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Simultaneous cardiocerebral infarctions: a five-year retrospective case series reviewing natural history

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ABSTRACT

Introduction: Concurrent cardiocerebral infarction (CCI), a rare condition defined as simultaneous occlusions in the cerebrovascular and coronary vessels, has high mortality but very limited literature on optimum treatment methods. A better understanding of the natural history and effect of treatment would improve patient outcomes.

Methods: Using our prospective stroke database from 2014 to 2018, ten consecutive patients with CCI were identified (incidence = 0.29%). We recorded patient demographics, cardiovascular risk factors, cardiac and cerebral occlusions, circumstances of admission and management of each patient. Patient notes and imaging findings were reviewed to determine the underlying cause of CCI.

Results: Median National Institute of Health Stroke Scale score was 15 (range 4–27). Mean patient age was 59 years and 90% were men. Two patients were treated with intravenous tissue plasminogen activator (IV tPA) only and three underwent endovascular treatment in both the cerebral and coronary vessels sequentially. One patient underwent percutaneous coronary intervention (PCI) only and two underwent PCI after IV tPA therapy. Two patients were conservatively treated due to poor premorbid status. At the three-month follow-up, five patients had excellent functional outcomes (modified Rankin Scale 0–1) while three died.

Conclusion: CCI is a rare but devastating clinical scenario, with high incidence of morbidity and mortality. Treatment strategy can impact patient outcome, and further research is warranted on the ideal acute and post-reperfusion treatments for CCI. In this series, IV tPA at stroke doses appeared to be the preferred initial step for its treatment, with subsequent coronary or cerebral endovascular therapy, if necessary.

Keywords: acute ischaemic care, endovascular, myocardial infarct, PCI, thrombolysis

INTRODUCTION

Coronary heart disease and cerebrovascular accidents are major causes of death regardless of ethnicity and gender.[1] While patients with ischaemic stroke have a subsequent risk of acute myocardial infarction (AMI) and vice versa, concomitant AMI and ischaemic cerebrovascular strokes have rarely been reported.[2] Concurrent cardiocerebral infarction (CCI) is a rare condition defined as simultaneous occlusions in the cerebrovascular and coronary vessels. There are two types of CCI: synchronous CCI (where both cerebrovascular and coronary vessels are affected at the same time due to the same pathology); and metachronous CCI (where infarction in either vessel precedes the other).[3]

CCI is not well described in the literature and this condition, although rare, can be devastating. We, therefore, wanted to better characterise the incidence of CCI and treatment modalities that can be provided to patients to guide their future management.

METHODS

In a cross-sectional study, we retrospectively screened our registry of 3,500 stroke admissions during the period 2014–2018. Information was collected on demographic variables, comorbidities, electrocardiographic and echocardiographic findings, cardiac and stroke treatments, as well as patient outcomes.

In terms of disease definitions, acute ischaemic stroke (AIS) was defined as an acute focal or global neurological deficit lasting over 24 hours or leading to death, and caused by vascular occlusion or stenosis.[4] AMI was defined as acute myocardial injury, with clinical evidence of ischaemia, a rise or fall in cardiac troponin values and at least one of the following symptoms: myocardial ischaemia; new ischaemic electrocardiogram changes; development of pathological Q waves; imaging evidence of viable myocardial or new regional wall motion abnormality suggestive of ischaemia; or presence of a coronary thrombus identified on

angiography.[5] All patients with concomitant ischaemic stroke and AMI that were diagnosed simultaneously during the presenting consultation were included. Patients with metachronous CCIs were excluded from the study.

Ethics approval was granted by the local institutional review board.

RESULTS

There were ten patients with CCI in the stroke database (Table I), giving an incidence of 0.29%. 9 (90%) patients were men. Four patients presented with a low diastolic blood pressure of around 60 mmHg. Coronary angiogram of seven patients showed stenosis or thrombosis of the left anterior descending (LAD) artery and circumflex arteries while six patients also showed occlusion of the middle cerebral artery (MCA) territory with early ischaemic changes.

