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Levodopa-induced myocardial infarction in a patient with Parkinson's disease and severe coronary artery disease

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Abstract

Levodopa is the most effective medical treatment for Parkinson's disease (PD) to date. As dopamine is known to increase cardiac inotropism and vasomotor tone, peripheral dopamine decarboxylase inhibitor is coadministered to suppress the peripheral conversion of levodopa to dopamine. Levodopa poses potential cardiovascular risks, thus its use in patients with existing coronary artery disease needs to be carefully monitored. We report a case of an elderly male with newly diagnosed PD who developed non-ST-elevation myocardial infarction following levodopa (Madopar) initiation.

Keywords: coronary artery disease, levodopa, myocardial infarction, Parkinson's disease

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Introduction

Parkinson's disease is a progressive neurodegenerative disorder characterised by bradykinesia, tremor, rigidity and postural instability. Levodopa was considered as a breakthrough treatment for PD in the 1960s and has remained the most effective medical therapy for controlling motor symptoms and some non-motor symptoms of PD. While the effects of dopamine on the cardiovascular system are established, there has been little data on the deleterious effects of levodopa on the cardiovascular system, especially in elderly PD patients. Here, we describe a PD patient with underlying coronary artery disease who developed an acute coronary syndrome following levodopa (Madopar) initiation.

Case presentation

A 77-year-old male with no previous medical illness, presented to the emergency department with recurrent left-sided chest pain associated with palpitations for 3 days. He was recently diagnosed with PD, although he had been symptomatic for 10 years. He was initiated on levodopa 100 mg thrice daily a few days prior to his presentation to the emergency department. Further history revealed that the chest pain started on the second day of taking levodopa and worsened with each dose. It occurred within an hour of taking levodopa, lasted for 3 hours and resolved gradually with rest. The chest pain became more intense and persistent with subsequent doses of levodopa. There was no family history of coronary artery disease. He was a chronic cigarette smoker for the past 30 years. On examination, blood pressure was 158/89 mmHg and pulse rate was 116 beats per minute. He had asymmetric parkinsonism with rest tremor, rigidity and bradykinesia consistent with idiopathic PD. The cardiovascular examination was unremarkable. The electrocardiography revealed a sinus rhythm with T-wave inversion in lead II, III, aVF, and ST-segment depression in lead V5 and V6. The serum troponin-I was markedly elevated at 2,383 pg/ml. Transthoracic echocardiography revealed left ventricular ejection fraction of 69%. There was no electrolyte or metabolic disturbance.

He was diagnosed with non-ST-elevation myocardial infarction possibly precipitated by levodopa. The levodopa was thus withheld. He was immediately treated with subcutaneous enoxaparin 60 mg twice daily, aspirin 100 mg daily, clopidogrel 75 mg daily and atorvastatin 40 mg every night. The chest pain resolved on the following day. Coronary angiography was performed and revealed a severe three-vessel disease (Figure 1). Percutaneous coronary intervention was subsequently performed to the left anterior descending and right coronary arteries (Figure 2). At 1-year review, he was angina free and his parkinsonism remained stable with selegiline and trihexyphenidyl.

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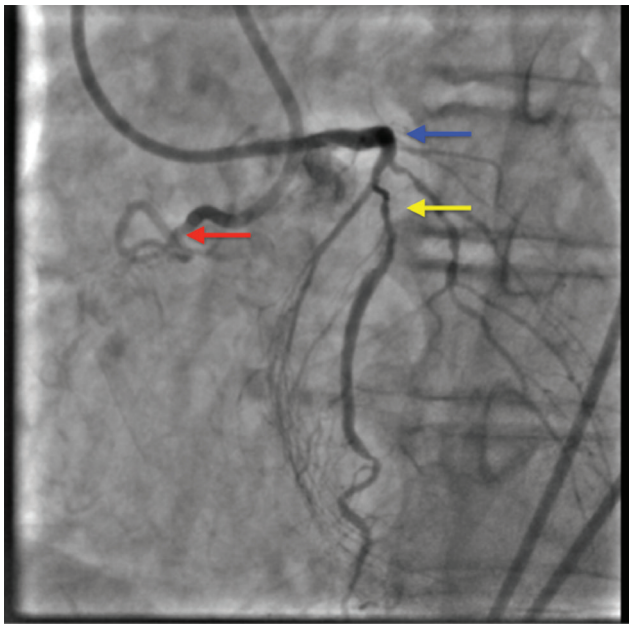
Figure 1 Coronary angiogram showed proximal chronic total occlusion in the right coronary artery (red arrow) and left circumflex artery (blue arrow). The left anterior descending artery showed severe proximal stenosis (yellow arrow)



