Pulmonary Thromboembolism (PTE) after Sinopharm vaccination

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February 22, 2024

Abstract

One of the serious side effects of COVID-19 vaccines is vaccine-induced immune thrombotic thrombocytopenia (VITT). A young man presented with pulmonary thromboembolism 7 days after receiving inactivated COVID-19 vaccine BIBP developed by Sinopharm/China. Close surveillance of possible adverse reactions a crucial step to encourage population to participate in vaccine campaign.

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The authors have given written consent form from the patient to publish the recording data.

Background

Development of vaccine against covid 19 was initiated as soon as the pandemic start, international research and development for the design and production of effective vaccines surged. A considerable number of pharmaceutical companies and research facilities began to work on the design and development safe and effective vaccines to prevent spreading of the deadly disease. A variety of approaches and platforms were designed. mRNA based vaccines such as Pfizer/BioNTech and Moderna, non-replicating viral vectors such as AstraZeneca/Oxford and Johnson & Johnson (J&J) vaccines and inactivated virus vaccines such as Sinovac, Bharat and Sinopharm are examples that have been launched and used in millions of people [1].

Medical intervention might accompany mild to severe side effects, in regard to vaccine which is used in healthy individuals to prevent a disease should induce limited side effects which balance the benefit of vaccination, various covid plat form vaccines have shown to induce side effects. There is a report from Saudi Arabia, in which the side effects of AstraZeneca vaccination ranged from mild fever, myalgia, fatigue, shortness of breath and headache to serious cases of cerebral venous sinus thrombosis, pulmonary embolism and cardiac arrest, the latter caused led to mortality in one patient[2]. In a systematic review conducted by Kaur *et. al.*

, the results of eleven vaccine trials were reviewed with aim to assess the frequency and severity of adverse events of 3 vaccines; five cases received Comirnaty (BNT162b1), three received AstraZeneca (AZD1222), and one individual received Covaxin (BBV152) showed serious adverse reactions [3].

One of the rare serious side effects of COVID-19 vaccines is known as vaccine-induced immune thrombotic thrombocytopenia (VITT) which might lead to thrombosis and embolism in different parts of the body, VITT reported different vaccines currently in use such as AstraZeneca/Oxford as well the J&J vaccine [4].

The present work is a case report of non-VITT associated PTE occurred after the second dose of Sinopharm vaccine in a seemingly healthy individual. To the best of our knowledge, there is no report of non-VITT associated PTE following the administration of Sinopharm vaccine.

Case report

A 26-year-old male with no prior medical history was admitted to the emergency ward with shortness of breath, pleuritic chest pain, and hemoptysis. Symptoms was first appeared 4 days prior to his admission, the patient has received second dose of Sinopharm COVID-19 vaccine (also known as BBIBP-CorV or BIBP vaccine) three days before the onset of his symptoms. The patient medication history includes pantoprazole 40mg and paroxetine 20mg once daily. The patient did not have familial history of venous thromboembolism. Patient vital signs were normal on admission, except for an O2 saturation of 93% detected via pulse oximetry. There were no other abnormal findings in the physical examination/history and also BMI was 25. There were not any signs of DVT in lower extremities.

Based on the fact that the patient had a high pretest probability for pulmonary thromboembolism (PTE) and hence a CT angiography was ordered and performed based on which a diagnosis of PE was confirmed for the patient.

The patient was treated with Enoxaparin)60mg in the morning and 80mg in the evening (and vital signs were also closely observed for the duration of hospitalization. The patient remained stable and was eventually discharged from the hospital one day after the admission in healthy condition and prescribed with 10mg Apixaban twice daily for one week. The medicine was maintained at 5 mg twice daily thereafter for the next three months.

Computed tomography of pulmonary angiography (CTPA) showed filling defects in the segmental branches of the left lower lobe (in comparison with normal contralateral pulmonary artery), with the presence of blurred lung tissue in the same segment indicating infarction (Figure 1a, b). An Echocardiography was also performed which showed elevated pulmonary atrial pressure (PAP=30 mmHg). As for the lab results, aside from the mildly elevated CRP and ESR levels, all the other lab results and markers including NT-PRO-BNP and troponin I were normal. Qualitative assessment of PF4 Antibody was inconclusive. A summary of the lab results is shown in (table 1).

Discussion

Incidence of vaccine-induced immune thrombotic thrombocytopenia is a rare but serious adverse event of several of the vaccines used for the prevention of COVID-19. In most of the cases, the condition has been reported to result following the administration of AstraZeneca vaccine, even though it remains very rare with an incidence of around 1 in 125,000 to 1 million [5]. As for other vaccines, VITT is reported following the Pfizer/BioNTech vaccine in a case series by Edler *et. al.* [6], As well as a case report by Al-Maqbali *et al.* A patient suffered from extensive DVT/PE after receiving first dose of Pfizer-BioNTech BNT162b2 mRNA COVID vaccine [7].