Eight of ten patients underwent acute treatment, while two patients were treated conservatively. Two patients received intravenous tissue plasminogen activator (IV tPA) alone while one had percutaneous coronary intervention (PCI) only. The patient who had PCI only had a low National Institute of Health Stroke Scale (NIHSS) score and no large vessel occlusion on computed tomography angiography. Among patients who underwent treatment for both conditions, two patients had PCI before cerebral endovascular thrombectomy, one patient had cerebral endovascular thrombectomy before PCI (non ST-segment elevation myocardial infarction [NSTEMI] with basilar occlusion and high NIHSS score) and two patients had IV tPA before PCI.

3 (30%) patients died during the same hospital admission. At the three-month follow-up, 5 (50%) patients achieved a good functional outcome, with a modified Rankin Scale (mRS) of 0–1. For patients who were treated for both conditions, three underwent endovascular treatment for both cerebral and coronary vessels. Two underwent PCI first, with mRS of 3 and 5, respectively, at three months, while one patient started with cerebral thrombectomy but died

during the admission despite successful recanalisation due to brainstem stroke. Another two patients underwent PCI after bridging with intravenous thrombolysis therapy, with a three-month mRS of 0 and 1. The two patients who were treated with IV tPA alone at cerebral doses (0.9 mg/kg) both had mRS 1 at the three-month follow-up. The remaining two patients who did not undergo any form of recanalisation therapy due to poor premorbid status had died by the three-month follow-up appointment.

DISCUSSION

We found the incidence of synchronous CCI at our hospital to be 0.29%, which was similar to an earlier study that reported a 0.52% incidence of stroke within 24 hours of AMI.[6] The male preponderance in our study correlated well with the existing literature, which cites higher age-specific stroke rates in men, with an incidence rate among patients hospitalised for AMI being nearly double among men when compared to women.[7,8]

A study of the extent and severity of atherosclerosis in the coronary and cerebral arteries during 200 consecutive autopsies showed that coronary atherosclerosis develops earlier than cerebral atherosclerosis, but with a significant correlation between the coronary and cerebral arterial beds.[9] The atherosclerotic process tends to start earliest in the LAD artery branch of the coronary arteries, but the basilar artery typically has the maximum degree of atherosclerosis, followed by the MCA. Progressive tight atherosclerotic stenosis in both cerebrovascular and cardiovascular trees places the patient at risk of simultaneous infarcts when systemic blood pressure falls with haemodynamic compromise (with an arrhythmia or myocardial infarction), causing hypoperfusion. This may be the cause of CCI, as seen in some of our patients with low diastolic blood pressure despite the occlusions.[9]

There are several other potential mechanisms of CCI (Table II). These include thromboembolism from the heart,[10,11] hypoperfusion during AMI, the aforementioned

hypoperfusion in the setting of critical coronary and intracranial atherosclerotic disease,[9] arrhythmias triggered by insular infarcts and paradoxical emboli among others,[12] with rarer causes being aortic dissection involving the ascending aorta, coronary ostia and carotid arteries.[13-15]

Table II. Cause of concurrent cardiocerebral infarction.

Cause	Mechanism
Embolic	Hypokinetic myocardial segment
	Thrombosis, with right-to-left shunt
	Ventricular thrombus
	Atrial fibrillation
Hypotensive	Myocardial infarct
	Atherosclerotic stenosis
	Insular infarct, with arrhythmia
	Aortic dissection

IV tPA has been shown to have greater benefit than placebo for myocardial infarction when used early after symptom onset.[16] Although some guidelines do state that an AMI within the previous three months is a relative contraindication for IV tPA use during acute stroke, IV tPA continues to be used as first-line therapy for patients with AIS and AMI.[17] In the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) registry[18] and Simplified Management of Acute Stroke study,[19] there were comparable outcomes for patients with and without recent AMI treated with IV tPA. IV tPA appeared to be effective in four of ten patients in our study, with all four patients treated with IV tPA having an excellent mRS functional outcome at the three-month follow-up despite three patients having cerebral proximal large vessel occlusions and two patients having very high NIHSS scores. No patient treated with IV tPA had any haemorrhagic complication in our series. When a patient presents with synchronous CCI, it may therefore be preferable to initiate a treatment strategy that is beneficial to both pathologies simultaneously, as suggested by the favourable functional outcomes observed with IV tPA in our small case series. In this series, patients were

administered the stroke dose of IV tPA, which is classically 0.9 mg/kg. We avoided cardiac doses of up to 1.0 mg/kg bolus (up to 100 mg) to potentially mitigate against the risk of an intracranial haemorrhage.

