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CASE REPORT

Neuro-ophthalmic complications with ChAdOx1 nCoV-19 vaccine-induced thrombocytopenia and thrombosis

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Introduction

A syndrome of acute thrombosis and thrombocytopenia can occur with the ChAdOx1 nCoV-19 vaccine (AstraZeneca). This article describes two patients who presented with neuro-ophthalmic complications related to the vaccine-induced thrombocytopenia and thrombosis syndrome. At presentation, both had low fibrinogen and raised D-dimer levels. One patient recovered without any visual defects, while the other remained with very poor vision in the affected eye.

Case report 1

A 37-year-old woman, previously well, with a body mass index of 17.9 kg/m^2, who was taking no regular medication, noticed bilateral headaches 5 days following her first dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). Ten days after vaccination, she awoke with profound left eye visual loss. She was thrombocytopenic with a platelet count of 21x10^9/litre and a raised D-dimer level of 28.4 mg/litre. Computed tomography scan of the head showed a left-sided ophthalmic vein thrombosis. A presumptive diagnosis of vaccine-induced thrombocytopenia and thrombosis was made, and 50 g intravenous immune globulin started. She was transferred to a tertiary centre, disorientated and slightly hypertensive with a sinus bradycardia, suggestive of raised intracranial pressure. Fibrinogen was 0.97 g/litre, she had a normal coagulation screen and her D-dimer level was 24 070 ug/litre FEU (fibrinogen equivalent units, normal range 0–550 ug/litre FEU). Radiological examination confirmed extensive venous sinus thrombosis, bilateral intracerebral infarcts with bilateral thrombosis of the internal carotid arteries. She was given further intravenous immune globulin and fibrinogen concentrate. Plasma exchange was started, with 500 g pulsed intravenous methylprednisolone and further intravenous immune globulin post plasma exchange. With improved platelet count, fondaparinux was commenced. Further imaging identified a right-sided pulmonary embolus and pelvic venous system thrombosis.

She had a normal acuity of 6/6 in the right eye but hand movements only in her left. She identified 15/17 of the Ishihara colour plates with the right eye but none in the left. She had a brisk left-sided relative afferent pupillary defect. Fundoscopy (Figure 1) revealed inner retinal pallid swelling and a cherry-red spot suggestive of retinal ischaemia, consistent with a central retinal artery occlusion in the left eye. The diagnosis was confirmed on optical coherence tomography, which showed thickening of the inner retina and sparing of the outer retina.

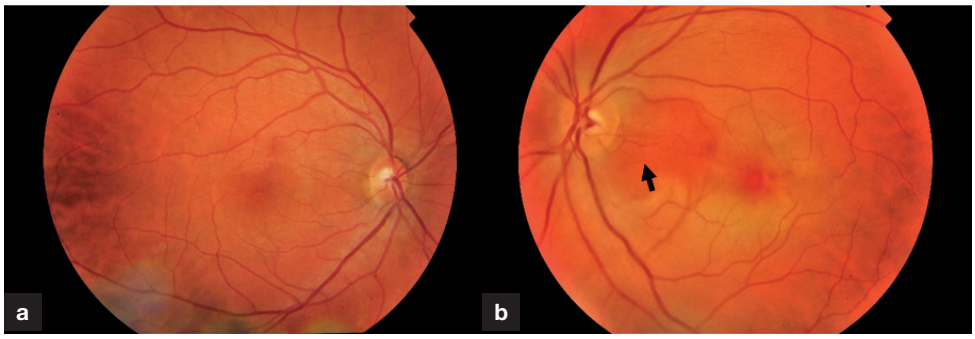

Figure 1. Colour fundus photography. a. Healthy right fundus. b. Retinal whitening from ischaemia with a cherry-red spot over the fovea and partial retinal sparing from the cilioretinal artery (arrow).

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Case report 2

A 23-year-old man, previously well, with a body mass index of 23.8 kg/m^2, developed headache and vomiting 10 days after his first dose of the ChAdOx1 nCoV-19 vaccine. Three days later, he developed right-sided weakness and confusion. His platelet count was 22x10^9/litre and his D-dimer level was 25.5 mg/litre. He was treated with intravenous hydrocortisone, intravenous immune globulin and fondaparinux. His Glasgow Coma Scale dropped to 6/15, likely related to a seizure, and he was intubated, ventilated and transferred to the authors' centre. Imaging confirmed extensive venous sinus thrombosis with intracerebral haemorrhage (Figure 2).