VITT usually presents after 6-14 days of vaccine administration, typically, presents lab findings including a low platelet count of less than 150,000 per microliter, increased D-dimer levels, and a decreased level of fibrinogen. As for the mechanism, it is proposed that similar to that of heparin induced thrombocytopenia (HIT), presence of antibodies against platelet-factor 4 complexes triggers a platelet activation via the Fc receptor [8]. In HIT, pathogenic IgG antibodies are known to target and bond complexes made of positively

charged platelet-factor 4 and negatively charged heparin and cause platelet activation via the FcγRIIA receptor [9]. Interestingly, considering the fact that many of the patients, never received heparin before, recently, reported that negatively charged molecules other than heparin may in fact trigger the same pathway which leads to thrombosis [10]. Anti PF4-heparin antibodies in fact were detected in several cases of patients vaccinated against COVID-19. As for the cause, the antibodies might either be elicited by the vaccine itself or by the inflammatory response caused by the vaccination [9].

As mentioned before, PTE (possible VITT) following Sinopharm vaccination was not reported in the literature. It seems this case is not compatible with VITT and probably is a non-VITT associated PTE. There are not clear evidences for causal relationship between patient drugs (pantoprazole and paroxetine) and PTE. The case presented here was a healthy young man with no prior medical conditions, no risk factor which makes it probable that the condition might be occurred as a result of the vaccination. Overall, further study is needed to clarify this matter.

Conclusion

Determination and close surveillance of possible adverse reactions regarding the use of COVID-19 vaccines is an important and crucial step to encourage general population to participate in vaccine campaign. To the best of our knowledge, the present study is the first to report the occurrence of pulmonary embolism after the administration of Sinopharm vaccine for the COVID-19 in a patient. Further research is therefore warranted for more understanding of vaccine effects in the general population.

Conflict of Interest

All authors declare that there are not conflicts of interest.

References

1. Tregoning JS, Brown ES, Cheeseman HM, Flight KE, Higham SL, Lemm NM, et al. Vaccines for COVID-19. Clinical & Experimental Immunology. 2020;202(2):162-92.

2. Esba LCA, Al Jeraisy M. Reported Adverse Effects following COVID-19 Vaccination at a Tertiary Care Hospital, Focus on Cerebral Venous Sinus Thrombosis (CVST). Expert Review of Vaccines. 2021(just-accepted).

3. Kaur RJ, Dutta S, Bhardwaj P, Charan J, Dhingra S, Mitra P, et al. Adverse Events Reported From COVID-19 Vaccine Trials: A Systematic Review. Indian Journal of Clinical Biochemistry. 2021:1-13.

4. Iba T, Levy JH, Warkentin TE. Recognizing Vaccine-Induced Immune Thrombotic Thrombocytopenia. Critical care medicine. 2021.

5. Pai M, Grill A, Ivers N, Maltsev A, Miller K, Razak F, et al. Vaccine-induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination. Science briefs of the Ontario covid-19 science advisory table. 2021;1(17).

6. Edler C, Klein A, Schröder AS, Sperhake J-P, Ondruschka B. Deaths associated with newly launched SARS-CoV-2 vaccination (Comirnaty®). Legal Medicine. 2021;51:101895.

7. Al-Maqbali JS, Al Rasbi S, Kashoub MS, Al Hinaai AM, Farhan H, Al Rawahi B, et al. A 59-Year-Old Woman with Extensive Deep Vein Thrombosis and Pulmonary Thromboembolism 7 Days Following a First Dose of the Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine. American Journal of Case Reports. 2021;22.

8. Oldenburg J, Klamroth R, Langer F, Albisetti M, von Auer C, Ay C, et al. Diagnosis and management of vaccine-related thrombosis following AstraZeneca COVID-19 vaccination: guidance statement from the GTH. Hämostaseologie. 2021.

9. Franchini M, Liumbruno GM, Pezzo M. COVID-19 Vaccine-associated Immune Thrombosis and Thrombocytopenia (VITT): diagnostic and therapeutic recommendations for a new syndrome. European Journal

of Haematology. 2021.

10. Tardy-Poncet B, Tardy B, Grelac F, Reynaud J, Mismetti P, Bertrand JC, et al. Pentosan polysulfate-induced thrombocytopenia and thrombosis. American journal of hematology. 1994;45(3):252-7.