After the initial bolus for thrombolysis has been administered, further intervention, such as PCI for the coronary arteries and clot retrieval for the cerebral arteries, can be rapidly arranged.[20] A large meta-analysis of prehospital thrombolysis for AMI showed that pretreatment with IV tPA does not decrease the coronary benefit of PCI and stenting.[21] Similarly, current guidelines for stroke recommend that IV tPA not be withheld if cerebral endovascular thrombectomy was being arranged.[22] For patients with contraindications to IV tPA or those who arrive out of the treatment window of 4.5 hours for IV tPA, treating physicians must then decide what to administer first.

Management of both AIS and AMI is extremely time sensitive. The decision to treat either first might result in detrimental consequences for the other pathology. For metachronous CCI, where it is apparent which vessels are the primary vessels affected, immediate care would generally be targeted towards the initial event. However, in a synchronous or nearly synchronous presentation, there are no clear recommendations for the order of management.[23] The patient's haemodynamic status can help to determine whether to treat the cerebral or coronary infarction first, with the cerebral circulation taking precedence in instances of low blood pressure or haemodynamic instability due to malignant arrhythmias or cardiogenic shock, while indications for prioritisation of neurological intervention would include signs of basilar occlusion or less severe coronary issues, such as NSTEMI.[20,23] A multidisciplinary team, comprising a stroke neurologist and cardiologist (both general and interventional cardiologists), should convene and discuss about the vascular bed that requires more urgent treatment and prioritise treatment appropriately.

The postprocedural management instituted following cardiac and cerebral acute treatments present several dilemmas in the clinical context of a CCI. Patients with AMI require dual antiplatelet therapy (DAPT), ideally aspirin and either ticagrelor or prasugrel, as this has been shown to be superior to clopidogrel.[22] However, for stroke patients, the current standard of care post thrombectomy is typically a single antiplatelet. DAPT after a large vessel occlusion stroke, in this case, aspirin and clopidogrel, are reserved for special scenarios, where plaques with emboli are seen on transcranial Doppler monitoring or if an intracranial stent has been deployed because of the increased risk of intracranial bleeding.[24] Furthermore, beta-blockers and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are beneficial for patients with AMI, but the lowering of acute blood pressure directly after stroke is still a controversial subject. Lowering of blood pressure would have a potential risk of hypotension and hypoperfusion leading to failure of the brain collateral circulation and worsening the infarct volume.[25] While anticoagulation is recommended for patients with AMI, this may increase the risk of haemorrhagic conversion in AIS and is typically avoided unless there is a strong indication, such as a left ventricular thrombus or a metallic valve.[26,27] However, some similarities do exist for follow-on management. Patients with both AMI and AIS require high intensity statin treatment and continuous telemetry electrocardiographic monitoring for arrhythmias is recommended for both.[24,27] Given the complexity of patients with CCI, it is essential for a dedicated team of cardiologists, with an interest in neurological disorders, and stroke neurologists, who understand cardiac conditions, to work together continuously using a multidisciplinary approach to optimise care for these patients.

In conclusion, synchronous CCI is an uncommon and devastating clinical scenario, with high incidence of morbidity and mortality. In our small case series, IV tPA at stroke doses appeared to be a potential initial step for the treatment of CCI, with subsequent coronary or cerebral endovascular therapy. Timely treatment would significantly impact the outcome for

patients presenting with CCI, and hence further research is warranted with regard to the ideal sequence and optimal treatment for CCI.

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Table I. Demographics, comorbidities, treatment modalities and outcomes of ten patients with CCI.

