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【 CASE REPORT 】

Moyamoya Disease Complicating Ebstein's Anomaly

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Abstract:
Ebstein's anomaly is an uncommon congenital disorder affecting the tricuspid valve. We herein report a 38-year-old woman who experienced consciousness and sensory disturbance during treatment for heart failure caused by Ebstein's anomaly. Urgent magnetic resonance imaging and cerebral angiography demonstrated acute cerebral infarction and internal carotid artery obstruction with the development of collateral arteries. We diagnosed her with multiple cerebral infarctions due to moyamoya disease. Ebstein's anomaly concomitant with moyamoya disease is extremely rare. However, we should consider the possibility of this rare but important concurrence when treating patients with heart failure due to Ebstein's anomaly to avoid excessive diuresis and vasodilation and irreversible brain injury.

Key words: cerebral infarction, Ebstein's anomaly, heart failure, moyamoya disease

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Introduction

Ebstein's anomaly is a rare congenital malformation of the tricuspid valve (TV) with an incident rate of about 1.0 per 20,000 live births (0.005%), accounting for less than 1% of all causes of congenital heart disease (1, 2). Ebstein's anomaly is defined as apical displacement of the septal leaflet of the TV from the insertion of the anterior mitral leaflet exceeding 8 mm/m^2 body surface area, resulting in atrialization of the right ventricle (3).

Moyamoya disease is a chronic cerebrovascular disease characterized by bilateral progressive stenosis and occlusion of a terminal portion of the internal carotid artery and/or proximal portion of the anterior cerebral arteries and middle cerebral arteries (4). Collateral vascular networks develop to compensate for moyamoya vessels (*moyamoya* is a Japanese word meaning 'hazy', like a puff of smoke). In Japan, the prevalence of moyamoya disease is 10.5 per 100,000 individuals and the incidence rate is 0.94 per 100,000 individuals (5, 6).

Ebstein's anomaly is often associated with other congenital cardiac diseases, such as atrial septal defect (ASD), ventricular septal defect (VSD) and pulmonary stenosis, and about 19% of cases are associated with non-cardiac defects (2). However, Ebstein's anomaly concomitant with moyamoya disease is extremely rare.

We herein report a case of Ebstein's anomaly complicated by cerebral infarction due to moyamoya disease during treatment for heart failure.

Case Report

A 38-year-old woman presented to our hospital with persistent cough and lower leg edema. She had been diagnosed with Ebstein's anomaly at nine months old and had been followed-up without intervention. Her subjective symptoms were classified as New York Heart Association (NYHA) functional class II, and her serum brain natriuretic peptide (BNP) levels were within normal range. At 25 years old, Caesarean section had been performed at 28 weeks' gestation for maternal adaptation due to the development of heart failure. An angiotensin-converting enzyme (ACE) inhibitor, mineralocorticoid receptor antagonist and loop diuretics were subsequently prescribed continuously for several years. However, the patient had suddenly stopped visiting the hospital six years before this presentation despite exercise intolerance.

