MEDICAL IMAGING—ORIGINAL ARTICLE

Impact of COVID vaccination rollout on the use of computed tomography venography for the assessment of cerebral venous sinus thrombosis

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Abstract

Introduction: Cerebral venous sinus thrombosis (CVST) is rare; however, it has been observed in patients with vaccine-induced immune thrombotic thrombocytopaenia syndrome (VITT) following the use of adenovirus vector vaccines against COVID-19. Adverse vaccine effects have been heavily addressed in mainstream media, likely contributing to vaccination anxiety. This study aimed to assess how the vaccine rollout and media coverage has influenced the use of computed tomography venography (CTV) in an acute care setting of a tertiary hospital.
Method: Single-centre retrospective cohort study from 30 March 2021 to 13 June 2021. Direct comparison to same calendar dates in the preceding 3 years.
Results: In 2021, 57 patients received CTV with headache being the reason in 48 (84%) and 40 (70%) had received ChAdOx1 nCov-19 (AstraZeneca COVID-19 vaccination). Only 20 of these patients received CTV after platelets and D-Dimer had returned, and only three patients met existing guidelines for imaging. Zero cases were positive. The number of CTV studies was 5.2 times than in 2020 and 2.7 times the mean number for the 3 preceding years.
Conclusion: The use of CTV in patients with headache has markedly increased at our centre since negatively biased vaccination influence of mainstream media. Headache is a common vaccine-related side effect and VITT is exceptionally rare. With the rates of vaccination increasing in the community, these results highlight the importance of strict adherence to established evidence-based guidelines. Otherwise, critical care capacity, and in particular imaging resources already under pressure will be strained further.

Key words: AstraZeneca; COVID; CVST; thrombus; vaccine.

Introduction

Cerebral venous sinus thrombosis (CVST) is rare, accounting for <1% of stroke admissions and a has a low population incidence of 0.22–1.57 per 100,000.[1,2] A small number of CVST have been observed in patients following vaccination against severe acute respiratory distress syndrome coronavirus 2 (SARSCoV2 or COVID-19) with adenovirus vector vaccines;[3,4] more specifically, following the use of either ChAdOx1 nCov-19 (AstraZeneca COVID-19) or Ad26.COV2.S (Janssen/Johnson & Johnson COVID-19).[3,4] The former is the only provisionally registered adenovirus vector vaccine for use in Australia at time of writing.[5] A second vaccine is provisionally registered in Australia, BNT162b2 (Pfizer-BioNTech), and is based on mRNA technology and not known to cause thrombotic thrombocytopaenic syndrome.[6,7]

This novel thrombosis syndrome known as vaccine-induced immune thrombotic thrombocytopaenia syndrome (VITT) is caused by autoantibodies to platelet factor 4 (PF4).[7] VITT is reported to be a rare condition occurring between day 5 and 30 post vaccination and results in thrombosis in both typical sites (e.g. pulmonary embolism) and unusual sites (e.g. splanchnic circulation

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Table 1. Thrombosis and Haemostasis Society of Australia and New Zealand diagnostic criteria for VITT[3]

Exposure to ChAdOx1 nCov-19, (AstraZeneca) within 4–30 days of symptom onset.
Thrombocytopenia or falling platelet count and elevated D-Dimer (>5 times upper limit normal) or reduced fibrinogen.
Thrombosis: Any deep vein thrombosis, pulmonary embolism or arterial thrombosis. Thrombosis in uncommon sites, such as CVST and splanchnic vein thrombosis, is strongly suggestive.
Antibodies detected against PF4/polyanion.
Functional assay indicating patient-derived plasma/serum induction of prothrombotic phenotype in healthy donor platelets.

and cerebral veins) with diagnostic criteria detailed in Table 1.[3] At time of writing, there have been 60 VITT cases in Australia, and two fatalities amongst 5.8 million doses.[8]

While the incidence of VITT is low, there has been significant coverage of adverse vaccine effects in mainstream media and this has likely contributed to anxiety for those who have been vaccinated.[9–11] At our institution, many patients have presented to the emergency department with concerns regarding potential vaccine-related effects, including headache, a common side effect.[12,13] Assessment of CVST using computed tomography venography (CTV) is standard of care in the acute setting; however, it has not been validated as a screening test. Unlimited scanning of patients with acute headache post vaccination carries considerable economic cost, including opportunity cost, radiation risk and risks of intravenous contrast-induced complications.

This study aimed to examine the effect of SARSCoV2 vaccination on CTV use in a tertiary Victorian healthcare provider.

Methods

Research ethics standards compliance

Ethical approval was provided by the institutional research and ethics committee, including a waiver of consent.

Population

Retrospective cohort study in an acute care setting for CTV between 31 March 2021 and 13 June 2021. Patients were identified through the Radiology Information System and Electronic Medical Record (EMR). This 75-day period begins at the date from early reported concerns in Australian media regarding CVST post vaccination. Further data were collected from the same calendar dates for the three consecutive preceding years, to allow for comparison. Patients were excluded if the indication for CTV was blunt force trauma. All other patients above the age of 18 years were included in the study.

