Progressive Memory Decline in a Patient With Atrial Septal Defect: Case Report and Literature Review

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ABSTRACT: Atrial septal defect (ASD) is a common congenital anomaly that increases the risk of heart failure as well as strokes which can lead to cognitive impairment. The risk of stroke is higher when pulmonary hypertension develops and there is reversal of shunt. Stroke in ASD may be due to paradoxical emboli from the right heart or a left ventricular thrombus which develops as a result of atrial fibrillation, a common arrhythmia in ASD. We present a case of a 32-year-old Ghanaian man with history of ASD who presented with progressive memory loss with magnetic resonance imaging scan of the brain showing multiple infarcts, microvascular disease, and cerebral atrophy.

KEYWORDS: Atrial septal defect, cognitive impairment, congenital heart disease, cardioembolic strokes, Kumasi

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Introduction

Certain cardiovascular diseases have been associated with increased risk of cognitive impairment.[1] Cerebral hypoperfusion as a result of cardiovascular disease such as left ventricular systolic dysfunction, pulmonary arterial hypertension, and obstructive sleep apnea may lead to cognitive impairment by causing loss of grey matter in certain areas of the brain.[2-5] Survivors of cyanotic congenital heart disease (CHD) also have increased risk of neurocognitive impairment which may persist beyond childhood.[6] For example, neonates with transposition of the great vessels and hypoplastic left heart syndrome have delayed structural brain development compared to controls.[7] Also, children with tetralogy of Fallot who survive after undergoing Fontan procedure have cognitive outcomes lower than the general population.[8] Pediatric patients with heart failure without underlying co-morbid cardiovascular risk factors exhibit similar changes.[6]

Interestingly, the risk of cognitive impairment is also found in acynotic CHD such as septal defects. Children with atrial or ventricular septal defect relatively have lower intelligence quotient, memory, perceptual reasoning, visuospatial scores as well as structural brain abnormalities on imaging even years after correction of the septal defect.[9]

Cognitive impairment in ASD may be due to cardioembolic causes from micro-thrombi causing microvascular disease or from stroke due to paradoxical emboli or left ventricular thrombus as a result of atrial fibrillation which is the commonest arrhythmia in ASD.[10-14]

As a result of improved medical and surgical management of patients with congenital heart disease, there is significant survival especially in developed countries, where adult congenital heart disease now make up 66% of total congenital heart diseases.[15] As much as 41% of these patients show impaired cognitive function compared to the general population (8%).[16] The more complex the CHD, the higher the extent of cognitive impairment, limitation in education and employment.[17]

We report a case of a young Ghanaian man diagnosed with ASD who later presented with gradual memory decline as a result of infarctive stroke and cerebral microvascular disease possibly from paradoxical embolus.

Case Report

A 32-year-old man with no known chronic medical illness presented to a private cardiac outpatient clinic in Kumasi, Ghana with increasing forgetfulness over a period of 1 year; affecting his work as a mobile banker. He had no known risk factor for cardiovascular disease such as hypertension, diabetes mellitus, or dyslipidaemia. He neither had history of head injury nor family history of dementia. He is single, lives with his mother, and does not take alcohol, smokes cigarette or takes recreational drugs.

On physical examination, he looked well, not cyanotic, afebrile and was not pale. His blood pressure was 104/61 mmHg with a pulse rate of 70 beat/minute, regular, and of good volume. On examination of the precordium, the apex beat was not displaced; there was a left parasternal heave, a thrill at the pulmonary area, normal S1, split S2, and a loud P2. He was oriented to time, place, and person, had no tremors, had normal cranial nerve and motor function. He however had Montreal cognitive assessment test (MoCA) score of 22/30 consistent

