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Vaccine-induced thrombotic thrombocytopenia (VITT) in COVID-19 vaccination: Demystified

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Abstract

The beacon of hope in the face of the COVID -19 pandemic has been the development of vaccinations. However, once these vaccines were administered to the masses, there were some rare complications reported. The most concerning among them was the development of a condition which presented with thrombosis, commonly in the cerebral and splanchnic veins in the presence of thrombocytopenia. This development led to a ban on some specific COVID-19 vaccines in certain countries. This thrombotic thrombocytopenia was elusive due to its clinical presentation that mimicked other diseases including COVID-19 infection.

This review was done following a methodical search in electronic databases including Google Scholar, Springer publication, World Health Organisation guidelines, PubMed and Cochrane. The data has been extracted and presented as a narrative review to help clinicians better understand and identify this post-vaccination phenomenon.

This study revealed a two-fold benefit, diagnostic and therapeutic. While evaluating a patient with thrombocytopenia and thrombosis it is prudent to consider VITT as a differential as it helps avoid a battery of investigations to prove the disease aetiology. Also the duration of anticoagulation can be restricted to 3 months in VITT which otherwise would need to be continued life-long in unexplained thrombotic events.

Key words: COVID-19, vaccination, thrombotic thrombocytopenia, vaccine-induced complications.

Introduction

COVID-19 has had an impact on the life of every individual as well as the global economy. This pandemic has caused unimaginable rates of mortality and morbidity.

From the outbreak of the COVID-19 pandemic in China in 2019, there are 235,242,311 confirmed cases with an active count of 18,418,977. The recovery count was 212,014,726 cases and death of 4,808,608 cases, as of October 2021[1].

Vaccination is a known prophylactic measure to prevent any infectious disease. Throughout history, vaccination has been used as a tool to combat the scourge of viral diseases and epidemics. Since the first appearance of COVID-19 in December 2019, there has been a world-wide race to come up with vaccines for COVID-19. We now have several approved vaccines which include mRNA-based vaccines (Pfizer-BioNTech and Moderna) and recombinant adenovirus-associated vector vaccines (AstraZeneca and Johnson and Johnson) and Whole-Virion Inactivated Vero Cell derived platform technology based indigenous vaccine from Bharat Biotech, India[2].

The mass vaccination campaigns in India and across the globe to ensure vaccination against COVID-19 is a huge effort. Billions of doses are being administered in a short duration to target a reduction in the number of severe cases and deaths. However, there has been a lot of concern regarding the thrombotic side effects of these vaccines. More particularly the AstraZeneca (AZ) vaccine, which though still approved by Medicines and Healthcare products Regulatory Agency (MHRA) and European Medical Agencies (EMA) has been in the eye of controversy due to the thrombotic complications. The first case of thrombosis was identified after the AstraZeneca vaccine in Feb'2021[3].

Justification for Review

With the emergence of this prothrombotic syndrome, several questions have been raised regarding the safety of these vaccines. Though the vaccines hold such promise, the threat of these thrombotic complications seem to overshadow it use among the masses. Therefore, it is imperative to examine the evidence available regarding these vaccine-associated complications and justify the use of these vaccines despite the risk.

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Methodology

First, the authors decided to go for a systematic review in this area, but due to the lack of authentic literature decided to represent the data in narrative review format.

Definition

Vaccine-induced thrombotic thrombocytopenia (VITT): Scully and his colleagues defined VITT as patients presenting with acute thrombosis and thrombocytopenia with elevated D-dimer following a COVID-19 vaccination[7].

Search methods

The data were searched through the popular electronic databases including Google Scholar, Springer publication, World Health Organisation guidelines, PubMed and Cochrane. All the articles were arranged as per the information they have provided and arranged in a systematic way.

Population

Data were searched for the population of > 18 years of age who received any COVID-19 vaccination irrespective of mortality status. The data for the population < 18 years of age and who did not receive any COVID-19 vaccination were excluded.