Patient details and definitions

Data collection included demographics, presenting symptom and diagnosis (positive or negative for CVST). For patients who were examined in 2021 additional collected data included platelet levels, D-Dimer, vaccination details (type of vaccination and number of days from injection to presentation), if applicable.

Outcomes

The primary outcome was to assess the number of positive CTV scans in 2021 to identify the incidence rate and compare this to preceding years.

Statistical analysis

Data were collated using Microsoft Excel (Microsoft, USA) and expressed as number (percentage), mean (SD) or median (IQR) according to the data type. Data were assessed for significance using Student's *t*-test and binary logistic regression according to the relative data type and outcome. A two-tailed *P*-value of <0.05 was considered statistically significant.

Results

A total of 57 patients were referred for CTV in an acute care setting between 31 March 2021 and 13 June 2021 (Figure 1) and there were zero patients diagnosed with CVST. The mean age was 54.3 years (SD 19.7), and the majority (80.7%) were females as shown in Table 2.

A total of 64 patients were identified in the same study period window for the three previous consecutive years combined, or 21.3 per year and there were two patients diagnosed with CVST. The incidence rate in 2018 was 1 per 27, 1 per 26 in 2019 and 0 per 11 in 2020. Significance testing comparing 2021 to the preceding years was not possible due to the zero incidence in 2021. The mean age for the 2018–2020 population was 41.5 years (SD: 15.2, $P < 0.001$), and majority of whom were female (73%, $P = 0.346$).

Headache was the primary presenting complaint for both the 2021 (84.2%) and 2018–2020 cohorts (76.6%, $P = 0.295$). Other presenting complaints included stroke symptoms, decreased consciousness, eye symptoms and facial or ear inflammatory processes.

Vaccination population details

As shown in Table 3, 40 of 57 patients were referred this year (2021) for CTV following EMR documentation of AstraZeneca vaccination at a median of 10 days following vaccination (IQR 7.25). No patients were referred for CTV in this study period following Pfizer vaccination. Thirty-two patients (80%) had both full blood count (including platelets) and a D-Dimer test in the emergency

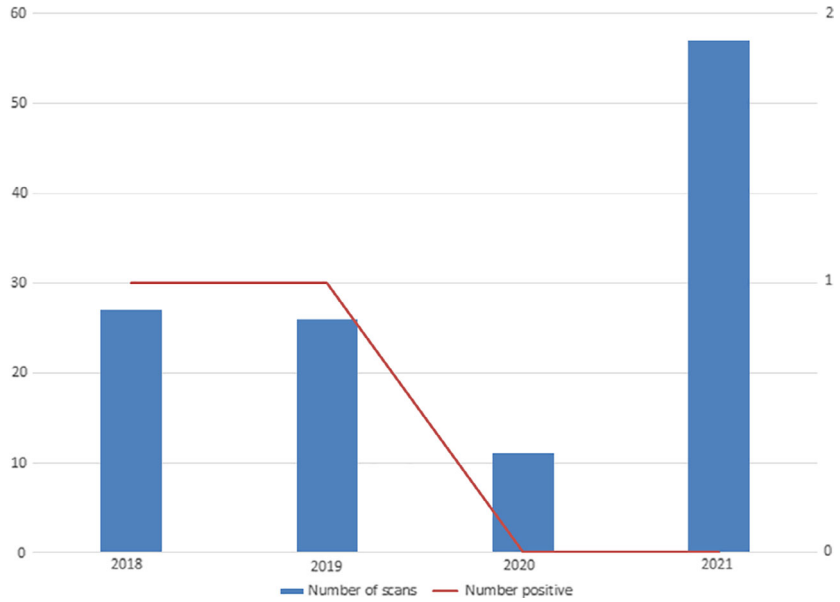

Fig. 1. CT brain venogram studies performed 31 March to 13 June in 4 consecutive years and their outcome.

Table 2. Comparison of CT brain venogram studies performed 31 March to 13 June in 4 consecutive years

	2021	2020	2019	2018	2018–2020 combined	*P*-value†
Female gender (*n*, %)	46 (80.7%)	8 (72.7%)	21 (80.8%)	18 (66.7%)	47 (73.4%)	OR 1.513, $P = 0.346$, 95% CI: 0.640–3.576
Age (mean, SD)	54.3 (19.7)	37.7 (14.8)	43.0 (16.4)	41.5 (14.4)	41.5 (15.2)	$P < 0.001$, 95% CI: 6.552–19.146
Headache as presenting symptom (*n*, %)	48 (84.2%)	8 (72.7%)	20 (76.9%)	21 (77.8%)	49 (76.6%)	OR 1.6, $P = 0.295$, 95% CI: 0.652–4.086
Number of scans (*n*)	57	11	26	27	64	N/A
Number of positive (*n*, %)	0	0	1 (3.8%)	1 (3.7%)	2 (3.1%)	N/A‡

†Comparing 2021 to 2018–2020

‡Unable to compare odds given the incidence of zero in 2021.