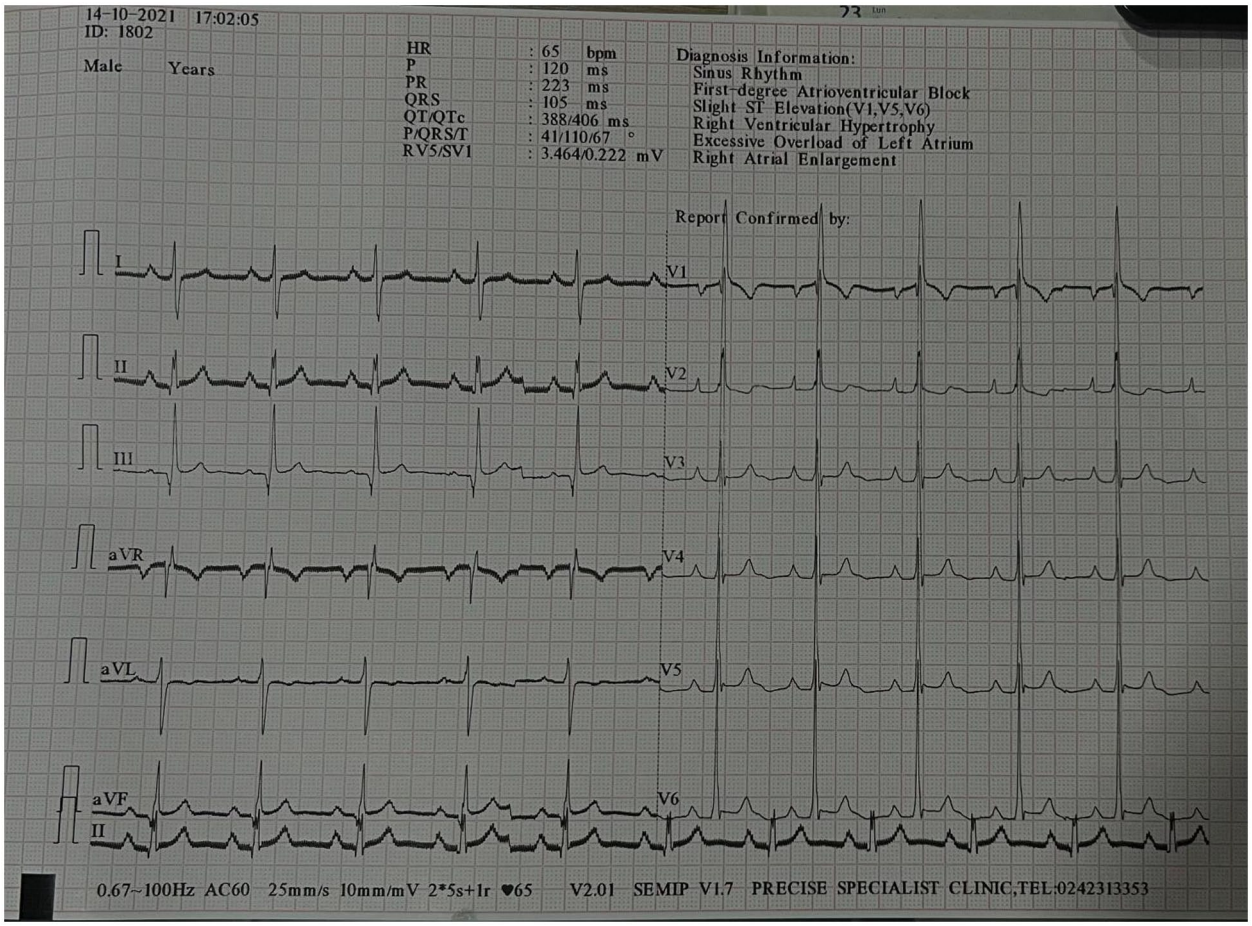

Figure 1. ECG of the patient showing regular sinus rhythm, with right atrial enlargement, and right ventricular hypertrophy.

with mild cognitive impairment with relatively lower scores in the domains of memory and delayed recall. Examination of all other systems was normal.