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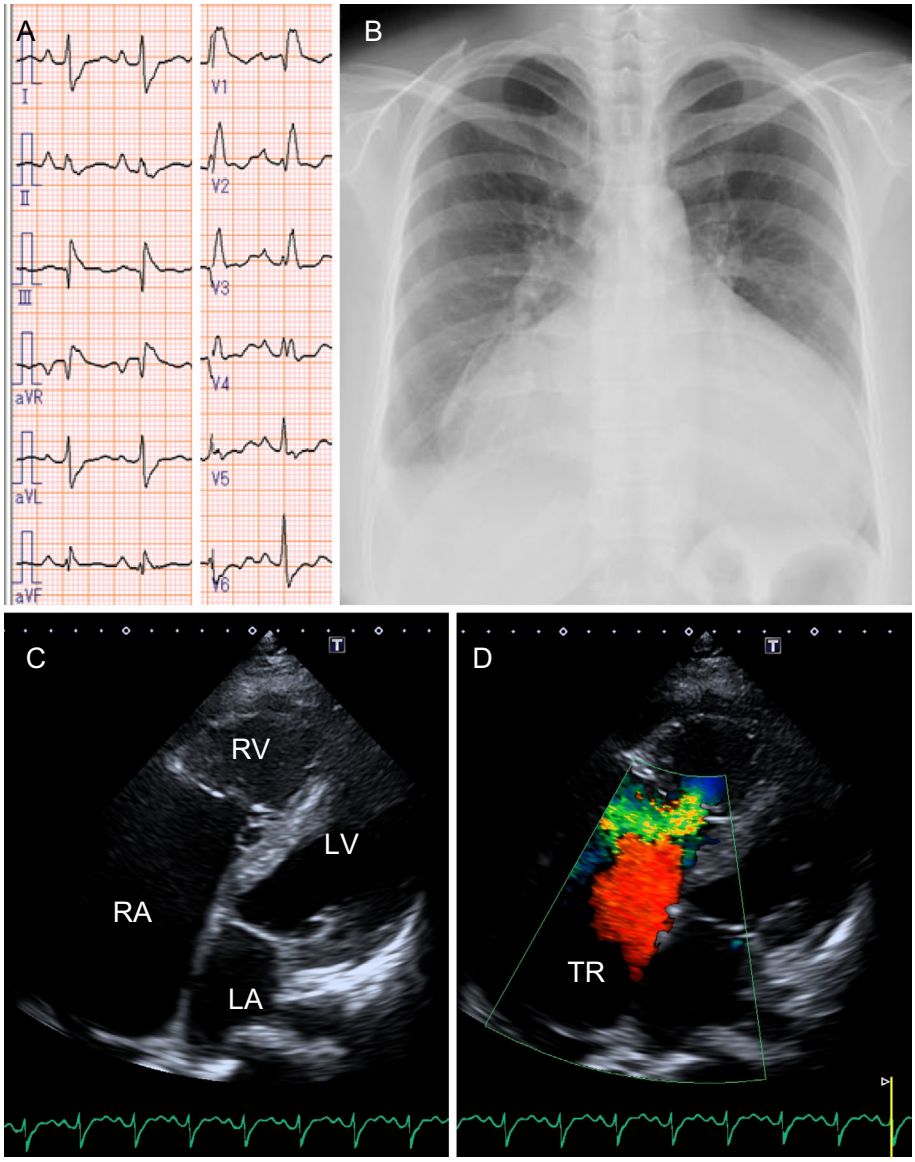

Figure 1. Multi-modal imaging demonstrating the findings in the present case. A: Electrocardiographic findings on hospital day 1 showing sinus tachycardia, pulmonary P waves in leads II and aVF and complete right bundle branch block. B: Supine chest X-ray showing prominent cardiomegaly and pleural effusion. C: Transthoracic echocardiography showing 29-mm (17.6-mm/m^2) apical displacement of the septal tricuspid leaflet from the insertion of the anterior mitral leaflet. LA: left atria, LV: left ventricle, RA: right atria, RV: right ventricle, D: Color Doppler imaging showing severe tricuspid regurgitation (TR).

One week before this presentation, she had developed dyspnea and exercise intolerance (NYHA III) with an increase of 5 kg in body weight. According to her, she had never complained of cyanosis, chest pain or presyncope. On admission, her blood pressure was 191/125 mmHg, her heart rate was 105 beats/min, and peripheral oxygen saturation was 98%. A physical examination revealed facial flushing, prominent jugular vein dilation and prominent leg edema. Auscultation showed regular tachycardia with gallop rhythm and systolic murmur (Levine II/VI) at the left parasternal area. Electrocardiography revealed sinus tachycardia, pulmonary P waves and complete right bundle branch block (Fig. 1A). Chest X-ray showed marked cardiomegaly with a cardiothoracic ratio of 83% and bilateral pleural effusion (Fig. 1B). Echocardiography showed apical displacement of the septal TV 29 mm (17.6 mm/m^2) into the right ventricle (RV) and mild pericardial effusion (Fig. 1C). The septal TV leaflet was tethered to the septum associated with severe tricuspid regurgitation (TR) and right atrial enlargement (53× 90 mm) (Fig. 1D). The left ventricular ejection fraction was 65%. No other cardiac malformations, including ASD, were detected. The BNP level was markedly elevated (707 pg/mL), and polycythemia (hemoglobin 17.9 g/dL) was observed. No diabetes or dyslipidemia was recognized. Mild renal dysfunction (estimated glomerular filtration rate, 39.5 mL/min/1.73 m^2; creatine, 1.25 mg/dL) and massive protein-

