

Case Report

Post COVID-19 Vaccination Fatality with Cerebral Involvement

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The vaccination is reckoned to be the most appropriate preventive measure to prevent COVID-19 pandemic infection. There are about seven varieties of Anti-COVID-19 vaccines available with relatively limited information about their effectiveness and adverse outcomes. We present a rare fatal case of severe postimmunization complication following COVISHIELD vaccination and is recorded as the first death postvaccination for COVID-19 in Sri Lanka.

The deceased was a 39-year-old previously healthy adult who succumbed to his illness following the second week of vaccination with thrombosis and thrombocytopenia. The findings may be helpful for the clinical management for prompt recognition and effective management of postvaccination reactions.

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Key words : COVID-19, Covishield Vaccine, Post vaccination reactions.

The SARS-COV-2, that appeared to be originated from Wuhan China has now been reported from almost all parts of the World. Following lineages of RNA virus has been detected in Sri Lanka: B.1.1.7 (UK variant), B.1.428 (Denmark/European/Middle East variant), B.1.411 (Sri Lankan variant), B.1.525 (Nigerian variant) and the B.1.351 (South African variant). Since there is no specific antiviral medicine for the disease so far, the symptomatic treatment is administered according to the severity and complications of the disease. There had been over 121,000 infected cases are reported and the number of deaths has gone over 1000 by end of April, 2021, in Sri Lanka since the onset of the pandemic in March, 2020. Apart from adherence to the Methods of Respiratory Hygiene, the Health Authorities of Sri Lanka have initially opted for AstraZeneca Oxford COVID-19 (COVISHIELD)¹ vaccine from Serum Institute of India under the COVAX facility of the World Health Organization (WHO) as the most effective method of Prevention and Control the Disease².

However, the adverse effect of the vaccine and its consequences should always be closely monitored and the serious complications are extremely rare but do occur, probably around five cases per one million vaccinated [There had been ~ one million doses given and five serious reactions including three fatalities]. The causal link between them with vaccination has led to hesitancy with regards the 'vaccine safety' among some populations.

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Editor's Comment :

- In midst of the COVID pandemic, Sri Lanka had opted for Covishield of all vaccines to Prevent & Control the disease.
- There has been very few serious complications recorded with only 3 fatalities against one million doses given.
- This case report deals with thrombocytopenia and intracerebral haemorrhage after 2 weeks of vaccination in a 39 years old previously healthy adult.

We report a case of a young adult died following vaccination for COVID-19 in the second week of the postvaccination period.

CASE REPORT

A 39-year-old previously healthy male hotel worker received the first dose of the COVISHIELD vaccine on 28th February, 2021 with no immediate reactions following administration. His postvaccination reactions which, began in 10-12 hours, comprised of usual discomforts such as mild fever, headache and myalgia for two days. However, his condition furthered over the next couple of days with severe headache, mild drowsiness, mild petechial rash on upper limbs and the platelet count was 130,000/ml while he was examined by a general practitioner on the 10th day of vaccination. He was admitted to the local hospital and the CT imaging showed mild intracerebral haemorrhage (Fig 1) in the right parietal lobe. He was suffering from severe headache while his consciousness became gradually altered. After initial management, the patient was transferred to the Tertiary Care Hospital in Galle for further management where his platelet count was found further decreased to 10,000 /ml. Intracranial haemorrhages progressed into the intraventricular spaces on repeated CT Scans. The serological investigations excluded Dengue and leptospirosis. The victim remained unconscious and had been managed conservatively. He succumbed to his

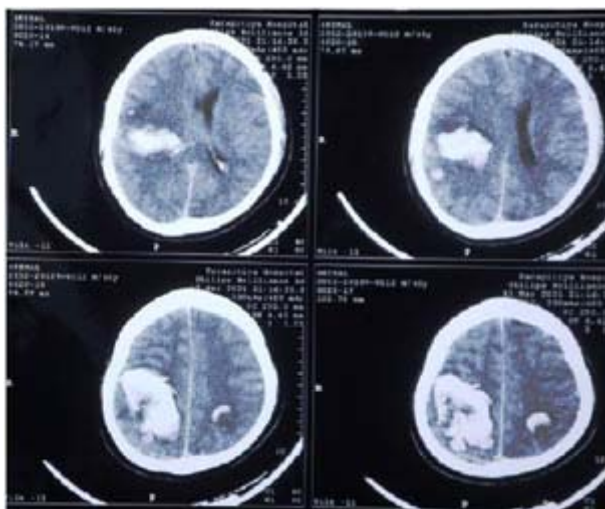


Fig 1 — CT images and brain shows intra-cerebral haemorrhages and sagittal sinus thrombosis (white arrow)

illness on the fifteenth day of vaccination in spite of medical management.

