Cerebellar and brainstem stroke possibly associated with booster dose of BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine

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SUMMARY

As COVID-19 vaccination becomes widely available and administered globally, there have been several reports of side effects attributed to the vaccine. This report highlights a patient who developed stroke 2 days following the administration of the COVID-19 vaccine, although its association remains uncertain. A man in his late 30s developed acute neurological symptoms 2 days after receiving the booster dose of the BNT162b2 (Pfizer-BioNTech) mRNA COVID-19 vaccine. History and neurological examination suggested a posterior circulation stroke, which was confirmed by MRI, as a right-sided posterior inferior cerebellar artery stroke. Full workup did not suggest other causes of the stroke. Due to the patient's age and well-controlled risk factors, it was presumed to be a rare adverse effect of the vaccine. Medical management with aspirin, statin therapy and rehabilitation led to the improvement of symptoms and enabled ongoing restoration of function. Further cases of stroke following administration of COVID-19 vaccine have been documented in the literature, but the association is yet to be established.

BACKGROUND

The COVID-19 pandemic has brought about a multitude of challenges and learning experiences for clinicians around the world. It has been well established that there are numerous pathological consequences because of the disease itself, and this has led to the development of vaccines with novel technology. The BNT162b2 (Pfizer-BioNTech) vaccine is an mRNA vaccine that encodes for the viral spike (S) protein of SARS-CoV-2, which has been approved for initial and booster dosing in Australia.[1 2] There have been a few reports of cerebrovascular accidents following vaccination,[3–11] though majority of these are following the first dose. These reports include vaccine-induced thrombotic thrombocytopaenia (VITT), repeated cardioembolic stroke, cerebral venous sinus thrombosis and other acute arterial thrombosis. In this report, we present a case of right-sided posterior inferior cerebellar stroke in a healthy patient who received his third (booster) dose of the Pfizer-BioNTech vaccine 1 day prior.

CASE PRESENTATION

A man in his late 30s developed sudden onset of sore neck, occipital headache, fatigue and leg cramps 1 day after receiving the third-dose (booster) of the Pfizer-BioNTech vaccine. Two days following vaccination, he presented to a hospital emergency department as he had a sudden onset dizziness, vertigo, ataxia, weakness of his right hand and constant diplopia, which led to a fall. The patient was afebrile and had no infective symptoms. His medical history included a 5-year history of well-controlled hypertension with regular review, childhood asthma and attention-deficit hyperactivity disorder (ADHD) diagnosed 4 years ago. He denied any recent illness, fever, neck trauma and no serious adverse effects following the previous two doses of the Pfizer vaccine. His regular medications prior to admission were irbesartan 75 mg once a day, budesonide/formoterol 200 µg/6 µg two times per day and dexamphetamine 5 mg three times per day. He had no significant family history of cerebrovascular or cardiovascular disease and was a non-smoker, with minimal alcohol intake and a balanced diet.

On examination, he was alert and oriented. Cranial nerve examination revealed a horizontal nystagmus with fast phase in all directions of gaze, associated with persistent diplopia. He also had right-sided ptosis and miosis suggestive of Horner's syndrome, along with decreased sensation to pain and temperature on the entire right side of the face. The remainder of the cranial nerve examination was normal, including speech and swallowing, with normal gag reflex, equal rising of the soft palate with no uvular deviation.

Upper limb examination demonstrated normal tone and power, and reflexes were equal bilaterally. There was reduced coordination on the right side, with dysmetria and intention tremor, but no dysdiadochokinesia. There was no loss of sensation in the upper limbs to pain, temperature, fine touch or proprioception.

Lower limb examination demonstrated a broad-based gait, truncal ataxia and decreased coordination of the right leg. The tone, power and reflexes in the lower limbs were normal and equal bilaterally. There was no loss of sensation to pain, temperature, fine touch or proprioception in the trunk or lower limbs.

The examination findings suggested a right-sided lateral medullary and cerebellar syndrome, and the patient was subsequently given aspirin 100 mg while awaiting diagnostic imaging.