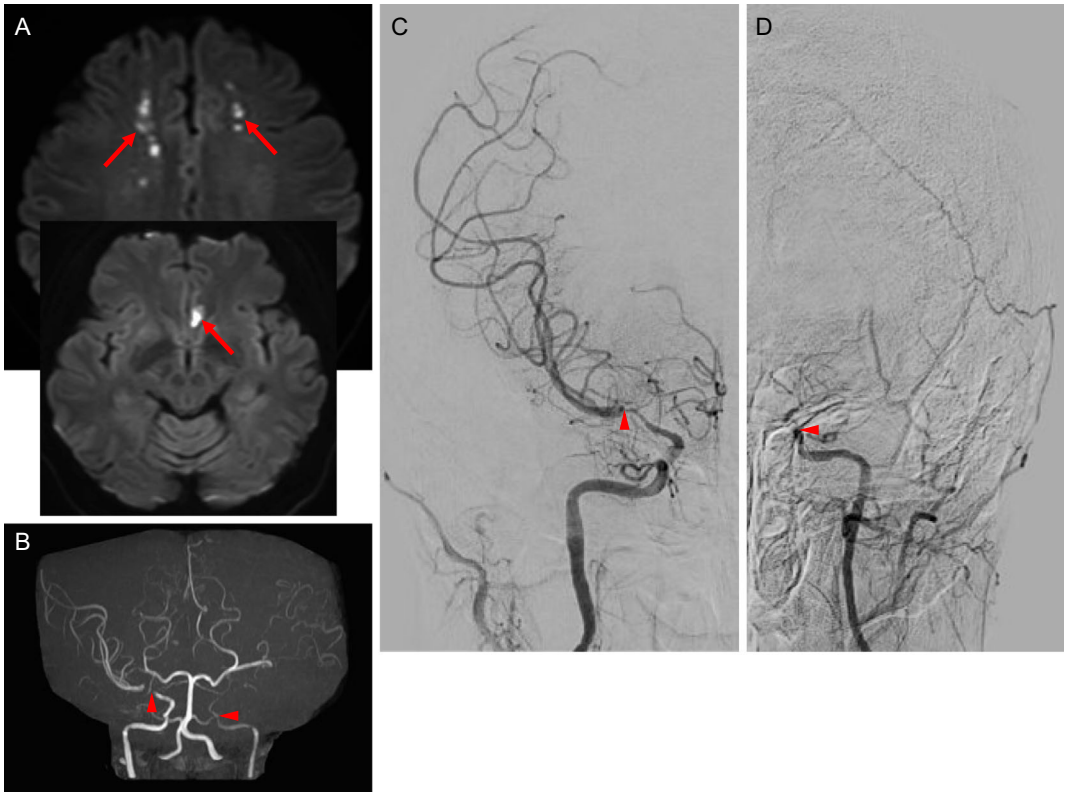

Figure 2. **Brain magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and selective angiography. A: Diffusion-weighted MRI showing acute ischemic infarction (red arrows) in the bilateral frontal lobes (upper panel) and in the left genu of the corpus callosum (lower panel). B: MRA showing stenosis and occlusion of the terminal portions of the internal carotid arteries (red arrowheads). C, D: Selective cerebral angiogram showing severe stenosis (red arrowheads) from the right internal carotid artery to the middle cerebral artery (M1 portion), occlusion of the left carotid artery, and right (C) and left (D) carotid injection, frontal views.**

uria (3.11 g/g·Cr) were identified.

She was admitted to our hospital with a diagnosis of heart failure due to Ebstein's anomaly. Administration of an oral antihypertensive (ACE inhibitor) and diuretics (loop diuretics and tolvaptan) was initiated. As hypertension persisted, we added isosorbide dinitrate and increased the dose of loop diuretics. Renal congestion subsequently improved, the renal function normalized, and the proteinuria disappeared. From the day after admission, the patient complained of headache and dysesthesia from the neck to the fingertips on the left side. She eventually became unable to maintain a sitting position due to mild headache and dysesthesia. Her blood pressure was 150-160/90-110 mmHg, and her heart rate was 80-100 beats/min without arrhythmias. Intravenous hydration was performed after isosorbide dinitrate tape and tolvaptan were discontinued.