Table 3. Vaccine statistics for patients in 2021 presenting with headache and receiving CT venography

Number of Pfizer vaccinations	0
Number of AstraZeneca vaccinations	40
Day of presentation post AstraZeneca (median, IQR)	9.5 (7.25)
AstraZeneca patients who met criteria for VITT (*n*, %)	3 (7.5%)

department. Twelve patients (40%) underwent CTV prior to pathology collection or results available for review. Three (7.5%) AstraZeneca patients met Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ) criteria for imaging.[3]

Discussion

Cohorts in this study were of similar gender and presenting symptom of which headache was the most common. In 2021, the mean age was significantly higher than for preceding years (54.3 vs. 41.5 years, $P < 0.001$) which likely reflects the older demographic who were eligible for vaccination during the early phases of rollout.[14]

The number of CTV performed in 2021 was 2.7 times the mean number from the preceding 3 years and 5.2 times the number in 2020. The cause of this increase is multifactorial. The major factor behind scanning is likely related to patient anxiety in the context of abundant media coverage of vaccination complications. However, emergency department practitioners are also placed in a challenging situation, where National Emergency Access Targets encourage early scanning sometimes prior to availability of relevant differentiating tests, such as platelets and D-Dimer.[15] In addition, it is likely that there is cognitive bias within emergency physicians whom are influenced by the community's hyper vigilance on the background of an unprecedented and uncertain pandemic. As a result, over 90% of the patients in this study following AstraZeneca vaccination did not meet imaging criteria for VITT-associated CVST as in Table 1.[3]

Computed tomography venography is the first-line investigation for CVST in Australia as it is accurate, reproducible and rapidly available. It has also been proven to be at as accurate as magnetic resonance venography (MRV) for the diagnosis of CVST without the costs and resources required to generate MRV.[2,16] However, the use of CTV is not without risk, including ionizing radiation exposure, contrast allergic reaction and contrast nephropathy.[2] Majoie et al.[17] estimate the effective dose for a CT venogram to approximate 1.4 mSv. This is below a threshold for tissue effects; however, stochastic effects are cumulative, and any potentially unnecessary ionizing radiation may contribute to a later lifetime risk of cancer. The risk of death following contrast administration is approximately 0.9 per 100,000.[18] In comparison, Australian authorities report the incidence of VTTS as 3.1 per 100,000 for <50 years and 1.8 per 100,000 for those 50 years, with death rate reported to be 25% for VTTS.[19,20] In Australia, at time of writing, there have been two confirmed deaths out of 3.8 million doses (0.05/100,000 doses).[21] A significant factor also to consider in a tertiary emergency department is opportunity cost when there are many other patients concurrently awaiting diagnostic scanning in a setting where resources are limited.

Worldwide understanding of VITT is rapidly increasing for this novel complication following SARSCoV2 adenovirus vector-based vaccines. Clinical guidelines and treatment strategies for VITT were first published in Australia by THANZ on 1 April 2021 and include advice for the use of radiological investigations in the assessment of organ-specific thrombosis.[3] Similar guidance has been released in June by the Australian College of Emergency Medicine.[22]

There is now a guideline from the Royal Australian and New Zealand College of Radiologists (RANZCR) based upon the THANZ principles, with practical considerations for emergency physicians and radiologists to follow.[23] RANZCR recommendations are for patients who have been given the AstraZeneca vaccine within the last 4–42 days, and present with persistent headache, visual changes, focal neurological symptoms, seizures or comatose. The use of diagnostic CTV is suggested in those where VITT is considered "possible" or "probable".[3] Practically, this is defined as D-Dimer > 5 times the upper limit of normal and platelets less than 150×10^9/L. Alternatively, where platelets are normal, CTV may also be considered if symptoms persist but should be based on clinical judgement.[3,23]

Based on this guidance, only three (7.5%) of AstraZeneca-vaccinated patients presenting to our institution in this study period met guidelines for investigation of organ-specific thrombosis. One patient was subsequently 'VITT confirmed' following evidence of thrombosis (positive CT pulmonary angiogram) and identification of PF4 antibodies on ELISA testing[3]; although this patient did not have CVST.

This retrospective study has limitations to acknowledge. It is reliant on the EMR and is thus prone to documentation error. The study period is short and underpowers assessment of trend analysis particularly in a rapidly changing environment. The understanding of VITT is rapidly evolving and decision-making guidelines take time to be developed, disseminated and educated prior to any change in medical care. Given that the THANZ guidelines were released at the beginning of the study period, they may not have been widely known at time of care delivery.

In conclusion, this study showed that the use of CTV in patients with headache has markedly increased at our centre since identification of VITT and the subsequent negatively biased vaccination influence of mainstream media. Headache is a common vaccine-related side effect and VITT is an exceptionably rare, serious and potentially fatal condition. With the rates of vaccination increasing in the community, these results highlight the importance of strict adherence to established evidence-based guidelines. Otherwise, critical care capacity, and in particular imaging resources already under pressure will be strained further.

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Data availability statement

Author elects to not share data.

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