INVESTIGATIONS

Initial investigation included a non-contrast CT head, followed by a CT angiogram head and neck,

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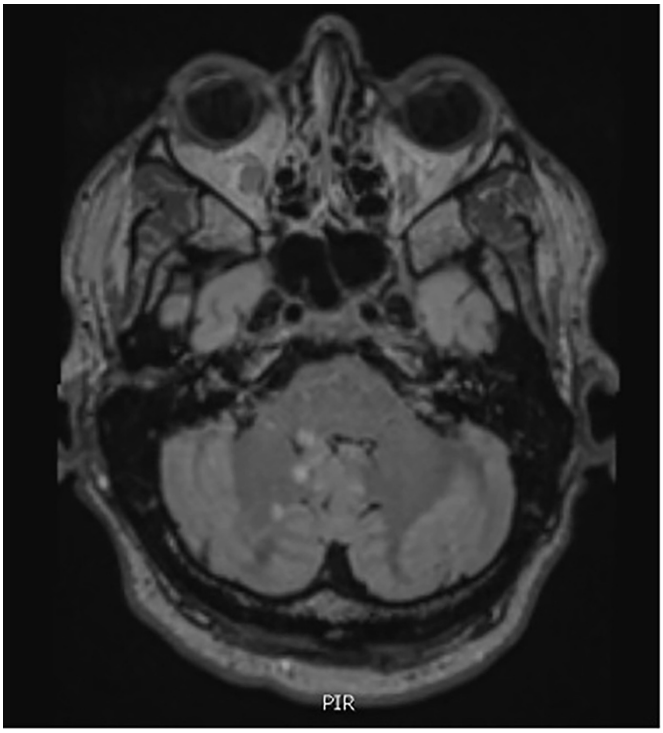

Figure 1 Axial image of MRI brain showing cluster of infarcts in the right posterior inferior cerebellar artery territory.

which revealed no abnormalities. ECG showed normal sinus rhythm, with no abnormalities. MRI brain and magnetic resonance angiography (MRA) head and neck vessels confirmed a cluster of infarcts involving the right posterior inferior cerebellar artery (PICA), including the caudal lateral medulla oblongata on the right side (figures 1–5).

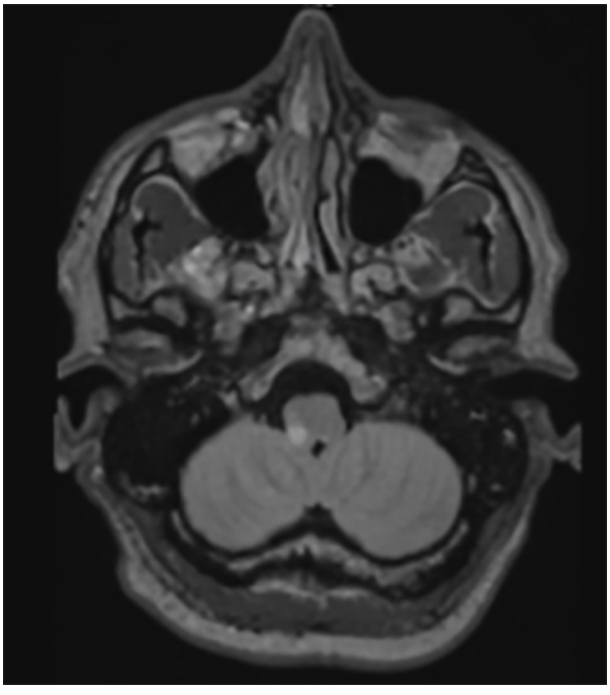

Figure 2 Axial image of MRI brain showing an infarct in the right lateral medulla.

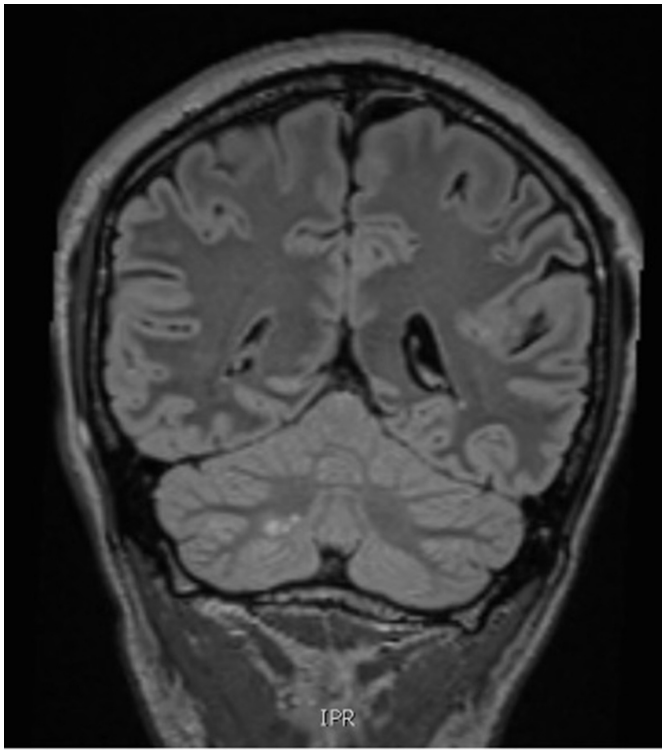

Figure 3 Coronal image of MRI brain showing cluster of infarcts in the inferior cerebellar peduncle, supplied by the right posterior inferior cerebellar artery.

