

Intracerebral hemorrhage in an adult patient with Tetralogy of Fallot

Case report and review of the literature

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Abstract

Rationale: Tetralogy of Fallot (TOF) accounts for approximately 5% of all congenital heart disease. However, only 1% of patients with TOF survive to the age of 40 years without undergoing surgery. Additionally, the relationship between intracerebral hemorrhage and unrepaired TOF remains unknown. We report a rare case of unrepaired TOF in a patient who presented with intracerebral hemorrhage, and we also present a literature review.

Patient concerns: A 40-year-old man presented with headache and right-sided limb weakness.

Diagnoses: He was diagnosed with TOF approximately a year prior to presentation and did not undergo any definitive treatment or any symptomatic management. Head computed tomography revealed an intracerebral hematoma in the left basal ganglia. The patient was drowsy, and his blood oxygen saturation was 77%.

Interventions: Owing to his poor cardiopulmonary status, the patient did not undergo surgery and was treated with only symptomatic supportive therapy.

Outcomes: After 2 days of therapy, his disturbance of consciousness and motor ability showed improvement.

Lessons: Literature reviews reveal that intracerebral hemorrhage is rarely observed in patients with TOF, and to date, only 3 cases have been reported. Furthermore, this patient was 40 years old and did not undergo cardiac surgery. Severe hypoxia, as well as low levels of platelets and coagulation factors in the blood could have led to intracerebral hemorrhage.

Abbreviations: ALGS = Alagille syndrome; APTT = activated partial thromboplastin time; BP = blood pressure; CT = computerized tomography; ICH = intracerebral hemorrhage; PT = prothrombin time; SpO₂ = oxyhemoglobin saturation; TOF = tetralogy of Fallot; VSD = ventricular septal defect.

Keywords: coagulation, intracerebral hemorrhage, oxygen saturation, tetralogy of Fallot

1. Introduction

Tetralogy of Fallot (TOF) is the most common congenital cardiac malformation observed in clinical practice.^[1] Owing to prolongation of life expectancy in patients with TOF, managing chronic multisystem diseases has become difficult.^[2] Intracerebral complications including brain ab-

scences, stroke, and subarachnoid hemorrhage (SAH) are relatively common and have been reported previously in patients with TOF.^[3,4] However, the occurrence of intracerebral hemorrhage (ICH) in patients with TOF has rarely been reported previously. Moreover, surgical repair is important to prevent chronic hypoxia, which can precipitate changes in the pathophysiological environment in the brain.^[5] The relationship between ICH and unrepaired TOF remains unclear. We report the case of a 40-year-old man with unrepaired TOF who presented with serious ICH. Additionally, we present a discussion regarding the pathomechanisms related to this condition.

2. Case presentation

The study was approved by the Biological and Medical Ethics Committee of West China Hospital, and written informed consent was obtained from the patient and his legal surrogate. A 40-year-old man was admitted to the emergency department with headache and right-sided limb weakness a day prior to presentation. He was diagnosed with TOF approximately a year prior and did not undergo any definitive treatment or symptomatic management. Physical examination was significant for the following findings: drowsiness, paralysis of the right upper and lower limbs, die blausucht, and clubbing of his digits. The muscle strength of right limb was second grade. The Glasgow Coma Score was 12. Blood pressure was 135/85 mm Hg, and heart rate was 68 beats per minute. The oxygen saturation (SpO₂) was 77% (on room air).

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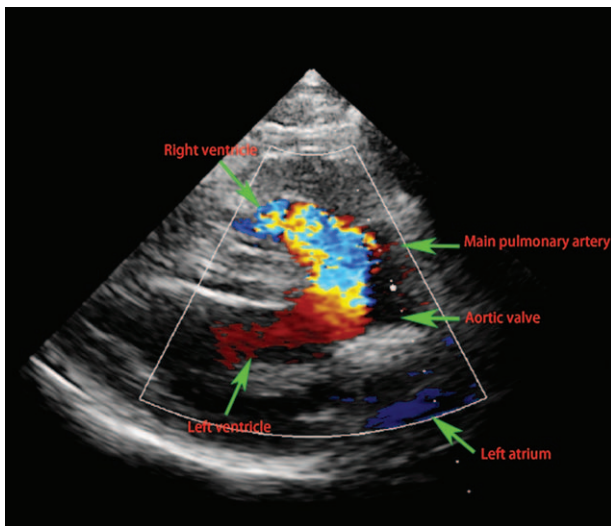


Figure 1. Echocardiographic images reveal a normal left ventricular ejection fraction (63%), over-riding of the aorta and a wide ventricular septal defect (VSD) with bidirectional shunting. The right ventricular systolic pressure is observed to be 120 mm Hg with right ventricular hypertrophy. Severe pulmonary stenosis is observed with a peak gradient of 97 mm Hg. VSD=ventricular septal defect.

