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CASE REPORT

A fatal seizure - A large cerebral abscess in a child with uncorrected Tetralogy of Fallot: A case report

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ABSTRACT

Cerebral abscesses are relatively common among children with cyanotic heart diseases. Tetralogy of Fallot is the leading cardiac structural abnormality which leads to cerebral abscesses. Despite recent reductions in mortality largely brought forth by early diagnosis and aggressive treatment protocols including surgery and/or parenteral antibiotics, such life-threatening cerebrovascular complications are still witnessed in low-resource settings such as Sri Lanka. The resulting mortality and morbidity is potentially preventable, with high degree of suspicion, directed history and examination, guided investigations and immediate surgical or non-surgical therapy, whenever appropriate. The presentation varies but fever, behavioral changes, and focal neurological signs are common and can point towards the diagnosis. This case report discusses a 2-year-old child diagnosed with Tetralogy of Fallot who initially presented with fever and generalized malaise, subsequently developed seizures and succumbed following a large cerebral abscess which was diagnosed post-mortem. The sequence of events following the initial medical contact suggest the potential reversible nature of the acute outcome, reinforcing the knowledge that first responders including doctors should be aware of life-threatening presentations of diseases.

Keywords: Congenital cyanotic heart disease, Tetralogy of Fallot, Cerebral abscess, Paediatric

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INTRODUCTION

Tetralogy of Fallot (TOF) is the commonest cyanotic heart disease, which predisposes to brain abscesses in the newborn and child[1-5]. These cyanotic heart diseases occur either as isolated anomalies or as a part of a syndrome and/or an association[6-7]. Complications following TOF are relatively rare at present especially in developed countries due to advances in palliative surgery and complete repair during infancy[7]. In contrast, these are not uncommon in developing countries due to inadequate resources and limited or delayed access to advanced cardiac care[1,2,8], which ultimately leads to increased morbidity and mortality among the affected. The delay in diagnosis of the underlying life-threatening cerebral abscess which is not an uncommon clinical presentations and potentially treatable, emphasizes the need for a high degree of suspicion and expedited investigation and treatment as it may be missed in non-specialized clinical settings.

CASE HISTORY

A 2-year-old boy diagnosed with TOF and ventricular septal defect (VSD), presented to a private hospital with fever, poor feeding, and drowsiness for about three days. There was no history of vomiting or fits on admission. He was born following vaginal delivery to non-consanguineous parents.

Examination revealed, a conscious, ill-looking, febrile child (Temp 102ºF), with a pulse of 110/min, blood pressure of 80/60 mmHg, parasternal heave, pan systolic murmur, moderate clubbing, and conjunctival congestion. An echocardiogram revealed 50% overriding aorta, stenosis of the pulmonary artery at the infundibular and valvular level, right ventricular hypertrophy. Infective endocarditis was excluded.

He was transferred to a government hospital based on financial, administrative, and clinical reasons after about 12 hrs. On admission to the second health care institution, the child developed one episode of generalized tonic colonic movements of a few minutes duration with spontaneous recovery. The child was treated empirically with intravenous ceftriaxone and metronidazole for sepsis. Arterial blood gas analysis revealed severe hypoxemia with metabolic acidosis. X-ray chest revealed right ventricular hypertrophy, uplifted apex, and oligaemic lung fields. CT brain was opted but was not available at this point. The child's condition rapidly deteriorated and he succumbed within six hours of admission.

The reports received after death showed a raised white blood cell count of 30,000/mm^3, (neutrophils - 87%, lymphocytes - 4.4%), platelet count of - 265,000/mm^3, haemoglobin level of 19 g/dl, hematocrit of 60%, and CRP of 133 mg/l.

He had been followed up and further investigated for the above condition at three-monthly intervals since birth and had been referred to a pediatric cardiothoracic surgeon for surgical correction at 12 months of age with suggestions for a Blalock (BT) shunt if significant desaturation developed before surgery. Surgery was planned at 18 months of age, but, was delayed twice due to the COVID-19 pandemic.

A Judicial postmortem examination was ordered by the inquirer into sudden death.

The autopsy revealed features of failure to thrive, fingernail clubbing, features of TOF during cardiac dissection revealing a large VSD with accompanying overriding of aorta, right ventricular hypertrophy and pulmonary stenosis, (**Fig. 1**).