Outcomes observed

Occurrence of thrombotic events following COVID-19 vaccination

Data extraction keywords

VIIT, Vaccine-induced thrombotic thrombocytopenia (VITT), thrombotic events and COVID vaccination, MACE following COVID vaccination, adverse events of COVID vaccinations.

Epidemiology of VITT

The incidence of VITT after 1st dose is 1.3 per million doses; and after the second dose is 2.7 per million doses with the age group of 18 - 49 years[4].

After the first case report in February 2021, in early April 2021, 6 cases of Cerebral Venous Thrombosis (CVT) were reported. The age group was between 18 and 48 years and the onset of symptoms was 6 - 13 days post-vaccination. FDA and CDC suspended the use of the Johnson and Johnson vaccine. By the end of April 2021, 169 cases of CVT and 53 cases of splanchnic vein thrombosis (SVT) were reported[5].

Due to the reports of VITT, Germany, Spain, Italy, the UK, France restricted the use of Vaxzervria (CoviShield in India). The UK advisory board suggested Vaxzervria should not be given to the age group below 30 years and whoever has taken the first dose may take a different vaccine for 2nd dose. In March 2021, Australia also suspended the use of Vaxzervria[5]. It is interesting to note that BBBP-CorV (SinoPharm, Shanghai, China), CoronaVac (Sinovac Biotech, Beijing, China), BBIBP-CorV and WIBP-CorV (Sinopharm, Beijing, China) did not report any cases of VITT.

In May 2021, the product information of Vaxzevria was updated with regard to the very rare risk of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS).

However, by August 2021, the European Medicines Agency (EMA) thoroughly assessed the data on the quality, safety, and efficacy of the vaccine and recommended granting a conditional marketing authorisation for people aged 18 and above.

Germany faced a different challenge as they attempted to use the surplus vaccination (over 2 milllion) on a reluctant population. This led the mass donation of unused vaccines by Germany to low-income countries in an effort to utilize vaccines before their expiry.

As of late September 2021, The Italian authorities also announced that all versions of the AstraZeneca vaccine are considered equivalent to the other vaccines that have already been approved for use by the country's authorities. The incidence of VITT among the various COVID-19 vaccines (AstraZeneca, Pfizer, Moderna, Sputnik, Covishield and Covaxin is shown in Table I.

Table I: Reports of thrombotic events per dose administered (data up to 31 July 2021, adapted from authentic resources).

Vaccine name	Total dose administered (Approx.)	Thromboembolic events report
VaxZevria (AstraZenca SKBio)	34 million	222
Pfizer BioNTech (USA)	54 million	35
Moderna (USA)	4 million	5
Janseen Ad26.CoV2 (Johnson and Johnson, USA)	7 million	6
Gamaleya Sputnik V (Russia)	943,000	2
Covishield (India)	68 million	26
Covaxin (India)	7 million	0

Pathogenesis

The indication of the similarities in Heparin-induced

thrombocytopenia (HIT) and Vaccine-Induced Thrombotic Thrombocytopenia (VITT) is due to the temporal association of symptom onset after vaccination, thrombosis at arterial and venous sites, as well as the thrombocytopenia[4].

Poi-Wei Chen *et al* proposed a mechanism that interaction between PF-4 and components of the COVID-19 vaccine could result in immune complexes[5].