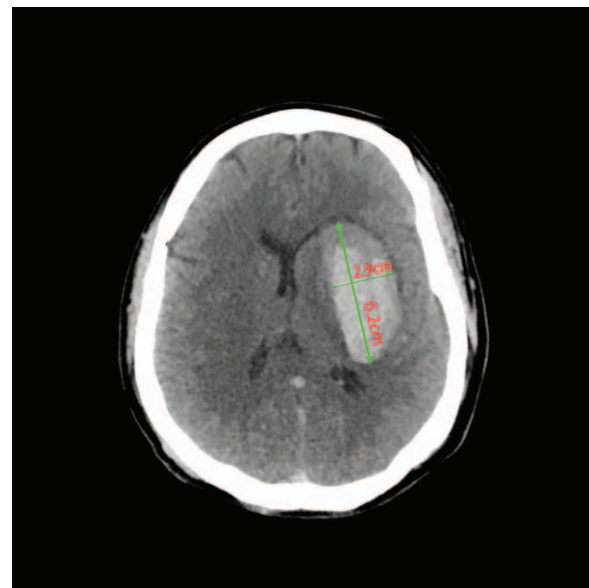


Figure 2. Head computed tomography (CT) scan upon admission shows an intracerebral hematoma in the territory of the left basal ganglia (measuring 6.2×2.9×4.7 cm in size with a volume of 42.2 mL), a midline shift, a reduction in the size of the left lateral ventricle and shallow sulci. CT = computed tomography.

Upon admission, laboratory tests revealed hemoglobin of 257 g/L and packed cell volume of 74.2%. The platelet count was at the lower range of normal at 99 to $111 \times 10^9/L$ on several occasions, creatinine was $290.0 \mu\text{mol/L}$, and urea was 11.80 mmol/L . Baseline prothrombin time (PT) and activated partial thromboplastin time (APTT) were observed to be elevated at 23 and 53.2 seconds, respectively.

His electrocardiogram suggested a sinus rhythm, right ventricular hypertrophy, and an incomplete right bundle branch block. Echocardiography revealed a normal left ventricular ejection fraction (63%), over-riding of the aorta, and a wide ventricular septal defect (VSD) with bidirectional shunting (Fig. 1). The right ventricular systolic pressure was estimated to be 120 mm Hg with right ventricular hypertrophy. Severe pulmonary stenosis (PS) with a peak gradient of 97 mm Hg was also observed. Head computed tomography (CT) revealed an intracerebral hematoma in the left basal ganglia (measuring $6.2 \times 2.9 \times 4.7 \text{ cm}$ in diameter with a volume of 42.2 mL), a midline shift, a reduction in the size of the left lateral ventricle, and shallow sulci (Fig. 2).

Based on the patient's poor cardiopulmonary function, the patient was considered a poor surgical candidate. Therefore, we strictly monitored the vital signs and took symptomatic treatment for the patient. Optimization of pharmacological treatment was performed with the administration of the following: mannitol 150 mL b.i.d., dezocine 5 mg b.i.d., and oxygen therapy. Clinical evaluation repeated 2 days after the institution of the aforementioned regimen showed that the patient's level of consciousness and SpO_2 had improved, and his Glasgow Coma Score was 14. After 10 days of treatment, the vital signs of patient were stable. The muscle strength of right limb tended to third-grade and the Glasgow Coma Score was 14. Then, the patient transferred to the local hospital and took symptomatic treatment for 1 month. Six months after onset, physical examination was significant for the following findings: clear consciousness, the muscle strength of right limb was fourth-grade. The Modified Rankin Scale (MRS)

was 2 and Glasgow Coma Score was 15. The patient did not receive any treatment for tetralogy of Fallot. The oxygen saturation (SpO_2) was 85% (on room air). The repeated non-enhanced CT showed the hematoma was absorbed without ischemic nidus.

3. Discussion

TOF is the most common congenital cardiac malformation, which accounts for approximately 5% of all congenital heart disease observed in clinical practice.^[1] It occurs in approximately 0.28 cases per 1000 live births. The key morphological abnormalities include:^[1] A malalignment defect, primarily a VSD,^[2] the aorta over-riding the VSD,^[3] right ventricular outflow tract obstruction,^[4] secondary concentric right ventricular hypertrophy. Only 1% of patients with TOF survive to the age of 40 years without surgical repair. Reportedly, the primary causes of death are hypoxic spells (62%), cerebrovascular accidents (17%), and brain abscesses (13%).^[6] Our patient was a 40-year-old man with an unrepaired TOF. In fact, longevity in such patients has been associated with the development of collateral circuits in the systemic-pulmonary circulation, balanced shunts between the right and the left ventricle, and balanced pulmonary valve stenosis, which allow sufficient passage of blood into the pulmonary artery.^[7,8] In our patient, although severe pulmonary valve stenosis and progressive right ventricular hypertrophy were observed, the progressive right ventricular hypertrophy could maintain sufficiency of the pulmonary vascular bed owing to hyperinflation (the so-called balanced PS). Additionally, an electrocardiogram showed a wide VSD with a bidirectional Doppler signal. The well-balanced shunt, almost at rest, and the presence of collateral circuits could have contributed to the longevity of our patient.

Cardiovascular accidents are common complications in patients with TOF. To date, 3 case reports^[9–11] in the literature have described patients with TOF presenting with ICH (Table 1).