Patient	Age (yr)/gender	Premorbid medical status	ECG and 2D-echo	NIHSS score at onset	Cerebral occlusion	Modality of acute treatment	Mechanism of CCI	Reason for choice of treatment modality	Postprocedural treatment	mRS at 3 mth	Follow-up duration (mth)
1	45/male	DM, HTN, HLD	Widespread T-wave inversions; LVEF 30%, LV thrombus	16	Right ICA	PCI of pLAD then penumbra aspiration EVT	Emboli from LV thrombus	Low LVEF and low BP-coronary intervention first	Aspirin and warfarin	3	14
2	53/male	DM, HLD	ST-elevation V2–5	23	Left proximal MCA	PCI of mLAD then EVT with stent retrievers	STEMI with AF	Refractory hypertension and on-site availability of cardiologist	DAPT and warfarin	5	8
3	71/female		ST depression inferior leads; LVEF 55%, LV thrombus	27	PCA	EVT with stent retrievers then PCI of mLAD and pLAD	Emboli from LV thrombus	EVT because of NSTEMI and severity of basilar occlusion	Nil	6	Nil
4	55/male		T-wave inversions V4–6	18	Left proximal MCA	IV tPA 0.9 mg/kg	Atherosclerosis	Simultaneous treatment	DAPT for 1 mth then aspirin	1	18
5	57/male		T-wave inversions V4–6	16	Left proximal MCA	IV tPA 0.9 mg/kg	Atherosclerosis	Simultaneous treatment	DAPT for 1 mth then aspirin	1	9
6	51/male	AF	ST elevation in V4–6; LVEF 35%	6, including aphasia	Left distal M2	IV tPA 0.9 mg/kg then PCI of pLAD	Emboli from AF	Distal M2 occlusion not amenable to thrombectomy	Rivaroxaban lifelong and DAPT for stent for 1 yr	0	3
7	70/male	Dementia, DM, HTN, HLD, renal impairment	ST-elevation V1–5 and ST depression	4	Basilar artery	Conservative management	Unknown	Poor premorbid state, with dementia	Nil	6	Nil

			in inferior leads LVEF 45%								
8	45/male		Deep T waves V2–6; LVEF 40%, LV thrombus	6	Left proximal MCA	IV tPA 0.9 mg/kg PCI RCA and LAD	Emboli from LV thrombus	Simultaneous treatment, with resolution of MCA occlusion	Warfarin lifelong and DAPT for stent for 1 yr	1	31
9	67/male	Asthma	ST elevation V4–6	4	No obvious occlusion	PCI of mLAD and pLAD	Atherosclerosis	Low NIHSS score and no occlusion on CTA, concomitant anterior STEMI	DAPT	1	3
10	76/male	DM, HTN, PVD	ST depression and later developed T-wave inversion; LVEF 30%	14	Right proximal MCA	Conservative management	Hypotension from MI and pneumonia	Poor premorbid state, with concurrent pneumonia	Nil	6	Nil

2D-echo: two-dimensional echocardiography; AF: atrial fibrillation; BP: blood pressure; CCI: concurrent cardiocerebral infarction; CTA: computed tomography angiogram; DAPT: dual antiplatelet therapy; DM: diabetes mellitus; ECG: electrocardiogram; EVT: cerebral endovascular thrombectomy; HLD: hyperlipidaemia; HTN: hypertension; ICA: internal carotid artery; IV: intravenous; LAD: left anterior descending artery; LV: left ventricular; LVEF: left ventricular ejection fraction; M2: Sylvian segment of middle cerebral artery; MCA: middle cerebral artery; MI: myocardial infarction; mLAD: mid-left anterior descending artery; mRS: modified Rankin scale; NIHSS: National Institute of Health Stroke Scale; NSTEMI: non-ST segment elevation myocardial infarction; PCA: posterior cerebral artery; PCI: percutaneous coronary intervention; pLAD: proximal left anterior descending artery; PVD: peripheral vascular disease; RCA: right coronary artery; STEMI: ST-segment elevation myocardial infarction; tPA: tissue plasminogen activator