Further investigations included repeat CT angiogram head and neck 2 days later, which showed that the right PICA remained occluded. A 24-hour Holter monitor did not reveal any cardiac arrythmias and a transthoracic echocardiogram with bubble

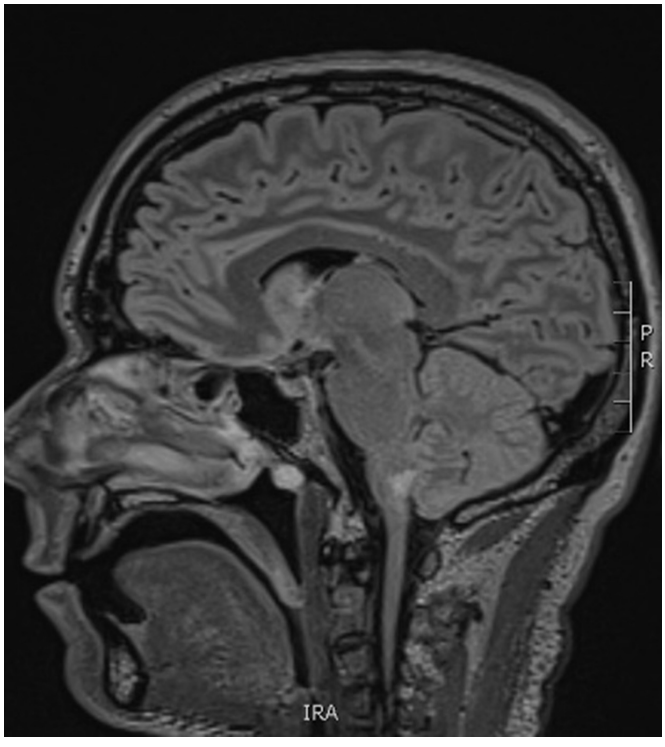

Figure 4 Sagittal image of MRI brain showing an infarct in the right posterior inferior cerebellar artery territory.

