CASE REPORT

The mystery of recurrent idiopathic cerebrovascular and coronary arterial thrombosis

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SUMMARY

A 46-year-old man presented to our hospital with ST elevation myocardial infarction (STEMI). Previous records revealed a history of recurrent non-STEMI, stroke and transient ischaemic attacks. He was thoroughly investigated with coronary angiography, a cerebral CT angiography, thrombophilia panel and autoimmune screening tests, all of which proved negative. His current episode of STEMI resulted while on dual antiplatelet therapy; the patient was investigated for P2Y12 receptor resistance, which was also negative. A diagnosis of idiopathic recurrent arterial thrombosis was established and the patient was discharged home on aspirin and warfarin. Routine follow-up has revealed no recurrence of symptoms.

BACKGROUND

ST elevation myocardial infarction (STEMI) with normal coronaries is an uncommon but recognised entity among patients with acute coronary syndrome (ACS). The common causes attributed include coronary vasospasm, hypercoagulable states, Takotsubo cardiomyopathy and perimyocarditis. Stroke of unknown aetiology termed cryptogenic stroke is a more common condition and enlists a long list of possible causes.

However, in our patient, the presence of recurrent episodes of ACS as well as ischaemic stroke brings to light an unusual presentation with no obvious aetiology despite numerous investigations. The absence of episodes of venous thromboembolism further mystifies our list of possible diagnoses. Therefore, physicians need to astutely assess their treatment options and priorities of care to maximise patient well-being and minimise the recurrence of symptoms.

CASE PRESENTATION

A 46-year-old Asian man presented in acute distress with a history of retrosternal chest pain radiating to the left arm, lasting for half an hour, and associated with sweating and nausea. ECG and cardiac enzymes corroborated a diagnosis of STEMI and he was subsequently thrombolysed with tenecteplase.

Medical history included two episodes of cerebrovascular ischaemic stroke in 2009 and 2012 with no persistent neurological deficits. The patient also suffered from non-STEMI (NSTEMI) in 2013. He has had mild dyslipidaemia and grade 1 hypertension since 1996. History also included rheumatic heart disease with mild mitral stenosis. There was no history of smoking, alcohol use or drug addiction.

Treatment history included a β -blocker, statin and dual antiplatelet therapy. On presenting to us, the patient was dyspnoeic and in pain. His vital signs were stable with no significant findings on cardiovascular and chest examination.

INVESTIGATIONS

ECG showed ST elevation in chest leads V1–V4, lead III and AVF. There were reciprocal ST depressions in lead I and AVL ([figure 1](#)).

Laboratory findings included: haemoglobin 14.7 g/dL, platelet count $257 \times 10^3/\mu\text{L}$, white cell count $14.8 \times 10^3/\mu\text{L}$, creatinine 1.3 mg%, potassium 4 mmol/L, random glucose 127 mg%, glycated haemoglobin 5.6%, total cholesterol 130 mg%, triglyceride 211 mg%, low-density lipoprotein 61 mg% and high-density lipoprotein 49 mg%. The peak cardiac enzymes were elevated and measured as creatine kinase 506 $\mu\text{U/L}$, creatine kinase MB 50 $\mu\text{U/L}$ and troponin 0.66 μL . Erythrocyte sedimentation rate was 20 mm in the first hour.

Homocysteine was 12.26 $\mu\text{mol/L}$. Autoimmune screening tests for anti-DNAse antibodies, antiribosomal antibodies, anti-nuclear factor antibodies, rheumatic factor IgM and anticardiolipin antibodies were all negative. Antithrombin III was 94%, activated protein C resistance 199, C4 complement level: 0.51 mg/L and D-dimer test was 0.09 mg/L. Protein C was 142% and protein S 91%. At the time of the patient's presentation, kits for factor V Leiden and lipoprotein(a) were not available in our centre so these tests could not be performed.

The P2Y12 receptor blocker resistance test for clopidogrel was negative.

Echocardiography was performed and revealed normal size cardiac chambers. The mid septum was thinned and akinetic. The basal septum, mid basal inferior and distal anterior were severely hypokinetic. Left ventricular systolic ejection fraction was 40%. Mitral valve leaflets were mildly thickened with mitral valve area of 2 cm^2 , consistent with a diagnosis of mild mitral stenosis of rheumatic origin. Mild aortic regurgitation was also present. There was no clot or vegetation detected on transoesophageal echocardiography.

The coronary angiogram showed normal left and right coronary arteries ([figures 2](#) and [3](#)). Carotid Doppler did not show any significant abnormality.

CT of the brain performed in 2009 showed a small hypodensity at the right anterior parietal lobe slightly above the level of ventricles in favour of a recent ischaemic infarct. CT of the brain repeated in 2012 reported bilateral frontoparietal periventricular and left cerebellar infarcts ([figure 4](#)).

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Figure 1 ECG at the time of admission showing ST elevation.

