Spontaneous Early Recanalization after Acute Innominate Artery Thromboembolic Occlusion Secondary to Abrupt Aspirin and Statin Discontinuation A Case Report

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ABSTRACT

Statin and antiplatelet drugs are widely used for prevention of ischaemic stroke and other cardiovascular diseases in high-risk patients. We report a rare case of a 49-year old man with a history of myocardial infarction and hyperlipidaemia who suffered an acute occlusion of his innominate artery (IA) accompanied by subclavian steal syndrome and cerebral infarction, on day seven after abrupt cessation of aspirin and statin, as confirmed by magnetic resonance and computed tomographic angiography of head and neck, and colour-coded Duplex ultrasonography (CCDU). Aspirin and atorvastatin were immediately re-started on admission. Spontaneous recanalization of IA was shown on repeat CCDU and digital subtraction angiography on day 10 after stroke onset. This case serves as a reminder that abrupt discontinuation of both aspirin and statin in patients with previous history of cardiovascular disease may increase the risk of ischaemic stroke.

Keywords: Aspirin discontinuation, innominate artery occlusion, statin discontinuation

Recanalización Temprana Espontánea después de la Oclusión Aguda Tromboembólica de la Arteria Innominada Secundaria a la Discontinuación Abrupta de Aspirina y Estatina

Reporte de un Caso

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RESUMEN

Las drogas estatinas y antiplaquetarias son ampliamente utilizadas para la prevención del accidente cerebrovascular isquémico y otras enfermedades cardiovasculares en pacientes de alto riesgo. Reportamos el raro caso de un hombre de 49 años con antecedentes de infarto del miocardio e hiperlipidemia, que sufrió una obstrucción aguda de la arteria innominada (AI) acompañada del síndrome de robo de la subclavia e infarto cerebral, el séptimo día después del cese abrupto de aspirina y estatina, según lo confirmado por resonancia magnética y angiografía tomográfica computarizada de la cabeza y el cuello, y ultrasonografía Dúplex codificada en colores (CCDU). La aspirina y la atorvastatina fueron inmediatamente reiniciadas tras el ingreso. La recanalización espontánea de la AI fue mostrada en CCDU repetidos y angiografía por sustracción digital el décimo día después del inicio del accidente cardiovascular. Este caso sirve como recordatorio de que la discontinuación abrupta tanto de la aspirina como de las estatinas en pacientes con antecedentes de enfermedad cardiovascular, pueden aumentar el riesgo de accidente cerebrovascular isquémico.

Palabras claves: Descontinuación de la aspirina, oclusión de la arteria innominada, descontinuación de la estatina

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INTRODUCTION

Statin and antiplatelet drugs are widely used in high-risk patients for prevention of ischaemic stroke and other cardiovascular disease (1, 2). We present a rare case of acute innominate artery (IA) occlusion accompanied by subclavian steal syndrome after abrupt cessation of chronic aspirin and statin use for one week. The spontaneous recanalization of the critical IA stenosis was observed on follow-up colour-coded Duplex ultrasonography (CCDU) and digital subtraction angiography 10 days after admission. The finding affected the subsequent clinical management of the patient.

CASE REPORT

The patient was a 49-year old, left-handed man with a history of myocardial infarction post percutaneous transluminal coronary angioplasty eight years earlier and hyperlipidaemia. Since then, he regularly took 100 mg of aspirin and 40 mg of atorvastatin daily. He did not have a history of any other medical disease, including atrial fibrillation and valvular heart disease.

Six months prior to admission, he had a vascular CCDU of his carotid arteries as part of his regular medical check-up with no remarkable findings. One week prior to admission, his regular medication finished and he did not refill. He was taken to the emergency room because of sudden onset of chest tightness and dizziness that was exacerbated by right arm exertion. His blood pressure was 126/78 mmHg in the left upper arm and 82/74 mmHg in the right. The suspicion of subclavian steal syndrome was raised.