An electrocardiogram (Figure 1) showed a regular sinus rhythm at 74 bpm, with right atrial enlargement and right ventricular hypertrophy. A 24-hour Holter showed sinus rhythm with low supraventricular extrasystole burden and no evidence of atrial fibrillation or other arrhythmias. An echocardiogram (Figures 2 and 3) revealed secundum ASD = 4.1 cm with left to right shunting and pulmonary flow to that of systemic flow (Qp/Qs) ratio of 1.7/1. There was right atrial dilation, right ventricular hypertrophy, and moderate pulmonary hypertension (right ventricular systolic pressure (RVSP) of 50.37 mmHg derived from tricuspid regurgitant maximum pressure gradient of 40.37 mmHg and estimated right atrial pressure of 10 mmHg). There was normal left heart dimensions and function as well as normal valvular morphology. Magnetic resonance imaging (MRI) scan of the heart (Figure 4) confirmed the ASD. Figure 5 shows MRI of the brain; (a) axial FLAIR showing left thalamic hyperintensity, (b) axial FLAIR showing minimal bilateral subcortical white matter hyperintensity, and (c) axial T2 showing chronic cerebellar infarct.

His complete blood count, liver biochemistries, renal function test, and thyroid function test were all normal. Syphilis and human immunodeficiency virus (HIV) screen were negative. His serum vitamin B12 and B6 levels were also normal.

He was started on medical treatment with tablet furosemide 40 mg daily, tablet sildenafil 25 mg 3 times daily with the aim of improving his pulmonary hypertension and subsequently referring him to cardiothoracic surgery for further evaluation and repair of the ASD. He was also started on anticoagulation (warfarin 5 mg nocte) to reduce the risk of stroke recurrence. At 3 months follow up, memory impairment had not changed, repeat echocardiogram showed a reduction of pulmonary artery systolic pressure from 50.37 to 41.12 mmHg.

He was referred to a cardiothoracic surgeon for further evaluation and possible repair of the ASD.

Discussion and Literature Review

Atrial septal defect (ASD) is a common congenital heart defect that affects approximately 2 out of every 1000 live births with a 97% chance of survival into adulthood.[18,19] ASD is classified into 4 types including ostium primum, secundum, sinus venosus, and unroofed coronary sinus.[20] It affects females more than males.[21] Most are asymptomatic for years.[22] However symptoms such as palpitations, shortness of breath, peripheral oedema may occur when it is complicated by pulmonary

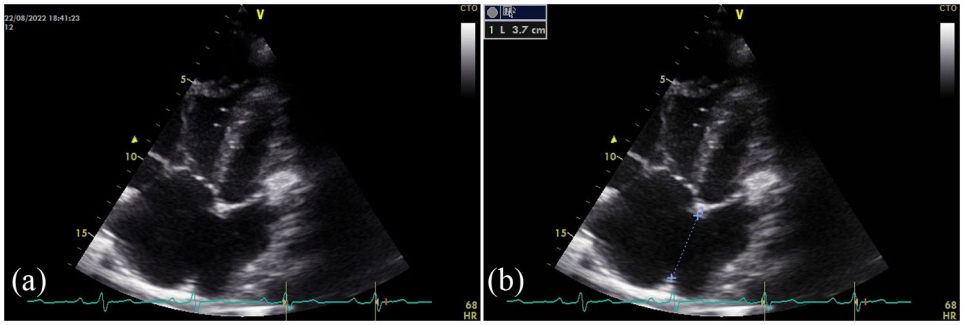

Figure 2. (a, b) Four-chamber trans-thoracic echocardiogram of the patient showing secundum ASD and right heart strain.

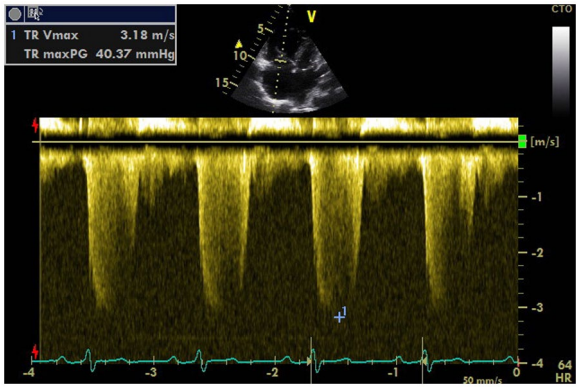

Figure 3. Tricuspid valve regurgitant spectral Doppler of the patient showing the tricuspid regurgitant maximum pressure gradient (TR maxPG) of 40.37 mmHg.

hypertension and right heart failure.[22,23] Our patient had the secundum defect which is the commonest type of ASD.[20]

