Acute ST-segment elevation myocardial infarction secondary to vaccine-induced immune thrombosis with thrombocytopaenia (VITT)

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SUMMARY

A 40-year-old man with no cardiac history presented with central chest pain 8 days after receiving the ChAdOx1 nCov-19 vaccine against COVID-19. Initial blood tests demonstrated a thrombocytopaenia (24×10^9 µg/L) and a raised d-dimer (>110 000 µg/L), and he was urgently transferred to our tertiary referral central for suspected vaccine-induced immune thrombocytopaenia and thrombosis (VITT). He developed dynamic ischaemic electrocardiographic changes with ST elevation, a troponin of 3185 ng/L, and regional wall motion abnormalities. An occlusion of his left anterior descending coronary artery was seen on CT coronary angiography. His platelet factor-4 (PF-4) antibody returned strongly positive. He was urgently treated for presumed VITT with intravenous immunoglobulin, methylprednisolone and plasma exchange, but remained thrombocytopaenic and was initiated on rituximab. Argatroban was used for anticoagulation for his myocardial infarction while he remained thrombocytopaenic. After 6 days, his platelet count improved, and his PF-4 antibody level, troponin and d-dimer fell. He was successfully discharged after 14 days.

BACKGROUND

Attempts to curtail the SARS-CoV2 pandemic have led to the development of several vaccinations against COVID-19. One such vaccine is ChAdOx1 nCoV-19 adenoviral vector vaccine against COVID-19 manufactured by AstraZeneca. It has been widely administered throughout the UK, with its use recently restricted to those over the age of 40 due to safety concerns.[1] It has been linked to rare but potentially fatal complications. The most concerning of these is vaccine-induced immune thrombocytopaenia and thrombosis (VITT). VITT is a rare syndrome of immune-driven thrombosis and thrombocytopaenia that appears to mimic heparin-induced immune thrombocytopaenia and thrombosis (HITT).[2–4] It affects patients of all ages, and both sexes without any apparent predisposing risk factors.[2 3]

VITT most commonly presents 5–28 days post-vaccination and is characterised by thrombocytopaenia, thrombosis, a raised d-dimer and the presence of platelet factor-4 antibodies.[1–4] The exact aetiology remains undefined, with its similarity to HITT reflected in current treatment strategies. Published reports describe the preponderance of cerebral venous sinus thrombosis, pulmonary emboli, splenic and portal vein thrombosis, and the potential for catastrophic intracranial haemorrhage.[1 4–6] Isolated coronary artery involvement appears to be rare with no previous cases published.

We describe the case of a 40-year-old man with no cardiac history who presented with isolated coronary artery thrombosis secondary to VITT. This resulted in left anterior descending artery occlusion and an ST-segment elevation myocardial infarction.

CASE PRESENTATION

A 40-year-old man presented to the emergency department with a 1-day history of central, crushing chest pain. He had received his first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine against COVID-19 8 days previously. In the 2 days following his vaccination, he reported transient myalgia and febrile symptoms that resolved within 48 hours. His medical history was significant only for smoking and previous gastric ulceration.

On arrival to the hospital, his initial ECG and troponin (28 ng/L) were normal. A full blood count demonstrated thrombocytopaenia with a platelet count of $24\times10^9\mu$g/L, polycythaemia (189 g/L) and a significantly raised d-dimer (119 000 μg/L). A diagnosis of likely VITT was made and the patient was transferred to our hospital that evening, the regional tertiary referral centre.

During transfer, the patient reported further episodes of heavy central chest pain. On arrival to our critical care unit, his chest pain had resolved but he began to develop ischaemic electrographic changes, with hyperacute T waves seen in leads V2, V3 and the beginnings of ST-segment elevation in V4–V6. Over the coming hours, this evolved to extensive ST elevation throughout his precordial leads; however, he remained pain-free (figure 1). His was hypertensive with a systolic blood pressure of >200 mm Hg and tachycardic at 100–110 beats/min. To optimise coronary perfusion, he was started on intravenous glyceryl–trinitrate and labetalol infusions to target a systolic blood pressure of <120 mm Hg and a heart rate of <80 beats/min.