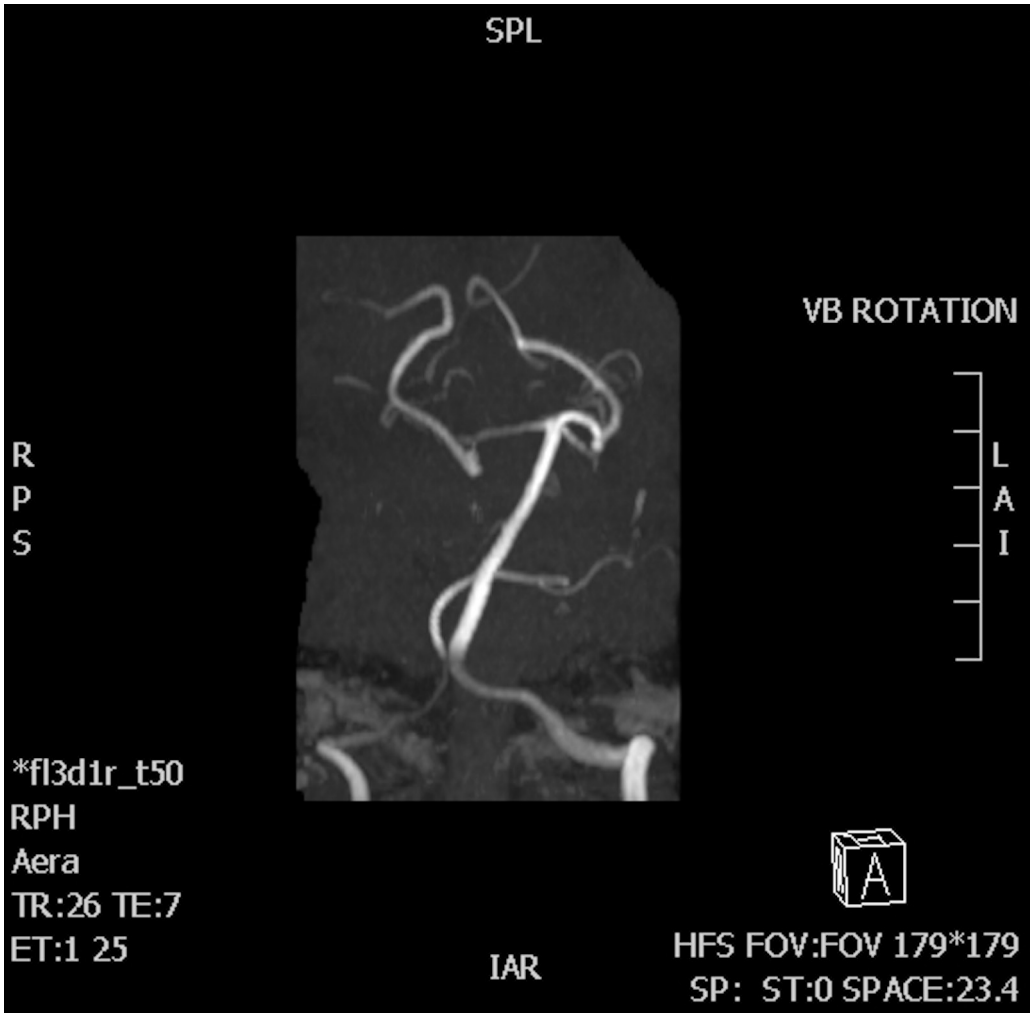

Figure 5 Three-dimensional reconstruction of magentic resonance angiography (MRA) circle of Willis showing an occlusion of the right posterior inferior cerebellar artery .

study showed no thrombus in the left atrial appendage or patent foramen ovale. Routine blood tests and CRP were normal, COVID PCR was negative, thrombophilia screen negative and vasculitis screen negative.

DIFFERENTIAL DIAGNOSIS

Given the cluster of infarcts, a cardioembolic source due to underlying arrhythmia was suspected, and hence a 24-hour Holter monitor was performed, which did not show any arrhythmias. CT angiogram showed patent vertebral arteries bilaterally. The patient's platelet levels were within normal limits on admission and throughout, rendering the possibility of VITT unlikely, though antibodies against platelet factor 4 were not tested.[12] A transthoracic echocardiogram with bubble study was performed, which did not identify any abnormalities. Vasculitis was considered as a potential cause, and a full screen performed, including ANCA, ANA, ENA, C3/C4, which was unremarkable.

TREATMENT

The patient was commenced on aspirin 100 mg once a day and atorvastatin 40 mg once a day. Prochlorperazine 5 mg three times per day was given for symptomatic relief of his vertigo but resulted in minimal benefit. Due to the ongoing nausea, ondansetron 4 mg was added as required. During the admission, dexamphetamine for his ADHD was withheld, and ongoing use to be reviewed by the patient's primary care clinician once symptoms resolve. Physiotherapy rehabilitation activities were commenced with the aim of regaining independence and improving balance following a stroke.

OUTCOME AND FOLLOW-UP

Throughout the length of the admission (13 days), his symptoms had improved. The patient was discharged from hospital for ongoing physiotherapy as an outpatient and to be followed up in stroke clinic.

DISCUSSION

At the time of writing, more than 55 million doses of the COVID-19 vaccine have been administered within Australia, which are primarily the monovalent Pfizer-BioNTech, ChAdOx-n1CoV-19 (AstraZeneca) and mRNA-1273 (Moderna).[13 14] These vaccines are encoded for the viral spike (S) protein against the original variant of SARS-CoV-2. Bivalent vaccinations such as tozinameran and famtozinemeran have also been developed, which targets the spike protein for both the original variant and Omicron BA.4–5.[15] Certain adverse effects following administration of the vaccines have been clearly documented, such as injection-site reactions, localised or generalised hypersensitivity reactions, myocarditis, pericarditis, diarrhoea, vomiting, paraesthesia and hypoaesthesia.[16]

The World Stroke Organization found that ischaemic stroke occurs in 1.4% of patients hospitalised due to COVID-19.[17 18] The risk of thromboembolic events as a complication of COVID-19 infection has been shown to be significantly higher than the risk following administration of an mRNA vaccine, as highlighted by a narrative review conducted by Abrignani *et al*.[4] These findings strongly suggest that the protective effect of the COVID-19 vaccine outweighs the potential risk of stroke compared with the disease itself, even without consideration of the other complications of COVID-19.