Discussion

Levodopa is an indispensable drug in the management of PD. Although it is a precursor of dopamine, its effect on cardiovascular system is not fully understood. Endogenous dopamine has been known to increase cardiac inotropism and vasomotor tone. The coadministration of peripheral dopamine decarboxylase inhibitor should have inhibited peripheral conversion into dopamine, thus reducing the potential cardiovascular risk.[1]

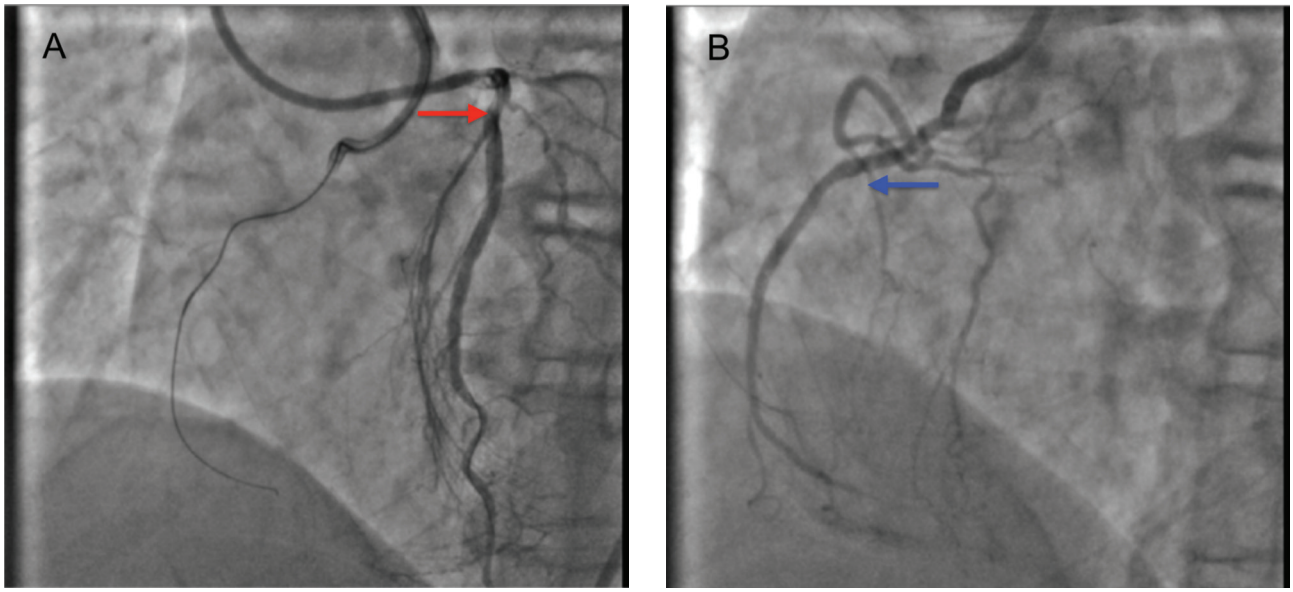
Although this might be a chance concurrence of two common pathologies, the temporal relationship of angina symptoms after the introduction and withdrawal of levodopa suggest that levodopa could have precipitated the myocardial infarction in this patient. As he had coexisting undiagnosed severe coronary artery disease, the levodopa initiation at 100 mg thrice daily might have caused a spill over of dopamine into the peripheries, giving rise to its deleterious effect on the already compromised coronary arteries and myocardium. In addition, unrecognised postural hypotension following levodopa ingestion could have led to reduced cardiac perfusion resulting in myocardial infarction.

Oxidative stress and systemic inflammation are known to play a major role in the pathogenesis of atherosclerosis. More recently, it was postulated that the production of oxidative stress mediators is pivotally involved in the molecular events between mitochondrial dysfunction and alpha-synuclein synaptic pathology.[2] An epidemiological study suggested that PD patients may have an increased risk of coronary artery disease, perhaps due to the shared pathogenesis involving oxidative stress and inflammation in both diseases.[3] Furthermore, chronic cigarette smoking was associated with elevated plasma homocysteine, which could promote atherosclerosis.[4,5] Thus, the development of severe coronary artery disease in this patient might have been a double-hit phenomenon due to the long-standing PD and cigarette smoking.

Conclusion

Although myocardial infarction precipitated by levodopa use in PD patients is rarely seen, we believe our case highlights the importance of recognising this association, especially in patients with high risk of cardiovascular disease. It is, therefore, important to assess cardiovascular risk profile in all PD patients prior to levodopa initiation, and those with high risk should be evaluated and followed up closely upon levodopa therapy initiation.

Figure 2 Postcoronary angioplasty showed good angiographic flow in the (a) left anterior descending artery (red arrow) and (b) right coronary artery (blue arrow). The left circumflex artery was small and nondominant



Informed consent

Written informed consent for the paper to be published (including images, case history and data) was obtained from the patient/guardian for publication of this paper, including accompanying images.

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