Daily plasma exchange was initiated, with intravenous immune globulin, 1 g intravenous methylprednisolone and neuroprotective measures. Following further epileptic episodes, he was started on levetiracetam. Low-dose argatroban infusion was started, normally used for heparin-induced thrombocytopaenia, an off-label use; fibrinogen levels normalised with fibrinogen concentrate. By day 3, his platelet count had improved to 79 x10^9/litre and argatroban infusion was increased. When his platelet count had improved and fibrinogen levels started increasing, plasma exchange and intravenous immunoglobulin were stopped and he switched to fondaparinux. Following extubation on day 8, he complained of headache and was referred to neuro-ophthalmology. On examination he had normal distance visual acuities of 6/6 bilaterally, normal colour vision, a slightly enlarged blind spot in his left eye and a normal visual field in his right. Fundoscopy (Figure 3) revealed acute haemorrhagic papilloedema in both eyes, with no associated retinal folds, choroidal folds or maculopathy. Spontaneous venous pulsation was absent in either eye, associated with significantly raised intracranial pressure (D'Antona et al, 2019). He had no ophthalmoplegia.

Oral acetazolamide 250 mg 4 times daily was started. Ten days later, he had normal visual acuities, colour vision and visual fields. Papilloedema was improving and spontaneous venous pulsation had become just visible (grade 1).

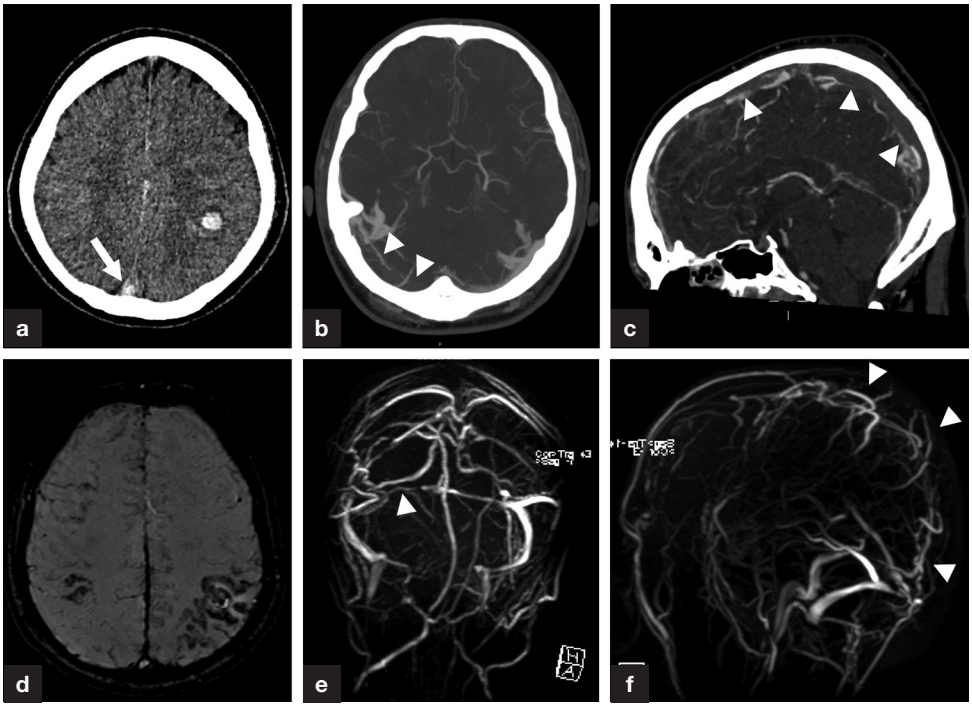

Figure 2. a–c. Computed tomography and (d–f) magnetic resonance imaging studies. a. Non-contrast computed tomography shows hypodense thrombus within the superior sagittal sinus (white arrow) and haematoma within the left parietal subcortical white matter. d. Susceptibility-weighted imaging acquisition shows increased susceptibility within the sulci of the right frontal and both parietal regions. b and c. Contrast-enhanced computed tomography and (e and f) three-dimensional phase-contrast venographic studies show absence of contrast with signal voids affecting the superior sagittal and right transverse sinuses (white arrowheads).