On physical examination, he was alert and complained of clumsiness of his left hand. He had Medical Research Council grade 4/5 muscle power and relative brisk deep tendon reflexes in the left-sided limbs with a positive Babinski's sign. His routine laboratory findings were within normal limits, including complete blood count, prothrombin and partial thromboplastin times, fibrinogen and antithrombin III concentrations, protein C, protein S, except for elevated serum cholesterol of 246 mg/dL (n: < 200 mg/dL), elevated low-density lipoprotein of 172 mg/dL (n: < 100 mg/dL) and increased C-reactive protein (CRP) at 1.55 mg/dL (n: 0–0.5 mg/dL).

Magnetic resonance (MR) imaging of the brain with diffusion-weighted imaging (DWI) revealed acute infarctions involving the right precentral and postcentral gyri (Fig. 1A). Time-of-flight brain MR angiography [MRA] (Fig. 1B) disclosed the absence of the right-sided vertebral artery (VA), common carotid artery (CCA) and its branches. Computed tomographic angiography (CTA) showed critical stenosis of the right IA with no contrast enhancement along the entire course of the right subclavian artery (SA) and CCA (Fig. 1C). His carotid artery vascular CCDU demonstrated absence of blood flow with only motion artifact within the right CCA (Fig. 1D), conspicuous decrease in blood flow with a broadened spectrum within the right SA (Fig. 1E), and reversal of flow within the right VA (Fig. 1F) and ophthalmic artery. The echocardiography revealed no thrombus formation or valvular abnormality within the heart.

After admission, his atorvastatin and aspirin were immediately re-started and intravenous fluid hydration was given. The patient showed great clinical improvement and both his National Institutes of Health stroke scale and modified Rankin scale returned to zero.

During hospitalization, invasive treatments such as open and endovascular management had been considered for the patient as two episodes of transient ischaemic attacks occurred on hospitalization days two and four. The patient and his family, however, were hesitant to undertake such an aggressive treatment.



Fig. 1: Day one after stroke onset.

A): Axial magnetic resonance imaging with diffusion weighted imaging shows hyperintense lesions in the right precentral and postcentral gyri. B): Magnetic resonance angiography of the neck vessels demonstrates non-visualization of the right carotid and vertebral arteries. C): Computed tomographic angiography reveals critical stenosis of the innominate artery (IA) [arrow] with almost no contrast enhancement of the proximal portion of the right common carotid artery (CCA) and along the entire course of the right subclavian artery (SA). D–F): Colour-coded Duplex ultrasonography of the neck vessels demonstrates absence of blood flow (with only motion artifact) within the right CCA (D), conspicuous decrease in blood flow with a monophasic waveform within the right SA (0 to 23 cm/sec) (E), and reversal of blood flow within the right-sided vertebral artery (F). On day 10 of hospitalization, follow-up CCDU revealed that the blood flow within the right CCA had returned to normal (Fig. 2A), but the monophasic waveforms within the right SA (Fig. 2B) and to and fro waveforms within the right VA (Fig. 2C) were still present. Follow-up MRA (Fig. 2D) and digital subtraction angiography [DSA] (Fig. 2E) confirmed the existence of partial recanalization with Antiplatelet drugs and statins are widely used in highrisk patients for stroke and cardiovascular disease prevention (1-2). Aspirin is an antiplatelet drug which exerts an irreversible inhibition of platelet aggregation by acetylation of platelet COX-1, which is sustained throughout the life of each platelet [approximately seven to 10 days] (8). The antithrombotic effect lasts for three days after a single-dose



Fig. 2: Day 10 (A-E) and at six months (F) after stroke onset.

