

COVID-19 Vaccination and Pregnancy: Single Hospital Case Report

L. Ratiani¹, N. Kintraia², P. Machavariani², K. Grigalashvili², T. Didbaridze³
N. Metskhvarishvili², M. Rizvadze², E. Shvelashvili², M.Gabadadze⁴

¹Director of Tbilisi State Medical University The First University clinic, Head of Anesthesiology/Resuscitation Department at TSMU, Full Professor (Georgia)

²Tbilisi State Medical University the First University Clinic, Department of Obstetric and Gynecology(Georgia).

³Tbilisi State Medical University, Microbiology Department, associated professor, MD, PhD (Georgia)

⁴Hematologist, MD



Abstract – Reported case has been taken under consideration because of its close relation to the fact of vaccination against COVID-19 (Pfizer BionTech) first dose.

Multiparous woman at age of 40 years with normal progressive 15 weeks of gestation, has been admitted to the University Clinic on the 10-th day after COVID -19 vaccination with general weakness, joint pain, severe to moderate head ache, fever, at the admission COVID-19 PCR testing occurs to be positive.

Following the protocol of COVID-19 pregnancy management anticoagulant treatment has been started (D-dimer 0.9 mg/dl). The patient were under observation of infectious disease specialist. Almost all other protocol based test results within normal ranges, on the 14-th day of vaccination gingival bleeding of moderate severity has been started together with progressive thrombocytopenia (63-10³ m/L later 57-10³ m/L), test of thromb agglutination was positive and the diagnose of idiopathic thrombocytopenia has been announced by hematologist. Dexamethasone treatment has been initiated with following progressive positive results of thrombocyte count. On the 12-th day of the admission with normal clinical and laboratory data's patient has been discharged from the hospital with biweekly follow up for 8 weeks. All follow up laboratory values and clinical data were normal during this period. Based on literature, vaccination induced thrombocytopenia is a rare complication although has been documented and only several of them has proven to be vaccination induced complication. The reported case after assessment of patient's history, clinical, lab data and VITT adapted scoring system revealed intermediate probability of VITT, coincidence of COVID-19 made difficulties for differentiation of thrombocytopenia reason which needs more accurate laboratory assessment, but unremarkable medical history and short time between vaccination and clinically revealed thrombocytopenia highly suspicious for VITT.

Keywords – Covid-19, Vaccination , Pregnancy, Thrombocytopenia.

I. INTRODUCTION

COVID-19 vaccination is one of the most important approach for resolving pandemic that has been aroused in 2019. Since this worldwide viral infection has been diagnosed, several vaccines become soon available. Showing promising results for ending pandemic. Available vaccines have proven highly safe and effective, but simultaneously various side effects leading to mortality and extended morbidity has also been reported. On February 2021 a prothrombotic syndrome was observed in a small number of individuals who received COVID-19 adeno viral vector vaccines – Astra Zeneca, University of Oxford and Serum Institute in India. Similar findings were observed with other adeno viral vector vaccine _Jansen, Jonson and Jonson. Other adeno

viral vector vaccine Moderna that has been massively used, reports a single possible case of VITT only. There is no reported case of VITT as a result of vaccination with Pfizer BioNTech vaccine. [1,2]

VITT new case series among 220 individuals been observed (August, 2021) [3]. In this series of patients with definite or probable VITT following features were noted: age between 19-79 y, 55% female gender, time gap 5 to 30 days. In the case of thrombotic complication site of thrombosis: cerebral veins, deep veins of leg, pulmonary artery. Platelet median count range 47.000 microL, fibrinogen median 2,2 g/L, D-dimer 5000 to 80000 FEU [4].