Autopsy findings :

Autopsy examination was conducted on the same day following negative postmortem PCR for COVID-19, the body was that of an average built adult male. External examination was unremarkable except for having a faded petechial rash over the lateral aspect of both upper limbs.

There were widespread petechial haemorrhages in serosal and mucosal surfaces. The brain was edematous and showed Cerebral Venous Thrombosis including the sagittal sinus (Fig 1) and massive intracerebral haemorrhage in the right parietal lobe, which was bursting into the intraventricular and subarachnoid spaces. There were multiple thrombi in pulmonary, renal and hepatic vasculature associated with hemorrhagic infarctions (Figs 2 and 3). The heart was flabby and showed multiple subepicardial petechial haemorrhages. Bone marrow was unremarkable. The findings were further confirmed with appropriate microscopic examination. (Figs 4 and 5). The COVID-19 antibodies were present in the postmortem blood sample. There were no signs of any other illness and all other primary and secondary causes for severe thrombocytopenia and bleeding

disorders were excluded (Figs 6-9).

DISCUSSION

Vaccination is a simple but most effective way of preventing people from harmful bacterial and viral agents, before they come into contact with them, using the body's natural defences to build specific antibodies against infections² Sometimes the combinations are used to enhance the protective efficacy of the vaccine³.

However, almost all vaccines are associated with side effects. In agreement with the World Health Organization, these reactions can be classified as follows, depending on the cause: vaccination-induced reactions (due to an effect of the vaccine itself or to an idiosyncrasy); reactions due to errors in storage, manipulation and/or administration and coincidental reactions (no causal relationship with the vaccine)⁴. The COVISHIELD vaccine is a mRNA compound of another virus of the adenovirus family that has been modified to contain the gene for making a protein from SARS-CoV-2 and the benefits of the vaccine outweigh its risks in adults of all age groups except for the very rare cases of blood clots with low blood platelets occurred following vaccination. According to the manufacturer's data of phase III clinical trials from the UK, Brazil and South Africa, COVID-19 Vaccine



Fig 2 — Brain shows thrombosis of superficial veins (yellow arrow)with bursting intracerebral haemorrhage into the subarachnoid space (white arrow)



Fig 3 — Remnants of thrombi in sagittal sinus (green arrow)



Fig 4 — Pulmonary thrombi (White arrows)

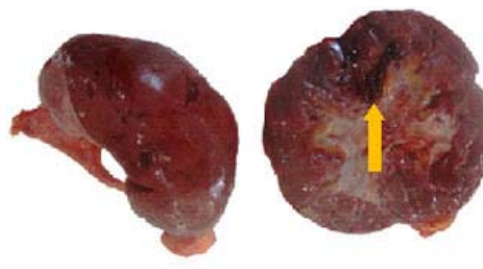


Fig 5 — Hemorrhagic infarction of kidney

AstraZeneca is safe and effective at preventing COVID-19 with no severe cases and no hospitalisations, more than 22 days after the first dose^{5,6}.

Nevertheless, the clinical history and autopsy findings of the presenting case are convincingly linked to the administration of the particular vaccine. The victim of this case, who was previously well, gradually developed severe thrombocytopenia together with the persistent postvaccination symptoms. A similar clinical scenario about postvaccination acquiring of unusual clotting defect known as Immune Thrombotic Thrombocytopenia mediated by platelet-activating antibodies against PF4 that may resemble autoimmune heparin-induced Thrombocytopenia⁷ is occasionally reported in the literature. It has also been referred to as Thrombosis with Thrombocytopenia Syndrome (TTS)⁸ which is very rare with a few reported fatal cases^{9,10}.