A cerebral CT angiography revealed no significant abnormal changes of cerebral vasculature.

DIFFERENTIAL DIAGNOSIS

- ▶ Prinzmetals angina
- ▶ Takotsubo cardiomyopathy
- ▶ Myopericarditis
- ▶ Antiphospholipid antibody syndrome
- ▶ Patent foramen ovale (PFO)
- ▶ Sticky platelet syndrome
- ▶ Metabolic syndrome X
- ▶ Coronary ectasia as a manifestation of vasculitis

TREATMENT

The patient was admitted to our coronary care unit and received tenecteplase as thrombolytic therapy for anterior STEMI. A coronary angiogram was subsequently performed revealing normal coronaries. During his hospital stay the patient received dual antiplatelet therapy, ACE inhibitor, statin and a β -blocker.

There were no complications and the patient's hospital stay was uneventful. On discharge, our team decided to continue the

patient on aspirin and warfarin as his previous dual antiplatelet therapy did not inhibit thrombus formation.

OUTCOME AND FOLLOW-UP

The patient was discharged after 1 week of treatment. He was advised to follow-up his international normalisation ratio (INR) between 2.0 and 3.0. At 2-month follow-up the patient showed good control of his INR and no further hospital admissions were needed.

DISCUSSION

Cardiovascular diseases, including coronary artery diseases and stroke, are the biggest contributors to global mortality and will continue to project similar trends in the future.¹ A number of risk factors contribute to these and are often grouped into non-modifiable factors such as age, gender, family history and modifiable factors such as hypertension, hypercholesterolaemia, diabetes mellitus, tobacco use, obesity, physical inactivity and unhealthy diets high in saturated fats. Besides these, there are now non-traditional newer emerging risk factors such as C reactive protein, small low-density lipoprotein, coagulation and haemostatic factors, lipoprotein(a), homocysteine, and apolipoprotein A and B, which have all proven to contribute towards coronary artery disease.²

Figure 2 Coronary angiography showing normal left coronary system.

Figure 3 Coronary angiography showing normal right coronary artery.

Figure 4 CT of the brain showing cerebellar infarction.

The most common aetiology for ACS is rupture of an unstable atherosclerotic plaque in a coronary artery. Prothrombotic factors released lead to rapid thrombus formation and ischaemia of the myocardium. Less commonly, it is caused by vasospasm or hypercoagulable states. ACS in young patients, particularly in the setting of suspected drug abuse, is oftentimes linked to cocaine use.³

Non-atherosclerotic causes of myocardial infarction are particularly common among a younger population of patients. Although rare, it has a number of differential diagnoses that the clinician must be aware of.

A small study of 41 patients by Neil *et al*⁴ found that there is increased frequency of factor V Leiden or prothrombin variant 20210A in patients under 50 years of age who had myocardial infarction and normal coronary arteries.

Another factor to be considered, particularly in this subset of patients, included elevated levels of lipoprotein(a). Banerjee *et al* studied ethnic variation in lipoprotein(a) among non-Hispanic whites, Asian Indians and Chinese populations. High lipoprotein levels correlated with ischaemic heart disease more particularly with Asian Indians and Chinese than non-Hispanic whites.⁵ Lentini *et al*⁶ cited a case report of a young man who had cryptogenic stroke due to high lipoprotein(a) levels.

Coronary ectasia is characterised by abnormal coronary vessel dilation and presents with angina, myocardial infarction and sudden cardiac death due to vasospasm, dissection or thrombosis.⁷ It is a recognised angiographic finding and was ruled out in our patient, who had normal coronary arteries.

For 10 years, Walid and Jeffrey studied 714 patients who had STEMI and found that 5.7% of them experienced STEMI with normal coronary arteries. The mean age of these patients was 44 years and the majority were males.⁸ Thirty-two per cent of these patients were finally diagnosed with peri-myocarditis and Takotsubo cardiomyopathy. A similar study by Brian *et al*, which included STEMI as well as NSTEMI patients, found 7.8% of the time the patients experienced myocardial infarction with normal coronary arteries. Females were more affected and their mean age was 57 years.⁹

Panduranga *et al*¹⁰ have published a case report of primary antiphospholipid antibody syndrome in a young patient who had recurrent coronary thrombosis and was treated with anti-coagulant medicine. A case report by Marques *et al*¹¹ elaborated the condition of a 48-year-old woman with antiphospholipid antibody syndrome causing acute carotid thrombosis leading to ischaemic stroke.

A majority of ischaemic strokes occur secondary to cardioembolism, atherosclerotic or small vessel occlusive disease. As per the TOAST classification, a stroke in the absence of any such causes is termed as a cryptogenic stroke and it is known that 30–40% incidences of ischaemic stroke fall in this category.^{12–13}

A small study by Dao *et al* found PFO as a significant risk factor for cryptogenic stroke and, less commonly, myocardial infarction.¹⁴ In our patient, PFO was ruled out by transoesophageal echocardiography.