The incidence of VITT is unknown but appears to be exceedingly rare. Most reports have described a small number of cases among tens of millions of vaccinated individuals [5],

The syndrome likely begins in narrow window post vaccination typically between 5 to 30 days, as awareness of the syndrome has increased, less typical presentation has emerged such as thrombosis without thrombocytopenia or thrombocytopenia without thrombosis [6, 7]

Reported case is multiparous woman 40 years old of age, vaccinated during pregnancy of 15 week of gestation by Pfizer BioNTech first dose. Followed by positive PCR test of COVID-19 and progressive decrement of thrombocytes within several days accompanied by moderate gingival bleeding. A diagnose of idiopathic thrombocytopenia has been announced by hematologist and dexamethasone treatment been initiated immediately, and shortly after progressive positive values of thrombocytes count been laboratory revealed. On the 12-th day of hospital admission patient has been discharged with normal clinic and laboratory values.

II. CASE DESCRIPTION

40 years old multigravida woman with current pregnancy of 15 weeks of gestation. Obstetric history is remarkable as current pregnancy is 9-th. She has 6 term vaginal uncomplicated deliveries, one spontaneous first trimester abortion and one preterm delivery on 28 week of gestation. Medical history also unremarkable (Table N.1), except recently done COVID-19 vaccination by Pfizer BioNTech one dose. After vaccination she has been under supervision of doctor for 40 minutes without any side effects. Menstrual function is normal and regular with normal blood loss. Menarche from 12 years old, family history unremarkable regarding diabetes mellitus, malignant systemic disease.

At the 5-th day after vaccination following symptoms occurred: flu (runny nose), general weakness, from 10-th day of vaccination mild to moderate joint pain, fever (38.5⁰C), malaise and moderate to severe head ache has been observed, by these symptoms patient been admitted to the TSMU first University Hospital emergency department. Patient undergone COVID-19 PCR testing occurred positive.

General condition in ER department has been assessed as moderate severity: SpO₂ 98%, pulse 92 min, T/A 126/70 mmHg, T 38.5⁰C. size of uterus coincident with gestation age, FHR 158-164 by ultrasound assessment, other US data's are also normal and compatible to gestation age, pathological vaginal discharge absent. History of any extra genital diseases are unremarkable, laboratory tests revealed soma changes. see (Table N 2). COVID-19 protocol based treatment been initiated-prophylactic dose of anticoagulant, infusion therapy, acetaminophen symptomatically for fever and head ache. Continuous monitoring of maternal warning symptoms was done: saturation, arterial blood pressure, pulse, consciousness, respiration, body temperature. All observed symptoms revealed normal stability. Laboratory tests were repeated every third day as per local protocol on the 6-th day from the admission and 14-th day of vaccination the following laboratory test results has been revealed: leukopenia 3,5 10⁹ g/L, erythropenia 3.6 10¹²/L, hemoglobin 9,9 g/dl, hematocrit 30.6, thrombocyte count 63.00 10³ m/L, ABG normal values, APTT normal values, PT decreased a little, INR decreased, fibrinogen normal value, D-dimer 0,7 mg/L. at the evening time patient reported gingival bleeding of moderate severity that has been stopped spontaneously but relapsed one hour later. Because of this alarming symptom CBC has been repeated and platelet count appeared markedly decreased till 57 10³ m/L patient has been consulted by hematologist. Thromb agglutinating test occurred positive and diagnose of idiopathic thrombocytopenia been announced. Immediately after episode of bleeding anticoagulation treatment was stopped and dexamethasone was prescribed 6 mg twice a day with infusion therapy and close monitoring of all vital signs. 24 hour later thrombocyte count occurred markedly elevated up to 106 10³ m/L. CRP < 5. D-dimer 0.6 mg/Dl, basic coagulation test within normal values. Patient has been retested again 48 hours later and thrombocyte count was increased up to 219 10³ m/L, basic coagulating tests and D-dimer were within normal values. Clinical symptoms regressed step by step. Dexamethasone dose was

decreased by step back mode within 10 days and kept on 4 mg twice a day under observation of family doctor and hematologist during consecutive 8 weeks. on the 12-th day of the admission patient has been discharged from the hospital. all clinical and laboratory values were within normal ranges. As dexamethasone management revealed fast positive result on thrombocyte count and clinical symptoms i/v immunoglobulin treatment was not prescribed.