In fact, the victim of this case exhibited the signs of cerebral involvement at the very early stages of the disease process due to the formation of venous thrombi in cerebral vasculature including the sagittal sinus. The CT imaging is quite easy to miss the early stages of Sagittal Sinus Thrombosis¹¹, the fact, which is obvious in the presenting scenario as well, hence needs a higher vigilance of clinical suspicion. Involvement of the renal vasculature indicates more severe forms of thrombosis as it is considered to be one of the critical sites at the end-stage. The findings are in keeping with the widespread intravascular coagulation apparently in response to ingestion of heterogeneous protein compound, though the exact biochemical initiating point of which is yet to be studied. The European postvaccination observations showed several cases of such thrombosis including unusual cases of Cerebral Venous Sinus Thrombosis associated with Thrombocytopenia. However, There the reported incidents of disseminated intravascular coagulation associated with severe cerebral haemorrhages following vaccination are very scanty. The thrombocytopenia, widespread intravascular coagulation and liver involvement would also have been contributed to the rapidly progressing extensive cerebral haemorrhages. Some experts do not accept the casual relationship of the adverse effects and express their view on these rare

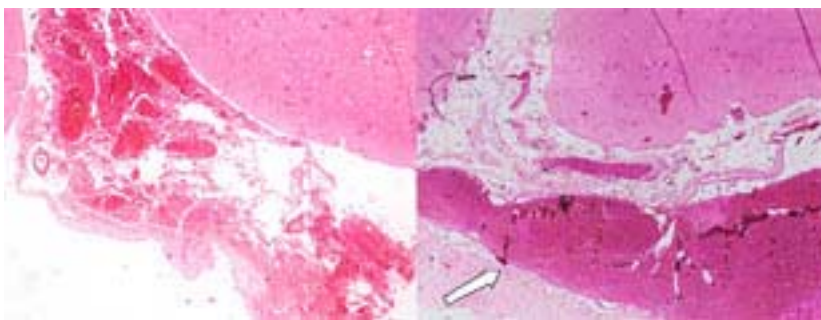


Fig 6 — Microphotograph shows the presence of subarachnoid hemorrhage (H&E X 50)

Fig 7 — Cerebral venous thrombosis (White arrow) with infarction of adjoining brain tissues (H&E X 50)

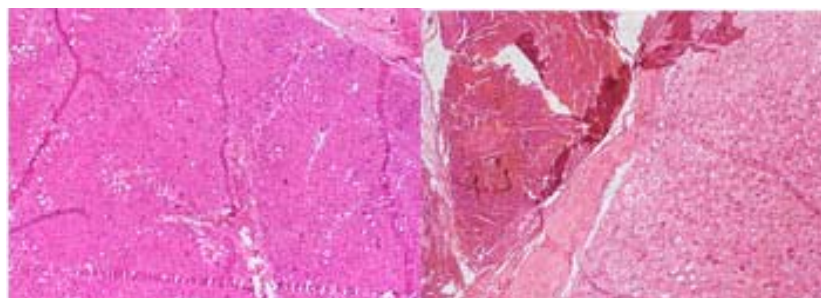


Fig 8 — Microphotograph shows the presence of fibrin thrombus in hepatic vasculature (H&E X 40)

Fig 9 — Renal tissues with adjacent infarction (H&E X 20)

occurrences as the normal complications of the disease the victims already suffered. Nevertheless, the deceased in this case was previously well and all the other possibilities responsible for his illness were excluded with antemortem and postmortem investigations.

However, the serious side effects from COVISHIELD are extremely rare and the risk of getting Thrombosis is much higher with COVID-19 infection. Incidents of severe anaphylactic reactions also hardly reported during the immediate postvaccination phase¹². Hence, it needs safety monitoring to be continued from weeks to months to identify the more possible side effects. This is the first reported and thoroughly investigated death following vaccination with COVISHIELD in Sri Lanka though there were three cases of recovery from vaccine-related thrombogenic complications. Policy decisions were made by the Epidemiology Unit in Sri Lanka and the Health Care and all the other frontline authorities were expected to report the suspicious Postvaccination case immediately for careful monitoring, thorough investigation whenever a patient present with unusual symptoms even after two weeks of vaccination.

CONCLUSION

The clinical features and the autopsy findings of the presenting case of a death of a healthy adult following two weeks of COVISHIED vaccination are in keeping with

the characteristic but rare fatal adverse outcome of COVID-19 vaccination. These findings may be helpful for the clinical management for prompt recognition and effective management of postvaccination reactions. Finally, the existence of rare complications against COVID-19 vaccination is outweighed by the benefits of forced immunization of the community.

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