ASD may cause cognitive impairment through microvascular disease or cardio-embolic stroke due to atrial fibrillation or paradoxical embolus.[10-14] Atrial arrhythmia, particularly atrial fibrillation, is one of the commonest complications of ASD with a prevalence of up to 19%[12] compared to 1% to 2% prevalence in the general population.[24] This risk of atrial fibrillation in ASD increases with age and persists even after closure of the atrial septal defect.[12,25] In the general population, atrial fibrillation has 1% to 20% annual risk of causing stroke influenced by the presence or absence of other cardiovascular commodities.[26] Even the existence of subclinical atrial tachyarrhythmia in the absence of clinical atrial fibrillation is associated with a 13% increased risk of ischemic stroke.[27] When patients with congenital heart disease develop arrhythmias, their risk of stroke doubles.[12] Apart from atrial fibrillation causing strokes and leading to cognitive impairment,[28] atrial fibrillation has also been associated with an increased risk of cognitive impairment regardless of whether or not there is the development of clinical stroke[29-31] possibly as a result of causing microvascular disease by showering of micro-thrombi into the cerebral circulation.[13,14] These suggest that patients with ASD are at increased risk of atrial arrhythmias that increases their risk of developing cognitive impairment through strokes or microvascular disease both of which happened in our patient.

Another cause of cardioembolic strokes in ASD is paradoxical embolus. This is when a thrombus embolizes through an intracardiac defect and subsequently lodges in the systemic circulation and causes occlusion of arteries.[32] Paradoxical embolism occurs in up 14% of patients with ASD; younger age and small ASD size increase the risk.[33] Patent foramen ovale (PFO), ventricular septal defect, and pulmonary arteriovenous malformation are other causes of paradoxical embolus.[32] The commonest cause of paradoxical embolism is PFO which is prevalent in up to 27% of the general population with an annual risk of stroke of about 0.1 to 1%.[34,35] The possible sources of the embolus are from a right heart thrombus or deep vein thrombus.[21] Stroke of undetermined etiology (cryptogenic strokes) are more likely to occur in patients with PFO and about 5-fold more likely to be associated with pelvic deep vein thrombosis.[36]

Paradoxical emboli is more likely to occur when there is reversal of flow, from right to the left atrium which can occur when right heart pressures are elevated as in the case of pulmonary embolism, Eisenmenger syndrome or momentary increased in right sided pressures during valsalva.[34,37] Paradoxical embolus, apart from stroke can lead to thrombosis of arteries in other organs such as renal artery thrombosis affecting the kidneys,[38] and the heart causing acute coronary syndrome.[39]

Cardio-embolic stroke is infarctive and tends to affect multiple territories of the brain.[40] This is consistent with the pattern of cerebral infarcts in our patient suggesting that he had cardio-embolic stroke. Our patient is young with no traditional cardiovascular risk factors, was in sinus rhythm, other common differential diagnosis for dementia in a young person (such as familial causes, vitamin deficiency, neurosyphilis, HIV, and head injury) were absent. With this pattern of infarct and microvascular disease, paradoxical embolus through the ASD is a likely aetiology which resulted in the vascular cognitive impairment. Although the first presentation of stroke in most cases is motor deficit,[41,42] our patient had no loss of motor function. The only neurological complain was memory loss which impaired his function as a mobile banker. Only 14% of

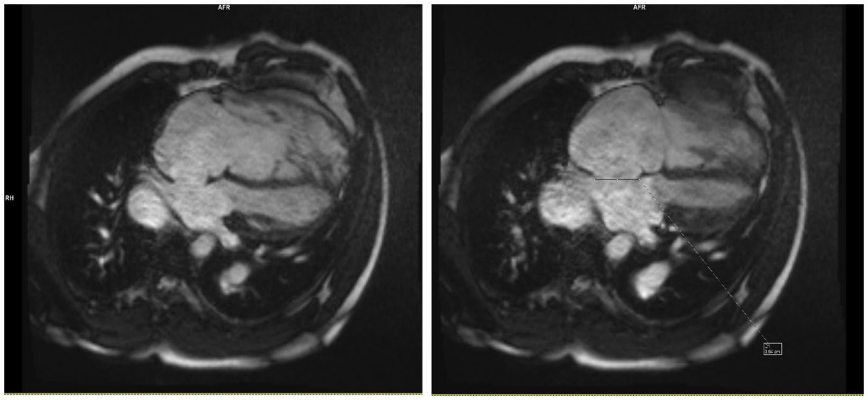

Figure 4. (a and b) Still frames from 4-chamber cine axial MRI of the heart showing atrial septal defect in the 32-year-old man.