Table N 1 Medical history

Childhood infections	Mumps, measles, rubella
Allergy	Negative
Blood transfusion	Negative
Hormone therapy	Negative
Medicine use	Negative
Kidney disease	Negative
Liver disease	Negative
Systemic disease	Negative
Viral diseases	Negative
CNS disease	Negative
Respiratory system disease	Negative
Digestive system disease	Negative
Urinary tract disease	Negative
Surgical interventions	Tonsillectomy (childhood age)
Vaccination	Season flu- 2017 Covid -19 PfizerBionTech 14/09/2021
Trauma	Negative
Infectious disease	Negative
Sexually transmitted diseases	Negative

Table N 2 Laboratory test results at the admission

Parameters	Results
ABO	A (II)
Rh	Positive
HbsAg	Negative
Anti HCV	Negative
Anti Tp	Negative
Anti HIV	negative

Troponin	1
LDH	148u/L
Creatinine	158 mmol/L
Urea	3.9 mmol/L
ALT	24.2 u/L
AST	18.5 u/L
Total bilirubin	15.7 mmol/L
APTT	36.3 sec
PT	14.3 sec
INR	1.13
Fibrinogen	3.0
D-dimer	0.9 mg/L
ABG	PCo2 decreased PO2 elevated K+ decreased Ca2+decreased
CBC	Thrombocytopenia 114 PCT decreased Eozinopenia Neutrophylolysis Erythrocytes –decreased Hb –decreased 10.7 g/Dl Ht- decreased
Urine test	Blood (+++)
Fe	N
CRP	39.0 mg/L

III. DISCUSSION

Vaccination remains the most important measure to prevent COVID-19 pandemic. There is board consensus among regulatory agencies and expert panels that benefits of vaccination overweight the potential of rare side effects [8].

An analysis of COVID-19 vaccination side effects (including mortality) versus COVID-19 illness complication (morbidity, mortality) was much higher in COVID-19 illness group 207 per million in COVID-19 illness group and 0.9 to 3,6 million in vaccinated individuals [9].

Common questions regarding prevention of vaccine induced thrombocytopenia includes: selection of vaccine, vaccination in individuals with history of thrombosis, vaccination during pregnancy and injection of second dose after VITT [10].

The real incidence of VITT is unknown because of underestimation as a result of decreased recognition and case reporting. Many countries all over the world do not have well established health registration system. Risk factors for VITT also unknown but possible risks are younger age, female gender, pregnancy. [11,12,13,14]. Typical presentation of severe thrombocytopenia is petechial or mucosal bleeding. One of the nonspecific signs of thrombosis is elevated D-dimer [14]. COVID-19 carries high risk of thrombosis and coagulation abnormalities in hospitalized individuals the same risks are documented after COVID-19 vaccination. Unlike VITT, COVID-19 associated thrombosis is not expected to cause a positive PF4 assay result. Thrombosis as one of the symptom of VITT has been excluded in reported case, by Doppler assessment of low extremities veins and normal data of basic coagulation [15, 16] in the literature both venous and arterial thrombosis have been described. As patient suffered of moderate to severe head ache from the day of hospital admission consultation of neurologist has been done to exclude any neurological abnormalities and results of checkup was normal. VITT begins in a narrow window 5 to 30 days' post vaccination [17] and flulike syndrome within the same time period possible suggests enhanced inflammatory response [18, 19]. Reported case shows onset of the flulike symptoms and gingival bleeding on the 10-th and 14-th days respectively after vaccination. The probability of VITT has been assumed by VITT scoring system see Tab N3. Total score of our case occurs to be 5 which shows intermediate probability of VITT.

Symptoms presented in the case description flue like symptoms, sever head ache, joint pain fever also characteristic for COVID-19, possibility of acquiring COVID-19 infection soon after vaccination increases because of immune fragility, positive PCR test confirmed COVID-19 infection in our patient. The fact of vaccination and COVID-19 infection makes difficult to clearly identify reason of thrombocytopenia. Although unremarkable medical family history and rapid irreversible elevation of thrombocyte count makes us to suspect vaccine induced thrombocytopenia, but reliable conclusions need further evaluation and assessment of the case.