However, there have been a few recent emerging reports of cerebrovascular accidents following administration of COVID-19 vaccines, though most are related to vaccine-induced immune thrombotic thrombocytopaenia (VITT) associated with the AstraZeneca vaccine.[3–8 11] The risk of stroke following AstraZeneca vaccine has been reported to be 8.11 times higher than the risk of stroke following Pfizer-BioNTech vaccine,[7] and risk has been shown to be higher in those under the age of 65 in a study that analysed European data for adverse events following COVID-19 vaccination.[8] In all of the aforementioned studies, the risk seems to be significantly higher in female patients.

There have been scattered reports of ischaemic stroke following administration of mRNA vaccines (Pfizer-BioNTech and Moderna), without VITT,[9 10] along with the case we have presented. While we are unable to draw a direct causal link between the administration of the mRNA vaccine and stroke in our case, there are no other clear causes, and therefore, vaccination is a possible cause. Preliminary studies from Israel and the USA have not reported an increased risk of stroke following these vaccines,[9] and there is insufficient data from other studies to determine the causal link between mRNA vaccines and stroke. However, the current management and our approach to the case presented is based on the Australian Therapeutic Guidelines for acute stroke and clinician expertise.[19] As rates of vaccination are increasing, the incidence of stroke in patients who have been recently vaccinated and lack other major risk factors should be cautiously monitored.

Recently, Pfizer and BioNTech have both released a statement stating that they were aware of limited reports of ischaemic strokes in people over the age of 65 following vaccination. However, currently, there remains no evidence to suggest an association with the use of their vaccines.[20]

Centers for Disease Control and Prevention Vaccine Safety Datalink investigation also suggests that patients who receive bivalent vaccines were more likely to have an ischaemic stroke in the 21 days following vaccination compared with 22–42 days following vaccination.[21] Other studies from the Vaccine Adverse Event Reporting System, Veteran Affairs Database, and the Pfizer-BioNTech global safety database, have all indicated an increased risk of stroke following an updated bivalent vaccine.[22]

Further studies are required to determine if these vaccines are associated with stroke. However, it is undeniable that the benefit of these vaccines far outweighs any potential associated risk at the population level. A recent meta-analysis published in the Lancet showed that the risk of haemorrhagic and thromboembolic strokes following vaccination is lower than that among SARS-CoV-2 positive cases.[23] Therefore, vaccination against COVID-19 remains an important public health intervention. This case has highlighted that, although very rare, the possibility of stroke following administration of COVID-19 vaccination should be considered.

Learning points

- Maintain a high index of suspicion of stroke in a patient who has strongly suggestive clinical signs following COVID-19 vaccination and in the absence of other significant risk factors, regardless of their age.
- Initial CT brain may not demonstrate the infarcts if they are small, and therefore, MRI brain and MRA head and neck vessels may be indicated if the symptoms persist and other causes are ruled out.
- As rates of booster vaccination increase worldwide, the rates of adverse events should be closely monitored.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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REFERENCES