On hospital day 5, the patient suddenly developed disturbance of consciousness (Glasgow Coma Scale score, E4 V2 M1) and convulsive seizures for 30 s despite a blood pressure of 149/104 mmHg and a heart rate of 80 beats/min. After 5 min, her consciousness fully recovered, and the patient reported weakness in the left arm. All neurological abnormalities faded spontaneously. We consulted a neurologist, and diffusion-weighted magnetic resonance imaging showed multiple patchy high-intensity lesions representing acute ischemic infarction in the bilateral frontal lobes and in the left genu of the corpus callosum (Fig. 2A). Magnetic resonance angiography revealed stenosis (right) and occlusion (left) of the bilateral terminal portions of the internal carotid arteries (Fig. 2B). Cerebral angiography confirmed severe stenosis from the right internal carotid artery to the middle cerebral artery (M1 portion) (Fig. 2C), and the occluded left carotid artery showed development of collateral arteries (Fig. 2D). Electroencephalography showed no abnormalities. Cerebral infarction was diagnosed due to moyamoya disease concomitant with Ebstein's anomaly. An antiplatelet drug and edaravone were started, and the dosages of ACE inhibitor and loop diuretic were further reduced.

We discussed this case with the heart and brain team and transferred the patient to the National Cerebral and Cardiovascular Center for combined revascularization surgery for moyamoya disease at the earliest opportunity. Once the neurosurgical condition has settled down, the patient will be considered for reconstructive surgery for Ebstein's anomaly.

Discussion

Ebstein's anomaly can present at any age and tends to be

severe in younger patients and mild in older patients. However, even in milder forms, patients often eventually develop easy fatigability and right heart failure, as in the present case (7). Our patient had not developed overt heart failure until this admission, probably because she had no other cardiac defects and only developed hypertension very recently. As much as 19% of patients with Ebstein's anomaly show non-cardiac defects, whereas about 50% are associated with other cardiac defects (2, 8). We therefore should consider the possibility that patients may have other defects when we treat patients with heart failure due to Ebstein's anomaly.

Non-cardiac defects involve the craniofacial region, central nervous system or limbs. To our knowledge, however, Ebstein's anomaly concomitant with moyamoya disease has not been reported previously in MEDLINE. Just one case was recognized outside of MEDLINE, in a 15-year-old girl presenting with seizure episodes (9). The coexistence of these two diseases is thus extremely rare. The exact embryological mechanisms remain unclear (10), and we cannot rule out the possibility that Ebstein's anomaly was only coincidentally complicated with moyamoya disease in this patient.

In contrast, moyamoya disease has been associated with congenital heart conditions such as coarctation of the aorta, VSD, aortic and mitral valve stenoses, and tetralogy of Fallot (11). The pathophysiological mechanisms underlying moyamoya disease also remain poorly understood. Previous experimental studies have supported the presence of abnormalities in angiogenic pathways and cellular proliferative signaling cascade at the base of both native revascularization and vessel stenosis or occlusion (12). We speculated that multiple gene mutations might have contributed to the development of both Ebstein's anomaly and moyamoya disease in the present case, as these entities are said to develop due to multifactorial causes, including gene mutations, chromosomal rearrangements and environmental factors (10, 11).

In the present case, we speculate that excessive diuresis and vasodilation exacerbated brain ischemia, leading to cerebral infarction and seizures. Indeed, dehydration may precipitate ischemic symptoms in moyamoya disease (13). Our patient was also unable to sit up due to headache and dysesthesia, probably because the sitting position prevented a sufficient venous return to maintain the blood flow to the ischemic cerebral area compared with the supine position.

In conclusion, we encountered an adult woman with Ebstein's anomaly complicating cerebral infarction due to moyamoya disease during treatment for heart failure. It is unnecessary to screen for cerebrovascular disease in all cases of Ebstein's anomaly in terms of cost-effectiveness and prevalence. However, when any minor neurological abnormalities appear, imaging studies, such as magnetic resonance imaging should be performed as soon as possible. We should take this rare but important coincidence into careful consideration to avoid excessive diuresis and vasodilation leading to irreversible brain damage.

The authors state that they have no Conflict of Interest (COI).

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