CASE REPORT

Extensive Cerebral Venous Thrombosis following by COVID-19 Vaccine with Concomitant COVID-19 Infection

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ABSTRAK

Vaksin penyakit Coronavirus 2019 (COVID-19) telah diperkenalkan sejak dua tahun lepas di seluruh dunia. Kebanyakan kesan sampingan yang dilaporkan selepas vaksinasi merupakan gejala ringan seperti sakit otot dan sakit pada tempat suntikan. Kesan sampingan yang serius seperti kejadian trombotik atau miokarditis jarang berlaku. Trombosis sinus vena serebrum (CVST) adalah komplikasi trombotik yang mungkin berlaku dalam tempoh satu hingga dua minggu selepas vaksinasi. Kami ingin melaporkan kes melibatkan seorang wanita muda yang mengalami sakit kepala dan sawan selepas vaksinasi. Keputusan imbasan otak menunjukkan CVST dan juga didiagnos dengan jangkitan COVID-19. Pesakit ini mempunyai platelet yang mencukupi. Oleh demikian, punca kejadian trombosis tidak berkaitan dengan tindak balas immuniti vaksin dengan platelet yang rendah Walau bagaimanapun, kejadian kesan sampingan tidak patut dijadikan sebagai alasan untuk meragui vaksinasi kerana faedahnya melebihi daripada risikonya pada ketika ini.

Kata kunci: COVID-19; thrombosis sinus vena serebrum; vaksin

ABSTRACT

Coronavirus disease 2019 (COVID-19) vaccines have been introduced to the masses for just over two years. Majority reported adverse events post vaccination are minor side effect such as pain or inflammation at local injection site. Serious side effects

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such as thrombotic events or myocarditis are rarely reported. Cerebral venous sinus thrombosis (CVST) is a thrombotic complication that may occur within one to two weeks from vaccine administration. We illustrated a case from our centre involving a healthy young lady who presented with headache and an episode of seizure following by vaccination. She was concurrently diagnosed with CVST and COVID-19 infection later with the aid of neuroimaging. The patient's normal platelet count made the diagnosis of vaccine induced immune related thrombotic thrombocytopenia unlikely. While serious adverse events are reported, such as our case, this should not support the growing vaccine hesitancy among the public as its benefits still greatly outweigh its risk at this juncture.

Keywords: Cerebral venous sinus thrombosis; COVID-19; vaccine

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic has transitioned to an endemic state, in part due to the efficacy of vaccines in mitigating severe illness and reducing mortality rates globally. Since 2020, COVID-19 vaccination initiatives have been implemented worldwide, encompassing a range of vaccine types, such as messenger RNA (mRNA) vaccines (Pfizer Comirnaty and Moderna vaccines) and Adenovirus vector vaccines (Oxford-AstraZeneca COVID-19 and Johnson & Johnson vaccines).

These vaccines have led to declining morbidity and mortality rates due to COVID-19 infections, particularly among elderly and immunocompromised individuals. However, there is still public concern on the safety and potential adverse effects associated with vaccination. (Solís Arce et al. 2021). Frequently reported were minor adverse effects following by vaccination, including fever, headache, myalgia, local pain and redness over the injection site. However, major adverse events, such as allergic reactions, venous thromboembolism, pericarditis, and myocarditis, were recorded but infrequent (Chirico et al 2022).

The scientific literature has reported several thrombotic events potentially linked to COVID-19 infection or vaccination, including a rare neurovascular event, cerebral venous sinus thrombosis (CVST) (Taquet et al. 2021). A high clinical index of suspicion is required to identify symptoms such as headache, vomiting, or seizures as manifestations of CVST. We described a case of a healthy young lady whom recently received vaccine then developed extensive CVST preceded the diagnosis of COVID-19 infection.