1 Therapeutic Goods Administration Australia. COMIRNATY COVID-19 vaccine. 2022. Available: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2021-CMI-02443-1&d=20220319172310101 [Accessed 20 Mar 2022].
2 Therapeutic Goods Administration Australia. COVID-19 vaccine: pfizer Australia – COMIRNATY (tozinameran) (mRNA). 2022. Available: https://www.tga.gov.au/covid-19-vaccine-pfizer-australia-comirnaty-tozinameran-mrna [Accessed 20 Mar 2022].
3 Pang E, Ghosh S, Chemmanam T, *et al*. Cerebral arterial and venous thrombosis due to COVID-19 vaccine-induced immune thrombotic thrombocytopenia. *BMJ Case Rep* 2022;15:e245445.
4 Abrignani MG, Murrone A, De Luca L, *et al*. COVID-19, vaccines, and thrombotic events: a narrative review. *J Clin Med* 2022;11:948.
5 Markus HS. Ischaemic stroke can follow COVID-19 vaccination but is much more common with COVID-19 infection itself. *J Neurol Neurosurg Psychiatry* 2021;92:1142.
6 Al-Mayhani T, Saber S, Stubbs MJ, *et al*. Ischaemic stroke as a presenting feature of chadox1 ncov-19 vaccine-induced immune thrombotic thrombocytopenia. *J Neurol Neurosurg Psychiatry* 2021;92:1247–8.
7 Cari L, Alhosseini MN, Fiore P, *et al*. Cardiovascular, neurological, and pulmonary events following vaccination with the bnt162b2, chadox1 ncov-19, and ad26.COV2.S vaccines: an analysis of European data. *Journal of Autoimmunity* 2021;125:102742.
8 Cari L, Fiore P, Naghavi Alhosseini M, *et al*. Blood clots and bleeding events following bnt162b2 and chadox1 ncov-19 vaccine: an analysis of European data. *Journal of Autoimmunity* 2021;122:102685.
9 Jabagi MJ, Botton J, Bertrand M, *et al*. Myocardial infarction, stroke, and pulmonary embolism after bnt162b2 mRNA COVID-19 vaccine in people aged 75 years or older. *JAMA* 2022;327:80–2.
10 Yoshida K, Tanaka K, Suto Y, *et al*. Repeated cardioembolic stroke after COVID-19 mRNA vaccination: a case report. *J Stroke Cerebrovasc Dis* 2022;31:106233.
11 Giovane R, Campbell J. Bilateral thalamic stroke: a case of covid-19 vaccine-induced immune thrombotic thrombocytopenia (vitt) or a coincidence due to underlying risk factors? *Cureus* 2021;13:e18977.
12 Datta P, Zhang F, Dordick JS, *et al*. Platelet factor 4 polyanion immune complexes: heparin induced thrombocytopenia and vaccine-induced immune thrombotic thrombocytopenia. *Thromb J* 2021;19:66.
13 Australian Government Department of Health. COVID-19 vaccination – vaccination data – 19 March 2022 [Australian Government Department of Health]. 2022. Available: https://www.health.gov.au/resources/publications/covid-19-vaccination-vaccination-data-19-march-2022 [Accessed 20 Mar 2022].

14 World Health Organisation. The moderna COVID-19 (mrna-1273) vaccine: what you need to know. 2022. Available: https://www.who.int/news-room/feature-stories/detail/the-moderna-covid-19-mrna-1273-vaccine-what-you-need-to-know [Accessed 20 Mar 2022].
15 Therapeutic Goods Administration Australia. COMIRNATY original/omicron BA.4-5 COVID-19 vaccine. 2023. Available: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent=&id=CP-2023-PI-01101-1&d=20230318172310101 [Accessed 18 Mar 2023].
16 Medicines.org.au. Australian product information – COMIRNATY (bnt162b2 [mRNA]) COVID-19 vaccine. 2022. Available: http://medicines.org.au/i/view/pfpcoviiPI [Accessed 20 Mar 2022].
17 Nannoni S, de Groot R, Bell S, *et al*. Stroke in COVID-19: a systematic review and meta-analysis. *Int J Stroke* 2021;16:137–49.
18 Markus HS, Martins S. COVID-19 and stroke-understanding the relationship and adapting services. A global world stroke organisation perspective. *Int J Stroke* 2021;16:241–7.
19 Therapeutic Guidelines Limited. Stroke and transient ischaemic attack. 2019. Available: https://tgldcdp-tg-org-au.eu1.proxy.openathens.net/viewTopic?etgAccess=true&guidelinePage=Neurology&topicfile=stroke-and-transient-ischaemic-attack&guidelinename=Neurology§ionId=toc_d1e175#toc_d1e175 [Accessed 20 Mar 2022].
20 Bloomberg News. Pfizer bivalent vaccine linked to strokes in preliminary data. 2023. Available: https://www.bloomberg.com/news/articles/2023-01-13/pfizer-bivalent-vaccine-linked-to-stroke-in-preliminary-data#xj4y7vzkg [Accessed 29 Jan 2023].
21 Centers for Disease Control and Prevention. Cdc and FDA identify preliminary COVID-19 vaccine safety signals for persons aged 65 years and older [National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases]. 2023. Available: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/bivalent-boosters.html [Accessed 29 Jan 2023].
22 Israel says has not found a link between pfizer COVID shot and stroke. 2023. Available: https://www.reuters.com/business/healthcare-pharmaceuticals/israel-says-has-not-found-link-between-pfizer-covid-shot-stroke-2023-01-19/ [Accessed 29 Jan 2023].
23 Chui CSL, Fan M, Wan EYF, *et al*. Thromboembolic events and hemorrhagic stroke after mRNA (bnt162b2) and inactivated (coronavac) COVID-19 vaccination: a self-controlled case series study. *EClinicalMedicine* 2022;50:101504.