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Autonomic dysfunction post-inoculation with ChAdOx1 nCoV-19 vaccine

Keyvan Karimi Galougahi *

Department of Cardiology, Royal Prince Alfred Hospital, 50 Missenden Road, Camperdown, Sydney, NSW, Australia

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ESC Curriculum 9.9 Cardiological consultations • 7.1 Haemodynamic instability • 5.1 Palpitations

A healthy 29-year-old male received the first dose of the ChAdOx1-nCoV-19 vaccine (AstraZeneca). Four-days post-inoculation, he noted intermittent paraesthesia in extremities, which gradually became persistent. He was completely asymptomatic prior to the inoculation, with no fever, cough, shortness of breath, or gastrointestinal symptoms, including since receiving the vaccine. There was no family history of autonomic neuropathy. Clinical examination, including neurologic exam, was normal. Blood count, electrolytes, inflammatory markers, thyroid function, and folate were normal. Polymerase chain reaction assay for COVID-19 was negative. B12 was mildly low [161 ng/L (200–1000)] with a negative intrinsic factor antibody. He was started on B12 injections and Amitriptyline for neuralgia. His symptoms, nevertheless, persisted. Two months post-inoculation, he noted increased heart rate on smartwatch (Apple Inc., *Figure 1A*), with a significant change when standing (80–120 b.p.m.) vs. lying (50–60 b.p.m.). He then developed intermittent

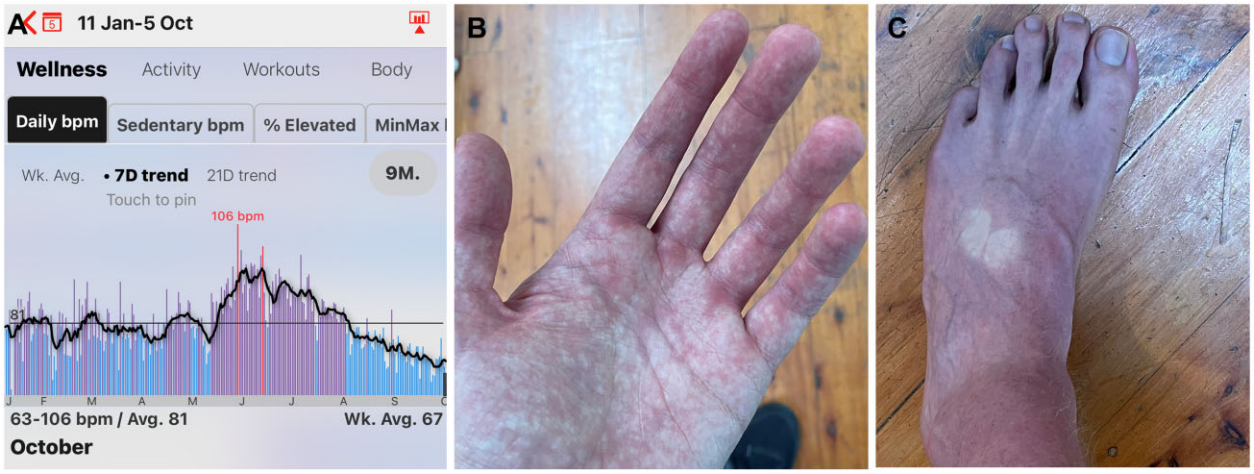

Figure 1 Autonomic dysfunction in a healthy 29-year-old male after a single dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). (*A*) A significant increase in the average daily heart rate was noted on a smart watch (Apple Inc.), starting around 2 months after inoculation with the first dose of the vaccine, which was associated with palpitations. With lifestyle modifications, palpitations and the increase in heart rate settled after 3 months. (*B*) Intermittent mottling in the hands and (*C*) blood pooling and dependent acrocyanosis with very sluggish capillary refill in the feet were exacerbated by orthostatic position for prolonged periods of time.

* Corresponding author. Tel: +611800651373; Email: Keyvan.karimi@hri.org.au
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skin colour changes (dark-blue/white/dark-red) in acral areas (hands/feet/penis), with mottling and blood pooling/dependent acrocyanosis with sluggish capillary refill (*Figure 1B and C*). He had intermittent palpitations, dizziness, and worsening of paraesthesia and skin colour changes especially with prolonged standing, exertion, food intake, or changes in the temperature in the environment, with no pre-syncope or syncope. He also developed difficulty achieving and maintaining an erection.

On examination, recumbent blood pressure/heart rate of 130/70 mmHg/75 b.p.m. changed to 130/70 mmHg/98 b.p.m., 120/80 mmHg/100 b.p.m., and 120/85 mmHg/106 b.p.m. on 1, 3, and 5 min of standing. Electrocardiogram and echocardiography were normal, with rare atrial ectopic beats on 24-h Holter monitor. On autoimmune serology, only antinuclear antibody (ANA) was positive at low titre (speckled pattern, 1:40) with elevated IgA level [5.06 g/L (0.60–3.96)], which did not fulfil the diagnostic criteria for an autoimmune disorder. Limbic encephalitis antibody panel, glutamic acid decarboxylase antibodies, anti-neuronal antibody, and anti-ganglionic acetylcholine receptor antibody were negative. Magnetic resonance imaging of brain-spine and nerve conduction study were normal. With a diagnosis of autonomic dysfunction/postural orthostatic tachycardia syndrome, he received an empiric 5-week course of steroid, with no change in symptoms. With lifestyle modifications, postural tachycardia improved, but paraesthesia and skin colour changes persisted at 6-months.

Autonomic dysfunction can occur secondary to viruses, including post-COVID-19,[1] and vaccines, with a single case reported after the Comirnaty BNT162b2 mRNA vaccine for COVID-19 (Pfizer-BioNTech),[2] although no cases have been reported with the ChAdOx1 nCoV-19 vaccine. Aetiology is unknown but may be mediated via autoimmunity against autonomic ganglia, fibres, or receptors[3]; or other receptors (e.g. ACE[4]). Further studies are needed to determine the prevalence, aetiology, and management of autonomic dysfunction secondary to COVID-19 vaccination.

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