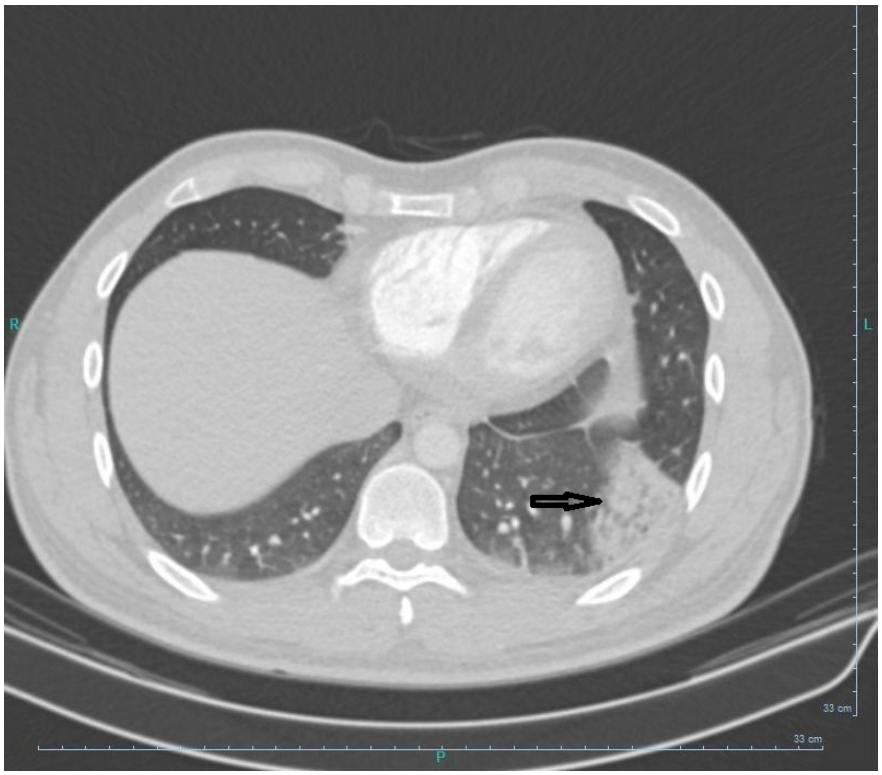
Table 1: laboratory findings of patient

Figure 1.a: PTE in CTPA (Computed tomography of pulmonary angiography) : filling defect in left descending pulmonary artery in mediastinal window

Figure 1.b: Pulmonary infarct in left lower lobe: Sub plural wedge pulmonary opacity in left lower lobe in parenchymal window

Table 1: laboratory findings of patient

Lab Test	Value	Lab Test	Value
WBC	8,000 (per mm^3)	Ca	9.1 (mg/dL)
Hb	12.8 (g/dL)	P	4.0 (mg/dL)
PLT	152,000 (per mm^3)	Mg	2.2 (mg/dL)
PT	14 (sec)	Na	140 (meq/L)
APTT	25 (sec)	K	3.3 (meq/L)
INR	1.16	Creatinine	1.2 (mg/dL)
AST	22 (U/L)	Urea	37 (mg/dL)
ALT	32 (U/L)	CRP	12 (mg/L)
ALP	158 (U/L)	ESR	52 (mm/h)
Bill.T	0.4 (mg/dL)	Troponin I	<0.2 (ng/ml)
Bill.D	0.2 (mg/dL)	NT-PRO-BNP	15.6 (ng/L)



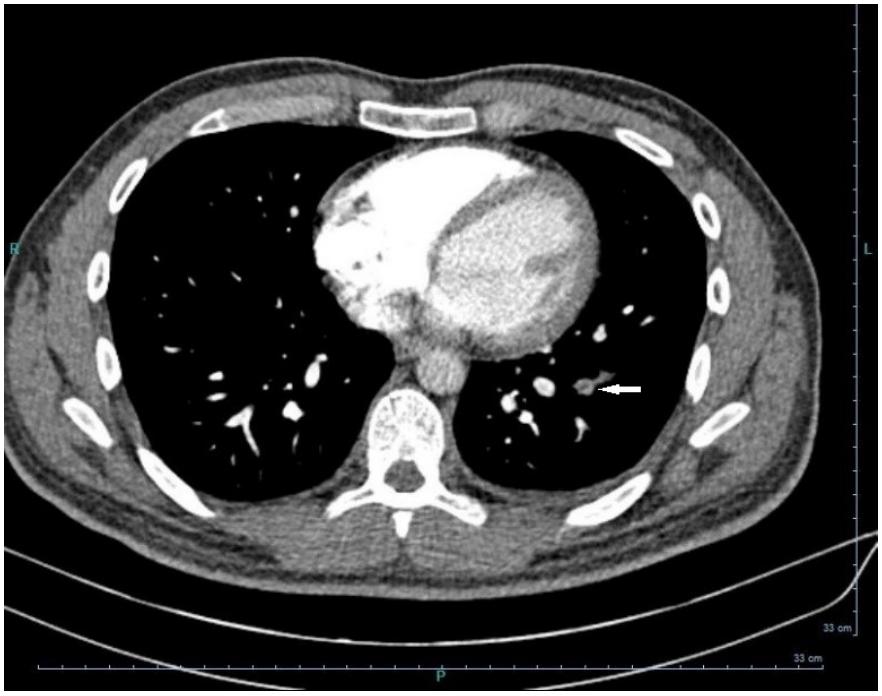


Figure 1. a Figure 1.b