REFERENCES

- [1] Pishko AM, Cuker A. Thrombosis After Vaccination With Messenger RNA-1273: Is This Vaccine-Induced Thrombosis and Thrombocytopenia or Thrombosis With Thrombocytopenia Syndrome? *Ann Intern Med* 2021.
- [2] Sangli S, Virani A, Cheronis N, et al. Thrombosis With Thrombocytopenia After the Messenger RNA-1273 Vaccine. *Ann Intern Med* 2021.
- [3] Greinacher A, Selleng, Wesche, Hendtacke et al. Preprint, <http://www.researchsquare.com/article/rs-440461/n1> (accessed on April 27/2021). Towards understanding ChAdOx1nCov-19 vaccine induced immune thrombotic thrombocytopenia
- [4] Schultz NH, Sorrol H, Michelsen AF. Et al. Thrombosis and thrombocytopenia after ChAdOx1nCov-19 vaccination. *M Engl. J Med* 2021:384-2124
- [5] Scull M, Singh D, Lown R, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1n Cov-19 vaccination. *M Engl J. Med* 2021. 384-2202.
- [6] Bayas A, Menacher M, Christ M et al, Bilateral superior ophthalmic vein thrombosis, ischemic stroke and immune thrombocytopenia after ChAdOx1nCov-19 vaccination. *Lancet* 2021. 397.
- [7] Muir RL, Kallam A, Koopsell SA, Gundabolu K. Thrombotic Thrombocitopenia after Ad26Cov2 vaccination. *M Engl. J Med* 2021, 384-0964.
- [8] Mahase E. AstraZeneca vaccine: Blood clots are "extremely rare" and benefits outweigh risks, regulators conclude. *BMJ* 2021; 373:n931.
- [9] Bikdeli B, Chatterjee S, Arora S, et al. Cerebral Venous Sinus Thrombosis in the U.S. Population, After Adenovirus-Based SARS-CoV-2 Vaccination, and After COVID-19. *J Am Coll Cardiol* 2021; 78:408.
- [10] Bhuyan P, Medin J, da Silva HG, et al. Very rare thrombosis with thrombocytopenia after second AZD1222 dose: a global safety database analysis. *Lancet* 2021; 398:577.
- [11] Greinacher A, Thiele T, Warkentin TE, et al. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. *N Engl J Med* 2021; 384:2092.

- [12]Schultz NH, Sørvoll IH, Michelsen AE, et al. Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. *N Engl J Med* 2021; 384:2124.
- [13]Pavord S, Scully M, Hunt BJ, et al. Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis. *N Engl J Med* 2021.
- [14]Bourguignon A, Arnold DM, Warkentin TE, et al. Adjunct Immune Globulin for Vaccine-Induced Immune Thrombotic Thrombocytopenia. *N Engl J Med* 2021; 385:720.
- [15]Scully M, Singh D, Lown R, et al. Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination. *N Engl J Med* 2021; 384:2202.
- [16]Sangli S, Virani A, Cheronis N, et al. Thrombosis With Thrombocytopenia After the Messenger RNA-1273 Vaccine. *Ann Intern Med* 2021.
- [17]Pishko AM, Cuker A. Thrombosis After Vaccination With Messenger RNA-1273: Is This Vaccine-Induced Thrombosis and Thrombocytopenia or Thrombosis With Thrombocytopenia Syndrome? *Ann Intern Med* 2021.
- [18]Bayas A, Menacher M, Christ M, et al. Bilateral superior ophthalmic vein thrombosis, ischemic stroke, and immune thrombocytopenia after ChAdOx1nCoV-19 vaccination. *Lancet* 2021; 397:e11.
- [19]Muir KL, Kallam A, Koepsell SA, Gundabolu K. Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination. *N Engl J Med* 2021; 384:1964.