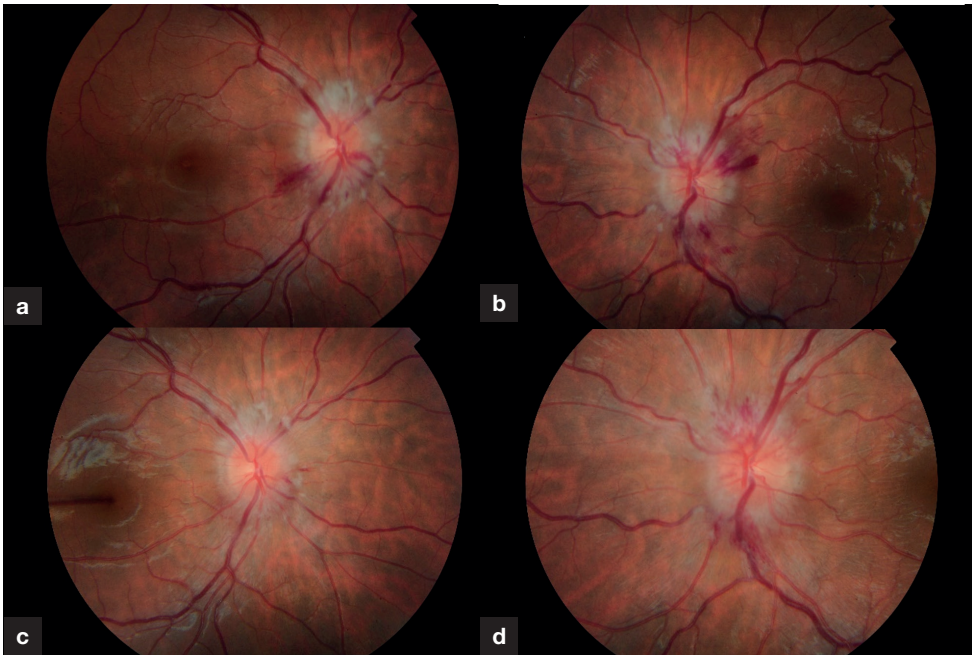

Figure 3. Disc colour photographs. a and b. Haemorrhagic papilloedema of the right and left disc respectively; the severity of papilloedema was graded according to the Frisén scale. The marked papilloedema with elevation of the entire optic nerve head, obscuration of all borders and total obscuration of a major blood vessel corresponds to grade 4. c and d. Improvement 10 days later to Frisén grade 3, which is moderate papilloedema.

Discussion

A syndrome of acute thrombosis and thrombocytopenia can occur with the ChAdOx1 nCoV-19 vaccine (AstraZeneca) (Bayas et al, 2021; Greinacher et al, 2021; Schultz et al, 2021; Scully et al, 2021). Patients with cerebral venous sinus thrombosis in the context of vaccine-induced thrombocytopenia and thrombosis present a significant clinical challenge, and early treatment decisions are critical. By day 3, patient 1 had improved D-dimer, platelet and fibrinogen levels. Plasma exchange enabled faster normalisation of platelet count. There is no effective treatment for central retinal artery occlusion presenting 4 hours after symptom onset, as irreversible damage occurs. Neovascularisation of the iris, iridocorneal angle or retina can occur, so careful follow up is needed. Despite her otherwise-excellent systemic recovery, the patient was very upset about her visual loss, and careful counselling was required during her reviews in the eye clinic to help her understand that her vision was not going to recover.

Patient 2, with vaccine-induced thrombocytopenia and thrombosis-related extensive venous sinus thrombosis and secondary intracranial haemorrhage, presented with weakness and seizures, requiring prompt intubation and ventilation. He was treated with intravenous immune globulin and daily plasma exchange and received intravenous methylprednisolone. He made a remarkable recovery and, before discharge, fondaparinux was stopped and apixaban started; he continued levetiracetam and acetazolamide. Optic nerve function remained good despite a significant degree of oedema. He remained well.

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Learning points

- Central retinal artery occlusion is a devastating potential consequence of vaccine-induced thrombocytopenia and thrombosis; this is the first reported case in the literature.
- In patients with venous sinus thrombosis from vaccine-induced thrombocytopenia and thrombosis or other causes, early ophthalmic assessment including acuity, colour vision, formal perimetry and optical coherence tomography is helpful. In this case, visual assessment prompted commencement of intracranial pressure-lowering medication, which may have contributed to his excellent visual outcome.

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