INVESTIGATIONS

Initial post-transfer blood tests demonstrated a rising troponin to 420 ng/L, worsening thrombocytopaenia with a platelet count of 5×10^9/L, and a strongly positive PF-4 antibody of 2.48 optical density units. An initial bedside transthoracic echocardiogram (TTE) demonstrated anterior septal hypokinesia but an otherwise normal heart. Initial

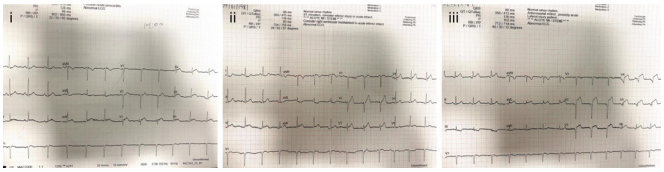

Figure 1 ECGs from the patient's first night of admission taken over a 4-hour period. Presented in chronological order from i to iii, demonstrating evolving ischaemic changes within the left anterior descending artery territory.

CT angiography of his head, chest, abdomen and pelvis was performed on arrival to investigate for the presence of any other thrombi, but none were found.

Throughout the night, his ECG continued to worsen and repeat echocardiography revealed new akinesia of his septal and anterior walls, in keeping with the ischaemic territory implicated by his electrocardiographic changes.

Further TTEs performed over the coming days demonstrated persistent akinesia of his anterior and septal walls, and the development of new tricuspid regurgitation with raised pulmonary artery pressures (45 mm Hg on TTE). His troponin rose to 3185 ng/L and his N-terminal pro B-type natriuretic peptide from 967 ng/L on admission to 4033 ng/L. He developed episodes of shortness of breath secondary to pulmonary oedema requiring supplementary oxygen and diuretics, with bedside lung ultrasound demonstrating bilateral pleural effusions.

A CT coronary and pulmonary angiogram was performed on day 5 of his admission. This demonstrated extensive thrombus from the origin of the left anterior descending coronary artery with moderate proximal stenosis and complete occlusion from the level of the first septal branch (figure 2), with a total coronary calcium score of 0. It also demonstrated a new right lower lobe segmental pulmonary embolism.

DIFFERENTIAL DIAGNOSIS

VITT was considered early following presentation, influenced by the timing of the patient's presentation postvaccination, the presence of severe thrombocytopaenia and a significantly elevated d-dimer with signs of new thrombosis, all coupled with the current drive to increase awareness of the syndrome. This was then confirmed by the presence of PF-4 antibodies.

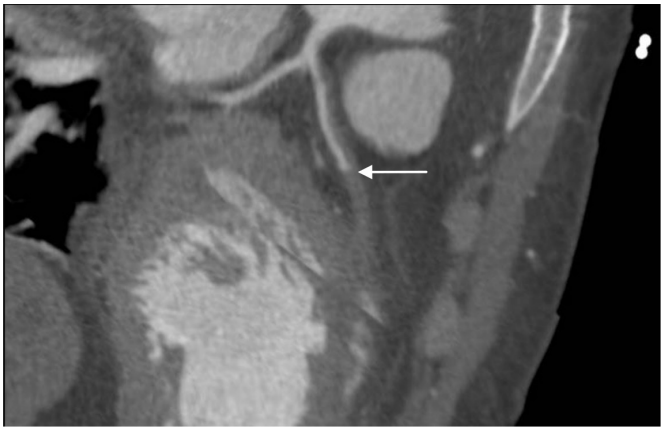

Figure 2 CT coronary angiogram demonstrating complete occlusion of the left anterior descending artery from the first septal branch (arrow).

The cardiac sounding nature of the patient's chest pain made the possibility of a myocardial infarction high despite the patient having no history of ischaemic heart disease, the initial normal ECG and troponin. When considering the aetiology of the occlusion, the diagnosis of VITT with myocardial infarction was key in guiding transfer and treatment. Current consensus is that despite the presence of myocardial ischaemia, the primary goal should be to treat the VITT in a specialist centre.