Table 1**Literature review of all the cases of TOF with ICH.**

Author, Year	Cause of ICH	Hemorrhage type	Age, years, Sex	Location
Fiorda-Diaz et al, 2017 ^[11]	ALGS with aneurysms	SAH	17, F	Right frontal lobe
Kaplan et al, 2006 ^[10]	Brain abscess	Intracavitary hemorrhage	6, M	Right temporal lobe
Imazumi et al, 2001 ^[9]	Chronic hypoxia	Intracerebral hematoma	2, F	Left frontal and temporal lobes

ALGS = Alagille syndrome, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, TOF = tetralogy of Fallot.

Kaplan et al^[10] described a patient with TOF who presented with hemorrhage into a brain abscess cavity. The incidence of brain abscesses is approximately 13% in patients with TOF.^[6] This is more likely to occur in those with TOF concomitant with pulmonary hypertension and predominantly right-to-left shunting.^[4] Although the related pathophysiological mechanisms are not well understood, severe inflammation around lesions is likely to damage the vasculature and the blood brain barrier.^[12] Moreover, a significantly elevated hematocrit level and hypoxia could also affect cardiovascular function, with consequent hemorrhage.^[4] Fiorda-Diaz^[11] reported the case of a patient diagnosed with Alagille syndrome (ALGS) and unrepaired TOF who developed a ruptured intracranial aneurysm with concomitant SAH. Approximately 12% of patients with ALGS accompany TOF.^[13] ALGS is a genetic disorder associated with multisystem dysfunction involving the hepatic, cardiovascular, and neurological systems with accompanying cerebrovascular abnormalities such as aneurysms and vascular stenosis.^[11] Intracranial bleeding is a significant cause of mortality in patients with ALGS; thus, patients with ALGS concomitant with TOF should be monitored closely for the risk of ICH.

To our knowledge, this is the first reported case of unrepaired TOF in a 40-year-old patient with ICH. In this patient, head CT showed no brain abscesses or aneurysms. Laboratory tests revealed that his platelet count was at the lower range of normal. Additionally, the PT and APTT were prolonged. Worsening hypoxia tends to cause chronic cyanosis that affects multiple organ systems. Therefore, patients are at a high risk for both, thrombosis and hemorrhage. These patients usually present with mild thrombocytopenia caused by ineffective thrombopoiesis and diminished platelet survival.^[14] Patients are also predisposed to bleeding secondary to alterations in the numbers and functions of platelets, as well as coagulation factors.^[15] Additionally, because of hepatic congestion and abnormalities in the vitamin K-dependent coagulation factors, PT and APTT are usually abnormal with an increase of 20%, which increases the risk for bleeding.^[16] Moreover, in our patient, the SpO₂ was only 77% on room air. Severe long-term hypoxia could damage the cardiovascular structure and function. Therefore, in our patient, a low platelet count and abnormalities of coagulation factors, as well as severe hypoxia could be considered contributory pathophysiological mechanisms that damaged his vasculature and led to an increased risk of ICH.

In patients with long-term hypoxia caused by TOF, all organs, particularly the brain (nervous tissue) tends to develop tolerance to the hypoxemia. Patients showing ICH with a large hematoma (a supratentorial hematoma with a volume >30 mL)^[17] always present with severe disorders of consciousness such as coma and need surgical treatment. However, our patient who presented with a supratentorial hematoma that was observed to be 42 mL in volume showed only a slight disturbance of consciousness upon admission. Additionally, the patient's SpO₂

was 77%, which was significantly lower than the threshold of hypoxemia (SpO₂ < 90%). All these findings could be explained by the fact that the brain tissue in this patient developed tolerance to hypoxemia secondary to the presence of a long-term right-to-left shunt. Selection of treatment is a balance of risks and benefits. The patient with a large supratentorial hematoma always needs surgical treatment. However, he also had high risks of surgical treatment owing to the poor cardiopulmonary function, abnormal coagulation factors and platelets and lower oxygen saturation. Therefore, the treatment needs to be carefully considered. In our case, the patient did not present disorders of consciousness and had stable vital signs. Under conservative treatment, the patient's condition remained stable. And after 6 months of follow-up, the oxygen saturation has improved and CT showed the hematoma was absorbed without ischemic nidus. These indicate that medical treatment might be a better choice for such patients.

4. Conclusion

In this case study, we describe a 40-year-old patient with unrepaired TOF who presented to the emergency department with ICH in the territory of the left basal ganglia. Although only 1% of patients with TOF survive to the age of 40 years without undergoing cardiac surgery, balanced pulmonary valve stenosis and the development of shunts could have contributed to the longevity of our patient. Current evidence suggests that severe hypoxia, as well as low blood levels of platelets and coagulation factors play an important role in weakening vessel walls and predisposing patients to a higher risk for hemorrhage. Although this patient could not undergo surgery for evacuation of the hematoma owing to his poor cardiopulmonary condition, his mental and motor condition improved after several days' symptomatic supportive treatment. Therefore, adults with unrepaired TOF are at a high risk of ICH secondary to severe long-term hypoxia. Symptomatic supportive treatment was effective in improving our patient's mental and motor condition.

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