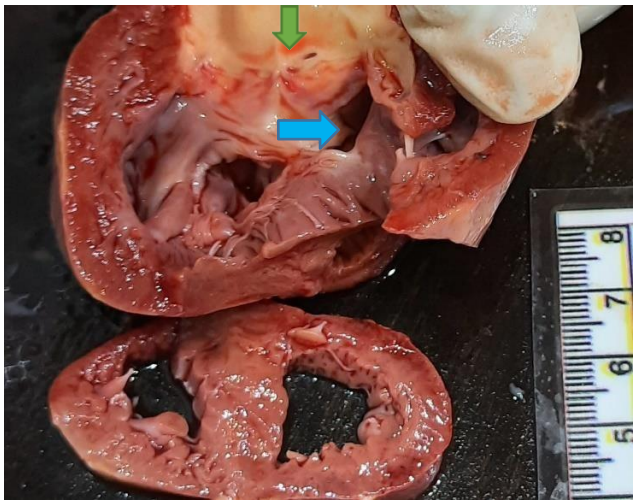

Figure 1: Large VSD (blue arrow) and 50% overriding aorta (green arrow), with right ventricular hypertrophy

There was oedema of the brain (weight of 1200 g), obliterated gyri and flattened sulci, a large purulent abscess (5x7x6 cm) within the right cerebrum which had ruptured into the right ventricle and purulent cerebrospinal fluid (CSF). (**Fig. 2, 3, 4**)

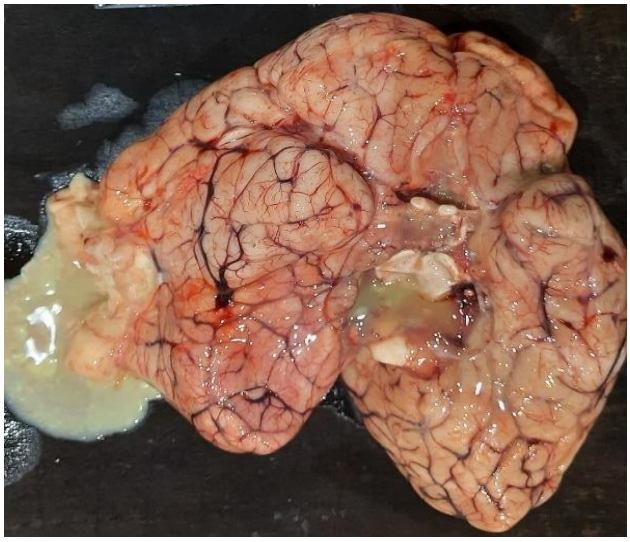

Figure 2: Turbid colour CSF leaking at the base of the brain and post mortem rupture of the abscess

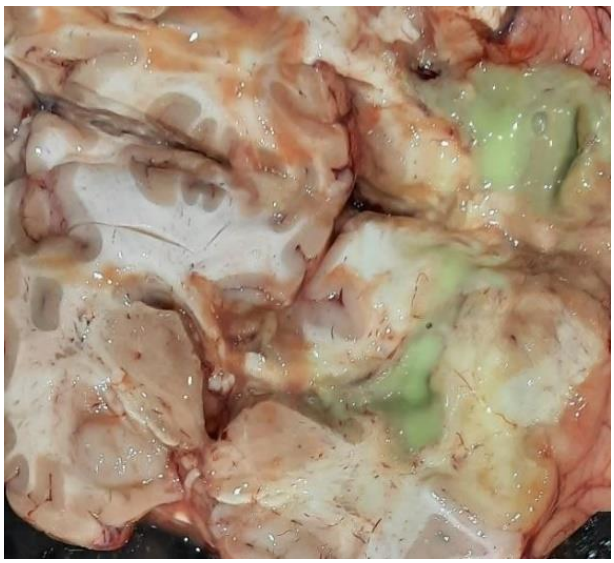

Figure 3: Isolated large abscess of right parietal lobe ruptured into lateral right ventricle

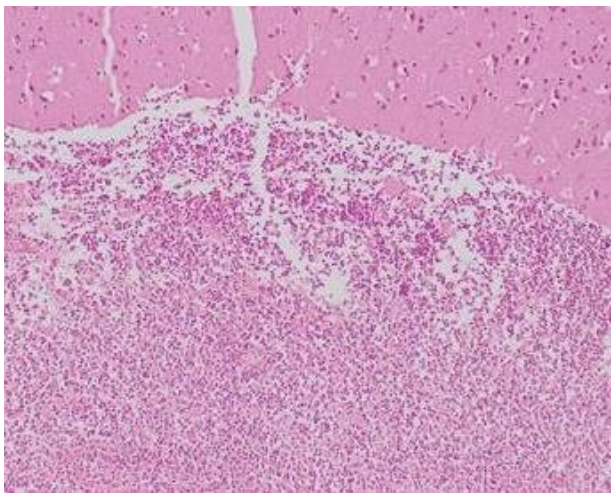

Figure 4: Collection of leukocytes with predominant neutrophil abscess with borderline brain parenchyma (H&E low power)

The spleen was diffluent and there were adrenal haemorrhages. Meninges were unremarkable. Blood and Pus culture did not yield any organisms. Full histological analysis of internal organs was performed and the cause of death was elucidated as sepsis following brain abscess in a child with Tetralogy of Fallot.