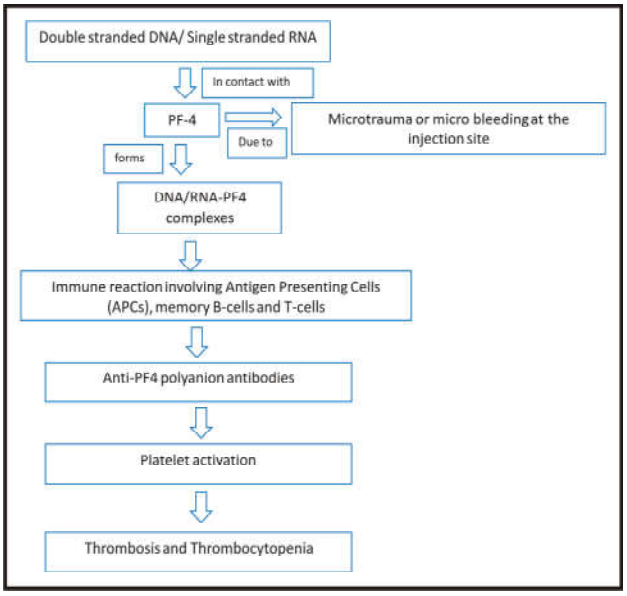


Fig. 1: *Proposed pathophysiology of VITT.*

A hypothesis stated that an autoimmune condition or pre-existing hypercoagulable status of an individual may trigger resulting in a cascade of thrombocytopenia and thrombosis. However, this was challenged when in a study on 11 patients, only 1 patient was found to have pre-existed Von Willebrand disease, anticardiolipin antibodies, and factor V Leiden[5]. Scully and his colleagues evaluated 23 patients with VITT and noted that they had no pre-existing prothrombotic condition or events to corroborate this hypothesis[7].

Schultz *et al* included 5 healthcare workers who presented with vaccine-induced thrombosis (four cases of CVT and one of portal vein) after 7 - 10 days following vaccination with first dose of AstraZeneca vaccine. All these patients had high levels of PF4-polyanion complexes[8].

Gonsalge *et al* reported an association of local tissue micro-trauma that occurred post-vaccination. They presented a hypothesis that contact of adenoviral DNA and PF-4 could lead to immuno-thrombosis due to increased anti-PF4 autoantibody. They proposed the concept of the Spike variant in the adenoviral genetic material that binds to endothelial cells and triggers platelet activation leading to thrombosis (as shown in Fig. 1)[9]

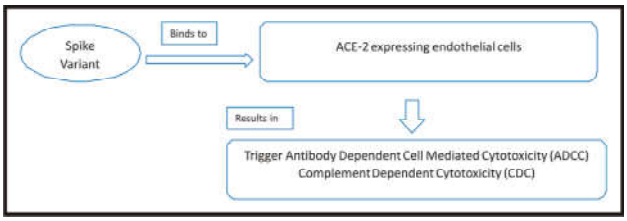


Fig. 2: *Pathophysiology of VITT involving the spike protein.*

Another possible hypothesis is that PF-4, a chemokine stored in platelet alpha granules is released due to activation of platelets and bind to high-affinity polyanions. This hypothesis was based on HIT, where heparin acts as hapten, i.e., production of specific antibodies is spurred due to the heparin binding to PF-4[10].

Predisposing factors

Host factors: This includes the female sex as reflected from early case reports this year. One series of VITT cases showed a female preponderance for 9 of 11 patients and another series reported 4 of 5 cases to be female[8,13]. Younger age also seems to have a predilection for VITT. It is suspected that as most of the vaccinated individuals were young women in the early phase of the vaccination campaigns, it is likely that the increased number of cases of VITT are due to a biased representation[8].

Vaccine factors: Two adenoviral vector-based vaccines have been implicated in causing VITT. The ChAdOx1 nCoV-19 (AstraZeneca, University of Oxford, and Serum Institute of India) has been reported to have more association with VITT[8]. The Ad26.COV2.S (Janssen; Johnson and Johnson) vaccine also has been implicated but to a lesser extent. The highest incidence of VITT in AstraZeneca as 1 in 26,000 in the Norwegian population. The Centre for Disease Control (CDC) reported that the Jannsen vaccine showed the incidence of associated VITT to be a mere 1 in 53,3333 vaccinated individuals.

Clinical features

Following the definition for VITT proposed by Scully and his colleagues, the largest study on cerebral venous thrombosis following vaccine for COVID-19 was done in the UK and a modified definition for VITT was proposed. They suggested that cases of CVT can be considered VITT-associated if the lowest platelet count recorded during admission was below 150×10^9 per L and, if the D-dimer was measured, the highest value recorded was greater than 2000 ¼g/L[11].