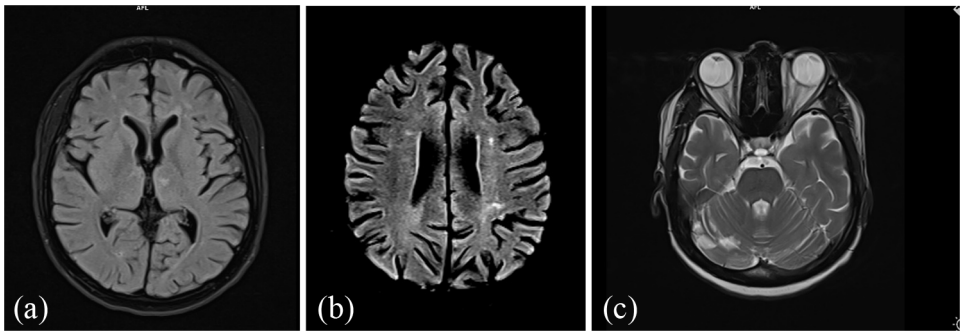

Figure 5. MRI of the brain: (a) axial FLAIR showing left thalamic hyperintensity, (b) axial FLAIR showing minimal bilateral subcortical white matter hyperintensity, and (c) axial T2 showing chronic cerebellar infarct.

patients with MRI evidence of brain infarct present with neurological deficit which is also influenced by the size and location of the infarct.[43]However whether clinical or subclinical stroke, infarcts increases the risk of cognitive impairment occurring in up to a third of patients with strokes.[44]

The diagnosis of ASD begins with history and examination and then confirmed with imaging. Transthoracic echocardiogram is a useful tool to evaluate the secundum and primum ASD. However sinus venosus and coronary sinus defects are better evaluated with transesophageal echocardiogram. In difficult cases, cardiac magnetic resonance imaging or cardiac computed tomography scan are helpful, especially in pulmonary venous connections that may be difficult if not impossible for echocardiogram to image.[45]

Generally, small asymptomatic ASD with no significant haemodynamic disturbance does not need to be corrected as they are not at increased risk of stroke, heart failure, pulmonary hypertension or arrhythmias compared to those who receive surgical correction.[46] However large ASD with ratio of pulmonary flow to that of systemic flow (Q_p/Q_s) greater than 1.5/1 requires surgical correction. For these patients, it is a class I indication to close the ASD if the pulmonary vascular resistance is less than 3 Wood Units (wu) and class II indication if 3 to 5 wu. However, for patients with very high pulmonary vascular resistance, with right to left shunting (Eisenmenger syndrome) targeted medical treatment (including pulmonary vasodilators such as prostaglandins, endothelin blockers, and phosphodiesterase-5 inhibitors) should be started initially to reduce the pulmonary hypertension before surgical correction is attempted, class III indication,[45,47] as those patients are at increased risk of pulmonary hypertension and increased long-term mortality after closure.[48,49] The closure can be done less invasively via transcatheter closure especially for ostium secundum and primum. However sinus venous and coronary sinus defect will require surgical closure.[45]

Conclusion

Unrepaired clinically significant atrial septal defects carry the risk of strokes from paradoxical emboli as well as that of atrial arrhythmia which can lead to cognitive impairment. Early diagnosis and closure of the defect before pulmonary hypertension develops will prevent such complications. Also, when evaluating cognitive impairment in young patients, other rare risk factors such as congenital heart disease may be also considered.

Author contributions

All authors made a significant contribution to this paper, whether that is in examination and management of this case. All authors also took part in the drafting, revising, and gave approval for the publication of this manuscript.

Consent

Permission was provided by the patient to publish this case.

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