A–C): Colour-coded Duplex ultrasonography of the neck vessels reveals a normal waveform within the right common carotid artery (CCA) (A), but persistent monophasic waveforms within the right subclavian artery (SA) (B), with to and fro flow within the right vertebral artery (VA) (C). **D):** Magnetic resonance angiography (MRA) of the neck vessels demonstrates a normal right carotid system but persistent non-visualization of the right VA. **E):** Digital subtraction angiography of the head and neck shows a U-shaped filling defect (arrow), measuring approximately 2.5 cm, straddling the bifurcation of right innominate artery, resulting in partial obstruction of the right SA and right CCA with no significant decreased flow beyond the filling defect. **F):** MRA with contrast of the neck vessels shows a patent innominate artery with total resolution of the U-shaped thrombus.

residual thrombus at the bifurcation of the IA, but no evidence of arterial dissection. The patient was discharged on day 17 with no residual neurologic deficit. Six months later, he underwent brain MRA (Fig. 2F) and CCDU which demonstrated total resolution of the thrombus within the IA. He has had no recurrent cardiovascular event while on regular medication for 48 months.

DISCUSSION

Innominate artery stenosis or occlusion is less common than SA disease in extracranial arterial atherosclerotic disease. Compared to SA lesions (which are primarily asymptomatic), IA lesions have a higher rate of clinical symptomatology. Lesions of the IA can present with variable symptoms including arm claudication, vertebrobasilar insufficiency and cerebrovascular accidents (3, 4). Previous angiographic studies have demonstrated that IA atherosclerotic lesions account for only 2.5% of extracranial and intracranial arterial occlusive disease, but another Doppler ultrasound study has shown that the incidence of IA occlusive disease (accompanied by haemodynamic insufficiency) can be as rare as 0.06% (5, 6). Diverse treatment alternatives are available for patients with acute symptomatic IA occlusion, including percutaneous transluminal angioplasty, intra-arterial thrombolytic therapy, or mechanical thrombectomy (3, 4, 7). However, early spontaneous recanalization of an extracranial arterial occlusion (especially an IA occlusion) has rarely been reported.

of aspirin administration, whereas an increased thromboembolic effect appears at eight to ten days after drug cessation due to new platelet formation with increased COX-1 activity and rebound inflammation (9–11). The studies of Sibon and Orgogozo (12) and Maulaz *et al* (13), have demonstrated that recent aspirin discontinuation is associated with increased stroke risk, with most strokes occurring between six and 10 days after aspirin cessation. However, early reuse of antiplatelet medication might be helpful for recanalization in patients with new thrombus formation within the large extracranial vessels (14).

Statins (3-hydroxy-3-methylglutaryl-coenzyme inhibitors) are cholesterol-lowering drugs. Acute discontinuation of statins in high-risk patients could increase thromboembolic events *via* platelet hyperactivity, rebound inflammatory effects evidenced by elevation of high-sensitive CRP, and reduction of nitric oxide bioavailability to the change in flow velocity (15–17). Furthermore, in patients with coronary artery disease, the decline in flow-mediated vasodilation ability could drop below baseline for as long as seven days and may exacerbate the haemodynamic insufficiency (18).

In the index case, we believe that the acute IA occlusion was due to abrupt cessation of aspirin and statin because the laboratory and image investigations of all causes of IA occlusion were negative, including no evidence of hypercoagulable status, cardiogenic embolism and diffuse artery atherosclerosis. The time span of seven days between

drug discontinuation and IA occlusion, vascular haemodynamic insufficiency symptoms and increased CRP were related symptoms after acute withdrawal of aspirin and statin. Newly formed soft thromboembolic plaque was evidenced by the appearance of CCA occlusion with motion artifacts on CCDU. However, the early reuse of aspirin and atorvastatin not only stopped the growth of thromboembolic plaque, but prompted spontaneous thrombolysis.

This case report emphasizes that acute cessation of the chronic use of aspirin and statins in at-risk patients may raise the risk of recurrent thromboembolic vascular events. Clinicians should ensure patient's adherence to evidenceproven medical treatment for prevention of recurrent cardiovascular events. In patients with acute large extracranial arterial occlusion, detailed clinical survey and a series of imaging studies may be helpful in the immediate evaluation of treatment options.

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