A 1-year follow-up study by Palomeris *et al* revealed that 15% of patients with stroke studied suffered from cryptogenic stroke. During the follow-up, 3 (2.75%) patients had recurrent cryptogenic stroke and 2 patients had myocardial infarction.¹⁵

Kannan *et al* reported a case of a 17-year-old boy who had thrombotic occlusion of coronary, cerebral and peripheral vessels. He was diagnosed to have sticky platelet syndrome.¹⁶

A review article by Chan *et al*, published in *Circulation*, mentioned that patients with recurrent arterial thrombosis in whom arterial thrombophilia was suspected need to be treated with a vitamin K antagonist. Long-term studies for such treatment options are, however, limited.¹⁷

The management of our patient was complex. In spite of taking dual antiplatelet therapy and without any resistance to clopidogrel, the patient had two episodes of stroke and two events of acute coronary syndrome. Our management team thus decided to continue him on long-term aspirin and warfarin.

Learning points

- ▶ Patients presenting with recurrent arterial thrombosis must be investigated thoroughly for hypercoagulable states or autoimmune diseases.
- ▶ In these patients, alternate diagnoses including perimyocarditis and Takotsubo cardiomyopathy should also be excluded.
- ▶ Long-term anticoagulation is required along with regular follow-up to assess the effectiveness of treatment and readmission.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 World health statistics. *Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health*. Chapter 2 p 49. Institute of Medicine (US) Committee on Preventing the Global Epidemic of Cardiovascular Disease: Meeting the Challenges in Developing Countries; Fuster V, Kelly BB, editors. Washington (DC): National Academies Press (US); 2010. Geneva: World Health Organization, 2009.
- 2 Chatterjee K. *Cardiology an illustrated textbook*. Vol 1. Jaypee Brothers Medical publishers. 2012:829.
- 3 Shah R, Duncan SJ, Ramanathan KB. ST segment elevation in patients with cocaine abuse and chest pain. *Acute Med* 2014;13:72–3.
- 4 Van de Water NS, French JK, Lund M *et al*. Prevalence of factor v Leiden and prothrombin variant g20210a in patients age <50 years with no significant

- stenoses at angiography three to four weeks after myocardial infarction. *J Am Coll Cardiol* 2000;36:717–22.
- 5 Banerjee D, Wong EC, Shin J, *et al*. Racial and ethnic variation in lipoprotein (a) levels among Asian Indian and Chinese patients. *J Lipids* 2011;2011:291954.
 - 6 Lentini A, Fornengo P, Bosco G, *et al*. Cryptogenic cerebral infarction in a young patient with very high lipoprotein(a) serum level as the only risk factor. *Neurol Sci* 2007;28:42–4.
 - 7 Aboeata AS, Sontineni SP, Alla VM, *et al*. Coronary artery ectasia: current concepts and interventions. *Front Biosci (Elite Ed)* 2012;4:300–10.
 - 8 Walid A, Jeffrey L. Acute ST elevation myocardial infarction with angiographically normal coronary arteries: causes and outcomes. *Int J Cardiol* 2008;128:131–3.
 - 9 Strunk B, Shaw RE, Bull S, *et al*. High incidence of focal left ventricular wall motion abnormalities and normal coronary arteries in patients with myocardial infarctions presenting to a community hospital. *J Invasive Cardiol* 2006;18:376–81.
 - 10 Panduranga P, Mohammed KM. Primary antiphospholipid syndrome with recurrent coronary thrombosis, acute pulmonary thromboembolism and intracerebral hematoma. *J Invasive Cardiol* 2009;21:E254–8.
 - 11 Marques MA, Murad FF, Ristow AV, *et al*. Acute carotid occlusion and stroke due to antiphospholipid antibody syndrome: case report and literature review. *Int Angiol* 2010;29:380–4.
 - 12 Lee BI, Nam HS, Heo JH, *et al*; Yonsei Stroke Team. Yonsei Stroke Registry. Analysis of 1,000 patients with acute cerebral infarctions. *Cerebrovasc Dis* 2001;12:145.
 - 13 Adams HP Jr, Bendixen BH, Kappelle LJ, *et al*. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. *Stroke* 1993;24:35.
 - 14 Catherine ND, Jonathan M. PFO and paradoxical embolism producing events other than stroke. *Catheter Cardiovasc Interv* 2011;77:903–9.
 - 15 Palomeras SE, Fossas FP, Cano OAT, *et al*. Cryptogenic infarct. A follow-up period of 1 year study. *Neurologia* 2009;24:304–8.
 - 16 Kannan S, Dhanasegaran SE, Raji V. Recurrent arterial thrombosis in a young male: sticky platelet syndrome. *Internet J Hematol* 2008;4:4.
 - 17 Mark YC, Felicita A, Richard CB, *et al*. Hypercoagulable states in cardiovascular disease. *Circulation* 2008;118:2286–97.

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