CASE REPORT

A 26 years old woman with no known comorbidities presented to the emergency department with her first episode of generalised tonic clonic

seizure three days after receiving her first dose of Comirnaty COVID-19 vaccination. She also had severe throbbing headaches and vomiting for three days. Otherwise, she denied fever, photophobia or other neurological symptoms. She had no history of COVID-19 infection or thrombotic events and denied the use of oral contraceptive pills or recreational drugs in the past. There was no significant family history of thromboembolic disease or malignancy.

On examination, she was alert, orientated and afebrile. Her vital signs were within normal limits. Neurological examination revealed no focal neurological deficits; other system examinations were unremarkable. Her initial blood investigations were unremarkable. Full blood count showed normal white cell count, hemoglobin of 13.5 g/dL and platelet count of 400 x 10^9 /L. Normal renal and liver function profiles. Her pre admission screening nasopharyngeal swab for COVID-19 Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was negative. A plain computed tomography (CT) brain scan revealed abnormal hyperattenuation at the superior sagittal sinus, right transverse sinus, and left internal cerebral vein, suggesting an extensive CVST. A subsequent contrast-enhanced CT brain and venogram (Figure 1 & 2) confirmed the diagnosis, demonstrating filling defects involving the superior sagittal, right transverse, right sigmoid sinuses and right internal jugular vein.

She was initiated on subcutaneous enoxaparin 60 mg (1 mg/kg) twice daily for CVST. Anticonvulsive agent Levetiracetam 500 mg twice daily was given for seizure control. Three days following hospitalisation, she developed new onset of cough and fever. A repeated nasopharyngeal swab for COVID-19 RT-PCR was

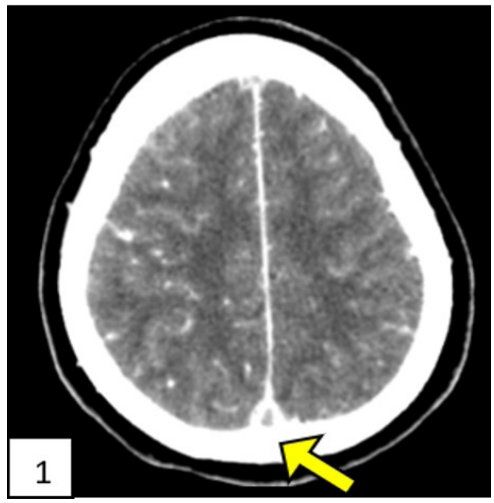

FIGURE 1: Axial contrast-enhanced CT brain showed the empty delta sign (arrow)

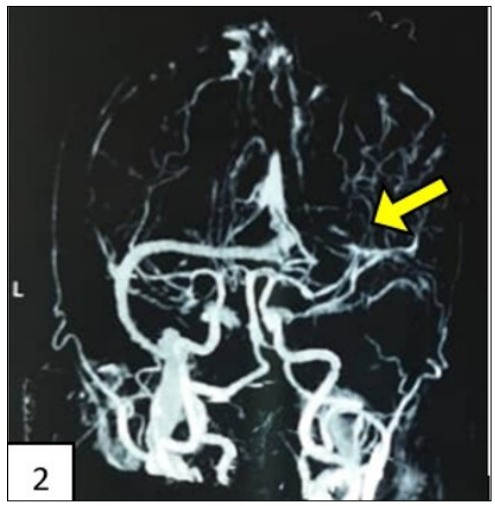

FIGURE 2: CT venogram showed lack of flow in the right transverse sinus, sagittal sinus, and internal jugular vein consistent with central venous sinus thrombosis (arrow)

positive with a cycle threshold value of 17. Chest X-ray (Figure 3) showed minimal peripheral ground glass opacities, and she was diagnosed with moderate COVID-19 infection. She was comfortable on room air and was treated symptomatically. She remained seizure free and her headache gradually resolved without needing analgesics. She was prescribed warfarin upon discharge. An outpatient review three months later, she was well and asymptomatic; return to daily office work. Her brain CT venogram showed resolution of venous thrombosis.