Other diagnoses to consider in patients with VITT include pulmonary embolism. Indeed, this patient presented with chest pain, tachycardia and a significantly raised d-dimer. However, his initial CT pulmonary angiogram (CTPA) demonstrated no conclusive evidence of pulmonary embolism and no signs of right heart strain were seen on echocardiography. It was the new tricuspid regurgitation and increased pulmonary pressures found on repeat TTE that led to a repeat CTPA being performed and identification of a new pulmonary embolism.

Given the extreme predisposition of patients with VITT to cerebral venous sinus thrombosis, portal and splenic vein thrombosis, and the patient's raised d-dimer, a CT cerebral venogram of the abdomen and pelvis was also performed. This was in accordance with VITT guidelines, but no further thrombi were found.[7]

TREATMENT

On arrival to our critical care unit, the patient was urgently treated with 1 L volume plasma exchange followed by 0.5 g/kg of intravenous immunoglobulin, and 1 g of methylprednisolone. An argatroban infusion of 0.5 μg/kg/min was used as anticoagulation for this patient while he remained severely thrombocytopaenic. Despite this, his platelet count remained $<10\times10^9$/L; his troponin continued to rise; and his cardiac function worsened.

He was discussed with the interventional cardiology team several times as his ischaemia evolved. It was concluded that his thrombocytopaenia meant he was not suitable for primary coronary intervention or antiplatelet therapy and treatment of his VITT should predominate. The decision was made to reassess initiation of antiplatelet agents and the need for a coronary angiogram once his platelet count reached $>50\times10^9$/L. This was revisited daily with the possibility of bridging platelet therapy to facilitate coronary angiogram considered. However, it was felt the risk of any acute intervention was outweighed by bleeding and restenosis risks, especially as his infarction was now established.

The patient was initiated on secondary prevention medications including bisoprolol and ramipril, alongside a titrated labetalol infusion to treat hypertension. He also required intermittently doses of furosemide to manage his fluid balance and avoid further episodes of pulmonary oedema.

His ongoing VITT treatment consisted of daily plasma exchange, further intravenous immunoglobulin (1 g/kg in total) and steroid treatment (3 g of methylprednisolone over 3 days followed by 1 mg/kg of prednisolone orally once a day. This was followed by a decrease in his PF-4 to 0.54 optical density units (normal), although no reciprocal rise in platelet count was seen initially, an unusual finding in the context of VITT. On day 3, the patient was started on rituximab, an anti-CD20 monoclonal antibody, receiving four 800 mg doses over a 10-day period.

OUTCOME AND FOLLOW-UP

An increase in his platelets was seen approximately 6 days after admission, increasing to 151×10^9/L by day 10 (after which his daily plasma exchange therapy was discontinued). This was accompanied by a fall in troponin to 826 ng/L (from 3185 ng/L) and d-dimer to 16 760 ng/L (from 26 270 ng/L).

By day ten the patient had no ongoing oxygen requirement, suffered no further episodes of chest pain or pulmonary oedema, and had been successfully weaned off labetalol. He completed a four-dose course of Rituximab and ten days of plasma exchange in total.

Once his platelet count recovered to >50×109/L, his argatroban was switched to treatment dose fondaparinux (with the view to switch to rivaroxaban on discharge); his prednisolone was weaned; and he was stepped down from critical care to the haematology ward. His TTE on discharge demonstrated mildly reduced left ventricular function with an akinetic mid to apical anteroseptum and apex with slow flow in these areas, and hypokinesia of the mid to apical inferoseptum. His right ventricular function remained normal with a follow-up TTE recommended to monitor for any changes.

The ongoing management of his myocardial infarction was discussed at the cardiology multidisciplinary team meeting. Due to the uncertainty surrounding his future platelet count trajectory, given the limited data available surrounding in VITT, it was decided the best option would be medical management with a cardiac magnetic resonance (CMR) scan in 4 weeks. Single antiplatelet therapy, in addition to rivaroxaban, was concluded as sufficient for the time being with ongoing review as his recovery progressed.