DISCUSSION

According to the most recent statistics, around 0.5-0.8 % of live births are complicated by congenital heart diseases (CHD)[7]. The incidence is tenfold higher in the stillborn[6]. Approximately 12% of the patients with CHDs have chromosomal defects. The causality is mostly multifactorial, precipitated by a complex interplay between genetic and environmental factors[6]. Implicated cardiovascular teratogens include maternal infections, drugs, and maternal diabetes which interfere with the normal development of progenitor cells of the primary and secondary heart field, neural crest cells, and endocardial cushions[6]. TOF represents 5-7% of all congenital heart diseases and 9.6/10000 live births[6-7]. This has been attributed as the leading cause of brain abscess in children[1,2,4].

The right to left shunting of blood in TOF results in bypassing the phagocytic activity of lungs which allows direct entry of this unfiltered blood into cerebral circulation, seeding of microorganisms, and consequent abscess formation[8,9]. Low perfusion of selected areas in the brain due to associated polycythemia leads to tissue hypoxia and acidosis[10]. Decreased oxygenation of blood due to pulmonary stenosis and pulmonary shunting through septal defects further aggravate the tissue hypoxia and acidosis.

In cyanotic congenital heart disease, microorganisms in shunted blood could lead to a cerebral abscess. [8] Most commonly, cerebral abscesses are caused by *Streptococcus milleri* and are rarely due to *Peptostreptococcus, Streptococcus intermedius, Bacillus* species, and *Staphylococcus epidermidis*[4,5]. Interestingly, however, no organisms have been identified in cultures in some studies[11] which is similar to our case, where blood and the pus culture revealed no growth. This may be due to the time lapse between death and postmortem examination, delays in collection, errors in sampling, delays in transport to the laboratory[11], and prior treatment with intravenous antibiotics. With regard to the outcome following cerebral abscess, the mortality is around 10-12% with significantly reduced long-term morbidity (up to 30 to 50%) in developed countries[13-17]. A large cohort study based on two centers in London and Paris which included 144 infants and children, reported a mortality rate of 4% and approximately 80% of acceptable outcomes[13]. The main explanations may relate to the availability of radiological studies (MRI) leading to early diagnosis, improvements in surgical techniques facilitating safer access to abscesses, and the utility of broad-spectrum antibiotics. If the cerebral abscess was diagnosed earlier with CT/ MRI scan, this child could have survived with timely, empirical antibiotics and/ or surgical drainage.

In contrast to developed countries where, ear, nose and throat infections are the commonest precipitants of cerebral abscess among children[13], cyanotic CHD is still largely responsible for the latter in developing countries[1-5]. This noticeable difference may be due to the early correction of congenital heart disease by advanced surgery in high-resource settings of developed countries. In this particular child, surgical correction had been planned but delayed due to longer waiting times and the ongoing COVID-19 pandemic.

In general, complications such as cerebral abscess and cerebral thrombosis usually occur after the age of two years in cyanotic CHD[7]. Several anatomical variants have been discussed in the literature, which might lead to differing clinical course and symptomatology. In 'Pink type TOF' minimal or no right ventricular out flow tract obstruction (RVOTO) is witnessed. 'Profound cyanosis TOF' denotes a complete RVOTO and the 'classic TOF' describes a partial RVOTO and overriding of aorta[19]. In autopsy studies in patients with TOF who present following sepsis, it is imperative to look for possible foci. Cerebral abscesses are the commonest foci. However, infective endocarditis and pulmonary infections should also be looked for.

There is a possibility of litigation regarding the outcome, delay in corrective surgery and diagnosis, and definitive treatment of this child. Increased demand for surgical interventions amidst limited skilled manpower and resources, reduced access to sophisticated investigations and therapy play an important role in determining outcomes in these time-critical medical conditions in developing countries.

CONCLUSION

Despite considerable advances in the diagnosis and management of TOF and resultant cerebral abscess, the incidence of mortality and morbidity is still high among the paediatric population in developing countries. Developing and upgrading relevant diagnostic and therapeutic modalities and enhanced and timely access to health care would have a definite and positive impact on the short and long-term outcomes.

CONFLICTS OF INTEREST

There are no conflicts of interest.

ETHICAL ISSUES

Informed, written consent was taken from the parents prior to preparation of the manuscript and publication of relevant medical details and clinical images.

AUTHOR CONTRIBUTIONS

SR: clinical work, conception, data acquisition, initial drafting, revising, final approval; **SP**: clinical work, initial drafting, revising, final approval; **BMM:** conception, initial drafting, revising, final approval.

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