CASE REPORT

Caseous calcification of the mitral valve annulus: a rare cause of bilateral cerebral and ocular embolisation

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SUMMARY

A 65-year-old woman presented with sudden bilateral visual loss of recent onset. She was recently diagnosed with multiple acute stroke syndrome for which she was commenced on antiplatelet therapy. Fundoscopic examination revealed bilateral inferotemporal retinal artery occlusions. The recent history of multiple cerebral infarcts combined with the current ocular findings prompted a transoesophageal echocardiogram which successfully revealed caseous calcification of the mitral valve annulus as the source of the numerous sequential emboli, a finding which the conventional transthoracic echocardiogram had failed to disclose as a result of suboptimal image quality. Transoesophageal echocardiography should always be considered as part of the diagnostic workup of retinal arterial occlusive disease, particularly in bilateral lesions, due to its higher yield in identifying posteriorly located cardiac valvular and aortic lesions.

BACKGROUND

This is the first reported case of multiple acute stroke syndrome and simultaneous bilateral branch retinal artery occlusions, resulting from the rarely encountered caseous calcification of the mitral valve annulus (CCMA), confirmed by transoesophageal echocardiogram (TOE) and cardiac CT. Although a hypothetical source of arterial embolisation, CCMA has not been thus far reported to provoke arterial occlusion of the ocular circulation, notably in a bilateral, simultaneous fashion.

CASE PRESENTATION

A 65-year-old woman presented with sudden, painless, bilateral vision loss over the preceding 6 hours. Medical history included well-controlled hypertension. No other atherosclerotic risk factors were present based on clinical and laboratory data. Best-corrected visual acuity was counting fingers (right eye—RE) and 6/18 (left eye—LE). Fundus examination of RE revealed inferotemporal branch retinal artery occlusion involving the macula, with a visible off-white embolic plaque which appeared wider than the blood column, large cotton wool spots, vessel attenuation and segmentation (figure 1A). LE funduscopy demonstrated a large cotton wool

spot and flame-shaped retinal haemorrhage along the inferotemporal arcade of the retinal artery, but no obvious embolus (figure 1B). A month before the onset of ocular symptoms, the patient had suffered multiple acute stroke syndrome involving anterior and posterior cerebral circulation, as evidenced by multiple infarcts localised at cerebral and cerebellar hemispheres bilaterally (figure 1C).

INVESTIGATIONS

Spectral domain optical coherence tomography disclosed macular hyper-reflectivity with thickening of the inner retinal layers, more prominent in the inferior quadrant of the Early Treatment Diabetic Retinopathy Study (ETDRS) macula map in the RE, and normal LE macula. Fluorescein angiography revealed bilateral inferotemporal retinal artery occlusions. The occurrence of multiple acute embolic lesions during the previous hospitalisation had prompted an intensified workup including tests for hypercoagulable status, autoimmune screen, carotid Doppler revealing absence of atheromatous disease and a transthoracic echocardiogram (TTE), showing mild calcification of the mitral and aortic valve. A 24-hour Holter monitoring was unremarkable for cardiac arrhythmias. In the light of the new embolic lesions, a TOE was performed, revealing an echo-dense mass containing central areas of echolucencies at the posterior perianular region of the mitral valve (MV), suggesting CCMA (caseoma, figure 1D). Although thoroughly assessed, no evidence of CCMA leakage was seen. MV function was normal, with mild left ventricular hypertrophy and no other structural or haemodynamic abnormalities. No patent foramen ovale or atrial septal defect were present. No significant atheromatosis was observed at the aortic arch and descending aorta. A cardiac CT confirmed the presence of a mass attached to the posterior MV with features supporting the diagnosis of CCMA (figure 1E).

DIFFERENTIAL DIAGNOSIS

Based on the above findings, a diagnosis of bilateral branch retinal artery occlusions secondary to CCMA was reached.

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Figure 1 (A, B) Coloured fundus photographs. (A) Visible embolus (long arrow) immediately after the first bifurcation of the inferotemporal arcade of the retinal artery in the right eye. (B) Large cotton wool spot adjacent to the inferotemporal arcade of the left eye (arrow). (C) FLAIR (Fluid-attenuated inversion recovery) imaging exhibiting multiple acute infarcts affecting several cerebral and cerebellar areas. (D) Transoesophageal echocardiogram; mid oesophageal long axis view clearly showing that the mass has a calcified rim (white arrows) surrounding an area of echolucency, finding consistent with a diagnosis of caseous calcification of the mitral annulus (CCMA). (E) Cardiac CT showing a well-defined crescent-shaped hyperdense mass with peripheral calcification along the posterior mitral annulus (white arrows), consistent with CCMA.