The outpatient CMR demonstrated extensive left anterior descending artery territory infarction with hypokinesis of the basal anteroseptum, thinning and akinesis of the mid-anteroseptal and inferoseptal walls, and akinesis of the apical anterior, septal, and inferior walls, and the true apex.

At a follow-up cardiology clinic 6 weeks post discharge, the patient's symptoms remained stable on medical therapy. The ongoing management plan included a repeat CT coronary angiogram to assess the left anterior descending artery thrombus and cardiology follow-up in 3 months.

DISCUSSION

This article describes the first published case of isolated coronary artery thrombus secondary to vaccine-induced immunological thrombocytopaenia and thrombosis. Over the past few months, a number of case series have been published, forming the basis of current international treatment guidelines.[2–4 7] Findings common to all cases include thrombocytopaenia, high levels of PF-4 antibodies, a raised d-dimer and the presence of thrombi, with common locations including cortical veins, venous sinus, splenic and portal vein thromboses.[1–4 7] Almost all cases have been seen 1–2 weeks following ChAdOx1 nCoV-19 adenoviral vector vaccine against COVID-19.[1–4 7] None had previously reported coronary artery thrombosis.

Due to the novelty of the disease, guidelines are continuously being re-evaluated and updated. The most recent guidelines published by the British Haematology Society emphasise the importance of urgent intravenous immunoglobulin, anticoagulation with non-heparin-based therapies (although this must be balanced with the risk of haemorrhage in such patients), consideration of plasma exchange, steroids, referral to a tertiary centre, and cerebral and abdominal imaging.[7] In patients not responding to initial treatment, rituximab may be considered, as was the case in this patient.[7]

To date, no incidents of isolated VITT-related myocardial infarction have been published, and guidelines on managing the disease continue to evolve. The patient was transferred to our hospital as a tertiary VITT centre and was treated as per the aforementioned guidelines but with little effect on his coronary vessel patency. As no specific guidelines exist on the management of VITT-associated ST-elevation myocardial infarction, his management plan was the result of ongoing discussion between the critical care, cardiology and haematology teams. The treatment emphasis remained on immunosuppression, plasma exchange and non-heparin-based anticoagulation. As he was initially unresponsive to the aforementioned treatments, the patient was started on the anti-CD20 monoclonal antibody rituximab. This has a well-established role in the management of autoimmune disease, but its use in VITT remains novel and is reserved for those not responding to other treatments.

As we continue to administer novel vaccines such as ChAdOx1 nCoV-19 adenoviral vector vaccine against COVID-19 to millions, we must remain cognisant of potential complications and the heterogenous nature in which they may present. Guidelines will continue to evolve and currently emphasise the importance of prompt investigation (specifically of headaches or abdominal pain) and expert consult. This case emphasises the potential for isolated coronary artery thrombus, even in those with no underlying coronary artery calcification. Thus, highlighting the importance of a low threshold for cardiac investigation in patients presenting with chest pain following vaccination and a multidisciplinary approach to decision making.

Patient's perspective

When I first felt the chest pain I felt shocked and panicked. I immediately thought it was related to the vaccine and because of everything I had seen on the news thought I was going to die. I was initially unsure about what treatment I would be given but felt relieved when I found out I was being transferred to a specialist hospital. My first night there was a blur, I remember meeting the intensive care team and feeling like it was a formula 1 pit-stop team whilst they organised my treatment. My main feeling now is one of frustration, that there is nothing that I can do to speed up my recovery and that I just need to wait for my body to fix itself. With regards to my feelings about the vaccine, I knew the risks when I was getting it and I know it is not anyone's fault. I wanted to get it to help the greater good so we could control COVID-19 and if anything feel bad now that I am using up more of the NHS' time being treated for the side effects.

Learning points

- Vaccine-induced immune thrombocytopaenia and thrombosis (VITT) is a rare but potentially fatal side effect of the ChAdOx1 nCoV-19 adenoviral vector vaccine against COVID-19.
- VITT may present with isolated coronary artery thrombosis leading to ST elevation myocardial infarction, even in patients with no underlying coronary artery calcification.
- We must remain open and adaptable in our approach to the treatment of VITT, with expert multidisciplinary team input at the heart of decision making.

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