On the 6th month of her diagnosis she presented to the clinic with a history of headache. Her PCV was 75% and her blood pressure was 130/110 mmHg. A diagnosis of polycythemia with hyperviscosity was made. A PEBT was carried out to reduce the PCV to 60%. The procedure was well tolerated and her blood pressure dropped to 110/80 mmHg and she was sent home after 6 hours on her regular drugs. She did not present a day after the procedure for the post PEBT PCV as was planned. Her father was contacted and patient was communicated with and she seemed well as she was in school earlier in the day. Information was sent to the hospital that she died the next day (2 days after the PEBT) after she returned from school.

Discussion

The cases reported above presented with Tetralogy of Fallot, heart failure and polycythemia. Heart failure is not a usual presentation of TOF [9]/ The heart failure in these cases may be as a result of many factors which include cardiomyopathy due to chronic hypoxia, myocardial infarction, severe hypoxia, polycythemia, infective endocarditis or systemic hypertension [10.11]. The two cases had oxygen saturation less than 80% at presentation and throughout the course of management. Case one at presentation, at the age of 3 years, already had heart failure while case two is believed to have developed heart failure at 6 years. Cardiomyopathy caused by chronic hypoxia has been reported to be the cause of heart failure in some children with TOF [23,24]. Case one was admitted on different occasions for sepsis which could have been infective endocarditis. An autopsy would have been helpful in confirming this assumption. There was no report of fever or admissions in case two. Case two presented with hypertension. Her blood pressure at presentation was 124/94 mmHg. Subsequently, her blood pressure ranged between 90/60 mmHg and 130/100 mmHg despite medications. Hypertension, hypoxic cardiomyopathy and infective endocarditis are documented causes of heart failure in TOF as reported by Ogunkule et al [10] and Choudhary et al [24]. This may have been a cause of heart failure in the patient.

Uncommon anatomical variants may also be implicated in these cases as a cause of the heart failure but cardiac catheterization and contrast imaging studies were not available in the hospital and this made confirmation of their presence difficult. The visiting surgical team also alluded to it when they planned to take case one abroad, for further investigations before corrective surgery. Tetralogy of Fallot is a cyanotic congenital cardiac defect that causes secondary polycytemia [17]. It is expected that the cases would have different levels of polycytemia due to the cyanosis and decreased blood flow to the lungs caused by pulmonary stenosis [3]. The recommended treatment of polycythemia in TOF is repair of the defects or PEBT when surgery is delayed or inaccessible [16-18]. Most of the patients with cardiac anomalies seen in our environment are from low socioeconomic background and present late, often with complications. Their only hope for surgical repair lies with Non-Governmental Organizations (NGOs) or individual donors, and this may never come. We therefore resort to conservative management, which is the only available option and this seldom provides the desired outcome. This was the case with UB and NV.

Management of polycythemia in TOF should not pose a challenge but the presence of polycythemia with heart failure imposes a therapeutic challenge [16]. They were placed on oral spirinolactone and furosemide for the heart failure but case one (UB) had episodes of cardiac decompensation with PEBT despite being on oral anti heart failure drugs. These episodes of heart failure were treated with intravenous furosemide which could have worsened the existing polycythemia [16]. Case one had several sessions of PEBT. There was cardiac decompensation on two occasions after PEBT necessitating the use of intravenous furosemide despite the regular oral anti failure drugs the patient was on. He had PEBT two day before demise; this may be attributed to the procedure [22].

Partial exchange blood transfusion has been shown to increase mean arterial pressure (MAP) and decrease oxygen carrying capacity [21]. Increased MAP increases oxygen demand by the heart and causes

damage to the heart muscles [21]. Therefore, the PEBT may have caused more damage to an already ailing heart and worsened the existing hypoxic state. This may have caused the decompensation after PEBT in the reported cases [22].

Case two had two sessions of PEBT without worsening of the preexisting heart failure. On each occasion she was observed for 6 hours before discharge. She was routinely on anti-heart failure and antihypertensive drugs. It was difficult to account for the events that led to her demise as she sounded well over the phone a day prior to her demise while conversing with her managing physician. She claimed to have no complaints and was in school that day. But she died in her sleep after school the next day. Deaths that occur within 7 days of PEBT are considered PEBT related deaths [22]. The cause of death in these two cases, is therefore, assumed to be PEBT related.

Conclusion

In children with Tetralogy of Fallot in heart failure complicated by polycythemia, the risk of cardiac decompensation with PEBT should be highly considered. We, therefore, recommend that caution should be applied in carrying out PEBT especially in patients with TOF, polycythemia and heart failure who are asymptomatic. This will include observing these patients closely for at least 48 hours in order to monitor their response to the procedure to avoid worsening of the heart failure or avoiding the procedure altogether in asymptomatic patients,

List of abbreviations

CHD – Congenital heart disease
ECHO – Echocardiography
GCS – Glasgow comma scale
PCV – Parked cell volume
PEBT – Partial exchange blood transfusion
RAE – Right atrial enlargement
RVH – Right ventricular hypertrophy
RVOTO – Right ventricular outflow tract obstruction
TOF – Tetralogy of Fallot
VSD – Ventricular septal defect

Declarations

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

No conflict of interest associated with this work.

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Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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