TREATMENT

Following the primary cerebrovascular event, antiplatelet therapy (aspirin 100mg) and secondary stroke prophylaxis with a statin and blood pressure control were commenced. The ensuing retinal embolism and unveiling of the cardiac pathology prompted initiation of anticoagulation (acenocoumarol) and referral to the cardiothoracic team for assessment and consideration of surgical excision and valve replacement, given the aggressive behaviour of the lesion.

OUTCOME AND FOLLOW-UP

In view of the patient's reluctance to undergo open-heart surgery with CCMA resection and MV replacement, she remains under regular follow-up by the cardiology team with adequate anticoagulation with no further stroke or other embolic recurrence.

DISCUSSION

This is a rare case of multiple acute stroke syndrome¹ followed by bilateral retinal arterial occlusions likely due to CCMA, which the initial TTE had failed to detect, mainly due to suboptimal image quality as a result of patient's anatomy. The bilaterality of lesions suggests a cardiac or great vessel source of emboli,^{2,3} while symmetry could be attributed to the smaller diameter of inferotemporal vessels. Although the embolus type cannot be reliably determined by clinical observation alone, the matte-white, non-scintillating and wider than the blood column appearance of the RE visible embolus in our case point towards a calcific rather than a cholesterol (Hollenhorst plaque) embolus, as described by Wray.⁴ This observation combined with the finding of CCMA on TOE led us to the assumption that CCMA was the main cause of the patient's multiple strokes. Our hypothesis was also reinforced by the fact that the rest of the patient's workup for alternative causes of stroke was negative and no significant atherosclerotic risk factors were present. CCMA is an uncommon variant of mitral annular calcification (MAC), found in 0.63% of all MAC cases and 0.067% of all echocardiographic examinations according to Dietl *et al.*⁵ It is usually an incidental finding on cardiac imaging with largely unknown prognosis. It is believed to run a benign course in the majority of cases, although MV dysfunction and systemic embolisation (cerebrovascular events, acute coronary syndrome) have been reported.⁶ Davidson and Cohn⁷ and Stamou *et al.*⁸ each reported a case of CCMA associated with unilateral retinal calcific embolisation, both successfully managed by prompt operative intervention. Sequeira *et al.*⁹ described bilateral branch retinal artery occlusion and cerebral embolisation in a young chronic haemodialysis patient, caused by both calcium and cholesterol emboli, who was also managed with MV replacement due to rapid progression of the lesion and systemic embolisation. This patient had risk factors for dystrophic calcification, with elevated calcium-phosphorus load and hyperparathyroidism. The optimal treatment of stroke occurring in patients with CCMA is unknown, especially since the mechanisms of stroke in these patients are likely multifactorial and not necessarily related only to thrombus formation.⁵ In our case, the fundus findings described above suggest calcium embolisation as the most likely mechanism of stroke, although other concomitant mechanisms cannot be ruled out (the fact that our patient responded well to anticoagulation also suggests that some form of thrombus substrate is likely present). In the literature, both antithrombotic therapy and/or surgical management have been used to prevent embolic recurrence.¹⁰ Considering our case, anticoagulation appeared to be a one-way road since antiplatelet treatment failed to prevent stroke recurrence and the patient was reluctant to undergo cardiac surgery. TOE has a higher yield compared with conventional TTE in the cardiovascular assessment of patients with retinal arterial occlusion by offering superior quality images due to placement of the probe in the oesophagus, which lies just behind the left atrium, thus overcoming artefacts from the ribs, lungs and breast.¹¹ Our case highlights TOE as an important adjunct to the routine evaluation of patients with bilateral cerebrovascular and retinal artery occlusions, especially when TTE images are suboptimal.¹² As highlighted by Dietl *et al.*, additional diagnostic imaging studies, including cardiac CT and/or MRI, may sometimes be necessary to establish the diagnosis of CCMA, which can even be missed by TOE.⁵ Our case highlights the alarming embolic

potential of CCMA, the challenge and importance of correct identification suggesting TOE as an irreplaceable adjunct to the routine evaluation of bilateral cerebrovascular and retinal occlusions, and comments on treatment options.¹²

Learning points

- ▶ Bilateral branch retinal artery occlusions have rarely been reported in the literature.
- ▶ When bilateral embolic events of the cerebral or ocular circulation occur, a cardiac or great vessel source of emboli should be investigated.
- ▶ Transoesophageal echocardiogram carries a higher yield compared with the conventional transthoracic echocardiogram in the cardiovascular assessment of these patients.
- ▶ Caseous calcification of the mitral valve annulus (CCMA) is an exceptionally rare cardiac lesion which is believed to run a harmless course in the majority of cases. This is a noteworthy case of a CCMA with aggressive systemic embolisation.
- ▶ Optimal management of such cardiac lesions is yet to be clarified with conservative management usually advocated for asymptomatic patients, while antithrombotic treatment or even surgical intervention may be indicated for aggressive lesions with systemic embolisation or mitral valve dysfunction.

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