The clinical manifestation of VITT is essentially the presence of the triad as shown in Fig. 3 occurring from 5 to 30 days

following COVID-19 vaccination.

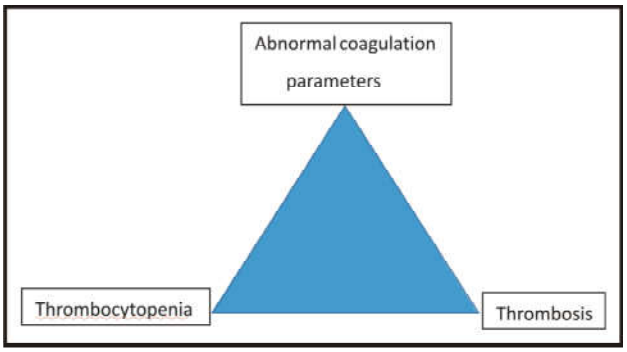


Fig. 3: *Graphical representation of VITT.*

In a large prospective cohort study done in UK, it was found that the mean baseline platelet count among the patients with VITT was only 47,000/cumm. Even though 5% of these patients had normal platelet count at the time of presentation, their counts dipped below normal during the course of hospitalisation. Thrombosis most commonly manifested as thrombosis of the cerebral veins (in upto 50%) of the patients. Deep veins of the legs were the next most common site of occurrence of thrombosis in these patients. Splanchnic veins are the most common site of thrombosis in the portal circulation[7]. The most common site for arterial thrombosis is the middle cerebral artery territory and less commonly the coronary arteries[14].

It was also noted that thrombosis with low platelet counts led to secondary complication of intracranial haemorrhage more commonly than thrombosis with normal platelet counts. Multivariate analysis identified the baseline platelet count and the presence of intracranial haemorrhage as being independently associated with death[7].

A study by Greinacher *et al* included 9 patients between 22 - 49 years. They had developed symptoms 4 - 16 days post-vaccination. Of these patients, 7 had CVT, 1 had pulmonary embolism, 1 had concurrent splanchnic and cerebral vein thrombosis. 4 patients succumbed to their complications and their reports showed positive anti-PF-4 antibodies and positive platelet activation assay[14].

Coagulation abnormalities such as DIC also can manifest in VITT. The spectrum of presentation ranges from clinically severe intracranial haemorrhage to mild bleeding tendencies such as petechiae and purpura. A majority of patients only have a transient thrombocytopenia.

As VITT clinically mimics a host of other conditions including Heparin-induced thrombocytopenia and Thrombotic thrombocytopenia purpura, it was important to have criteria to define this condition. The Case Definition Criteria for Vaccine-Induced Immune Thrombocytopenia and Thrombosis (VITT), according to an Expert Haematology Panel has been described in Table II[7].

Table II: Criteria for diagnosis of VITT.

Type of VIIT Description	Criteria
Definite VIIT	All five of the following criteria: 1. Onset of symptoms 5 - 30 days after vaccination against SARS-CoV-2 (or ≤ 42 days in patients with isolated deep-vein thrombosis or pulmonary embolism) 2. Presence of thrombosis 3. Thrombocytopenia (platelet count < 150,000 per cubic millimeter) 4. D-dimer level > 4,000 FEU 5. Positive anti-PF4 antibodies on ELISA
Probable VIIT	D-dimer level > 4,000 FEU but one criterion not met (timing, thrombosis, thrombocytopenia, or anti-PF4 antibodies) or D-dimer level unknown or 2,000 - 4,000 FEU and all other criteria met.

Once the diagnosis of VITT has been confirmed, the clinical severity can be assessed by the 4Ts score which is adapted from the scoring system for Heparin-induced thrombocytopenia. The scoring chart is summarised in Table III. This table is adapted from the 4Ts score for HIT, which has been validated in various populations. This adapted scoring system has not been validated, and the incidence of VITT is very low, making validation challenging. As a result, the interpretations do not carry a specific risk for VITT or correlate with a specific likelihood of positive PF4 antibody testing.