DISCUSSION

The incidence of CVST among hospitalised COVID-19 populations was 231/1,000,000 person-years (McCullough-Hicks et al. 2022). According to a study, the risks of developing CVST were higher among these patients who were men, older than 50 years or had more than two comorbidies (Ohaeri et al. 2022). The likely mechanism behind this thrombotic occurrence is related to an increase in the release of inflammatory markers, triggering the activation of complements which promote a hypercoagulable state, leading to the formation of microvascular thrombosis.

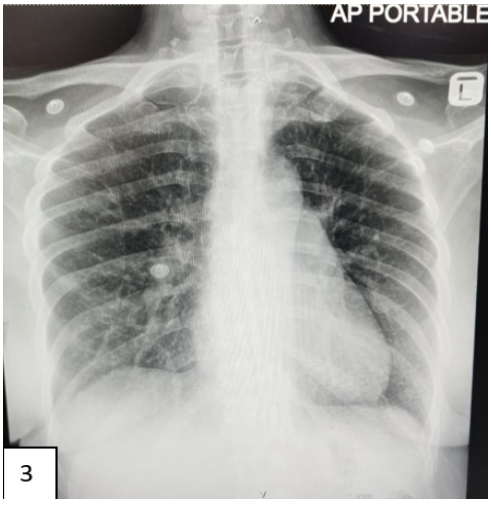

FIGURE 3: Chest X-ray showed bilateral minimal peripheral pulmonary infiltrations

Vaccines have positively affected the outcome of the pandemic. However, a lack of uptake in specific populations still exists, likely due to vaccine hesitancy. It could be attributed to a lack of confidence in vaccine safety and fears of possible side effects following vaccination. CVST is a rare and severe adverse event following by COVID-19 vaccination. The event rate of CVST was slightly higher in the population receiving adenovirus vector vaccines (1.1%) compared to those receiving messenger RNA vaccines (0.4-0.9%) (Smadja et al. 2021). Neurological symptoms commonly present within one to two weeks following by vaccination.

As far as we know, there is no data reported on thrombosis related to post vaccine with concurrent COVID-19 infection. This case was peculiar as it was still questionable on the cause of CVST which to be related to COVID-19 vaccine or infection itself. The exact mechanism of CVST post-COVID-19 vaccination remains unclear, but few theories have been proposed (Alhashim et al. 2022). One possible mechanism is the close relationship between vaccine-induced immune thrombotic thrombocytopenia (VITT), which has a similar mechanism as Heparin-induced thrombocytopenia

(HIT). It is associated with vector vaccines due to autoantibody formation towards platelet factor 4 (PF4), leading to thrombotic events and thrombocytopenia (de Gregorio et al. 2022; Douxfils et al. 2021; Elfil et al. 2023; Greinacher et al. 2021; Rao et al. 2022).

There are incidences of CVST reported among post vaccinated young adults in the absence of thrombocytopenia (Alhashim et al. 2022; Elfil et al. 2023). The thrombogenesis cascade in mRNA vaccine may be due to the platelet aggregation triggered by virus spike glycoprotein. Regardless of the risk of thrombotic risks due to vaccines, it is prudent to recognise that several studies suggest that up to ten times higher event rate reported on CVST to be associated with COVID-19 infection than vaccination; in particularly those hospitalised patients with severe illness (Ohaeri.et.al. 2022; Taquet et al. 2021; Tu et al. 2022). The mean time from COVID-19 symptoms onset to CVST diagnosis is between 7 to 11 days (Al-Mufti et.al. 2021; Novaes et al. 2022). There is no data on CVST during pre-symptomatic period. However, CVSTs were reported in patients with mild to moderate COVID-19 symptoms (Novaes et al. 2022). Therefore, concerning to thrombotic events alone, the overall benefits of vaccination still outweigh its risk.

CONCLUSION

This report highlights the uncommon thrombotic complications that might occur secondary to COVID-19 infection or vaccination. The take-home message is the importance of a high index of clinical suspicion on events like CVST for those at risk. As in the case with our patient, who has no identifiable prothrombotic risk besides recent vaccination and concurrent infection, her recovery was uneventful following prompt diagnosis and treatment.

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