Table III: The 4TS score for clinical severity in VITT.

Variable	Score
Thrombocytopenia	
Platelet count fall > 50%	2
Platelet count fall 30 - 50%	1
Platelet count fall < 30%	0
Timing of onset	
Within 4 - 16 days of vaccination	2
> 2 weeks of vaccination	1
No history of vaccination	0
Thrombosis	
New thrombosis post-vaccination	2
Progressive/recurrent thrombosis	1
No thrombosis	0
Other causes of thrombocytopenia	
None	2
Possible	1
Definite	0
Total score	
0 - 3: Low probability	
4 - 5: Intermediate probability	
6 - 8: High probability	

Table IV: Comprehensive clinical overview of VITT after COVID-19 vaccination[15-17].

Age/Gender	Vaccine	Symptoms	Laboratory tests	Treatment
44 Male[14]	AstraZeneca	Day-8: Fevers, fatigue, foggy head, abdominal discomfort, increased bowel frequency.	Low platelet count; elevated D-dimer; CT-thrombosis with complete occlusion of portal and splenic veins and protrusion of thrombus into superior mesentric vein.	Fondaparinux,IVIGMethyl-prednisolone
26 Female	AstraZeneca	Day-8: Severe headache, thrombocytopenia.	Slightly elevated D-dimer, positive PF-4 antibodies.	Platelet transfusion, Heparin, IVIG Dexamethasone Apixaban
29 Female[15]	Astrazeneca	Severe headache, left orbital swelling, blurred left eye vision, fever.	Thrombocytopenia, high D-dimer, elevated CRP, MRI: hype T2 signal in left superior ophthalmic vein (SOV); PF-4: positive	IVIG Antibiotics Rivaroxaban Prednisolone
30 Female[13]	Janssen	Day-10: Headache, neck pain Day-17: lower extremity pain and weakness	Thrombocytopenia, CT: subtle increasing density of right transverse and sigmoid sinuses suspective of dural sinus thrombosis; Duplex U/S: Acute DVT involving posterior tibialis and popliteal veins; MR and CT Venography: large near occlusive thrombus in right transverse sinus extending to right sigmoid sinus & jugular bulb.	Agartoban Bivalirudin Apixaban
62 Female[13]	Pfizer	Day-9: headache and vomiting	CT: increasing size of haemorrhagic right cerebral venous infarcts with early hydrocephalus requiring decompressive craniotomy.	Unfractionated Heparin Low Molecular Weight Heparin Warfarin

There was also an association noted between the presence of the above mentioned predictors of VITT and mortality. In the UK prospective cohort study, it was noted that intracranial haemorrhage and cerebral venous thrombosis had a univariate Odd's ratio of 4.7 and 2.7 respectively with a 95% CU. Thrombocytopenia (every 50% drop) and low fibrinogen level had a univariate ODD's ratio of 1.7 each[7].

Apart from the AstraZeneca vaccine, some mRNA vaccines-Moderna and Pfizer BioNTech also were associated with immune thrombocytopenia and bleeding with thrombosis as reported in August 2021[14].

A comprehensive summary of the reported cases has been presented in Table IV.

Autopsy studies

Several autopsy studies have also been done on patients with post-vaccination symptoms and venous thromboembolism at unusual sites, i.e., cerebral and abdominal veins. There was a concomitant presence of haemorrhage and consumption coagulopathy with low plasma fibrinogen, highly elevated D-dimer, and strongly positive PF-4/heparin antibodies. All of this was associated with poor prognosis and higher mortality.

Anatomic dissection showed a catastrophic picture with multiple sites of venous thrombosis with intracranial bleeding. The usual sites showed involvement of large venous vessels far more extensive than predicted imaging. Microvascular findings showed vascular thrombotic occlusion in multiple organ microcirculation and increased inflammatory infiltrates.

Immunohistochemical analysis was done and vascular and perivascular expression of adhesion molecules such as VICAM1 was noted. Also, the presence of $CD66b^+$, $CD163^+$, and $CD61^+$ activated inflammatory cells indicated the activation of the innate immune system and complement pathway. This promotes inflammatory processes leading to microvascular damage of multiple organs[18-20].

The clinical history and course in the hospital for 2 patients of VITT who succumbed are summarised in Fig. 4a and 4b.

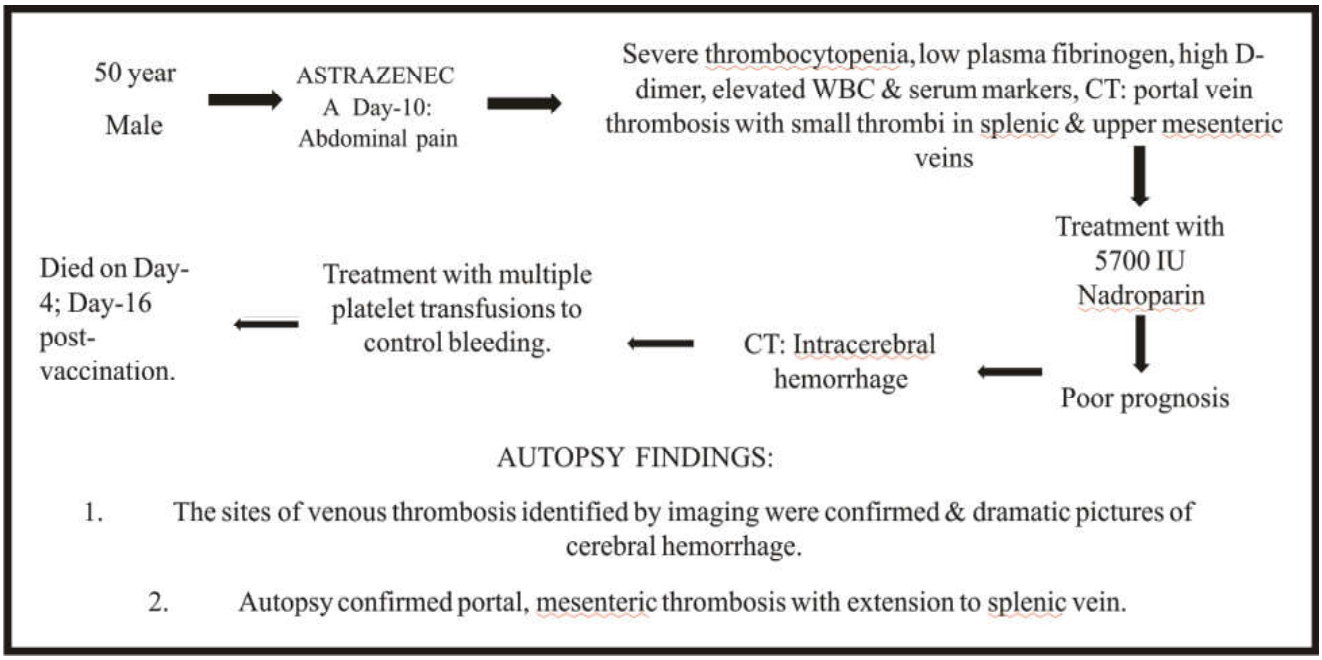
Evaluation of VITT

VITT must be suspected in all patients who have received vaccine with an interval of 5 to 30 days associated with thrombosis and thrombocytopenia.

However, the diagnosis needs laboratory evaluation which includes:-

1. Complete blood count: To look for thrombocytopenia (to look for fall in serial counts).
2. Coagulation parameters: Prothrombin time (PT) and activated partial thromboplastin time (aPTT), D-dimer and Fibrinogen.
3. PF4 antibody testing: Confirms the diagnosis of VITT in conjunction with the thrombocytopenia and D-dimer.

   However, it must be remembered that PF4 antibody can be positive with normal platelet counts and the patients are usually asymptomatic in this cohort. PF4 assays can be done using the Enzyme-linked immunosorbent assay method, Seratonin release assays and rapid HIT assays[7].



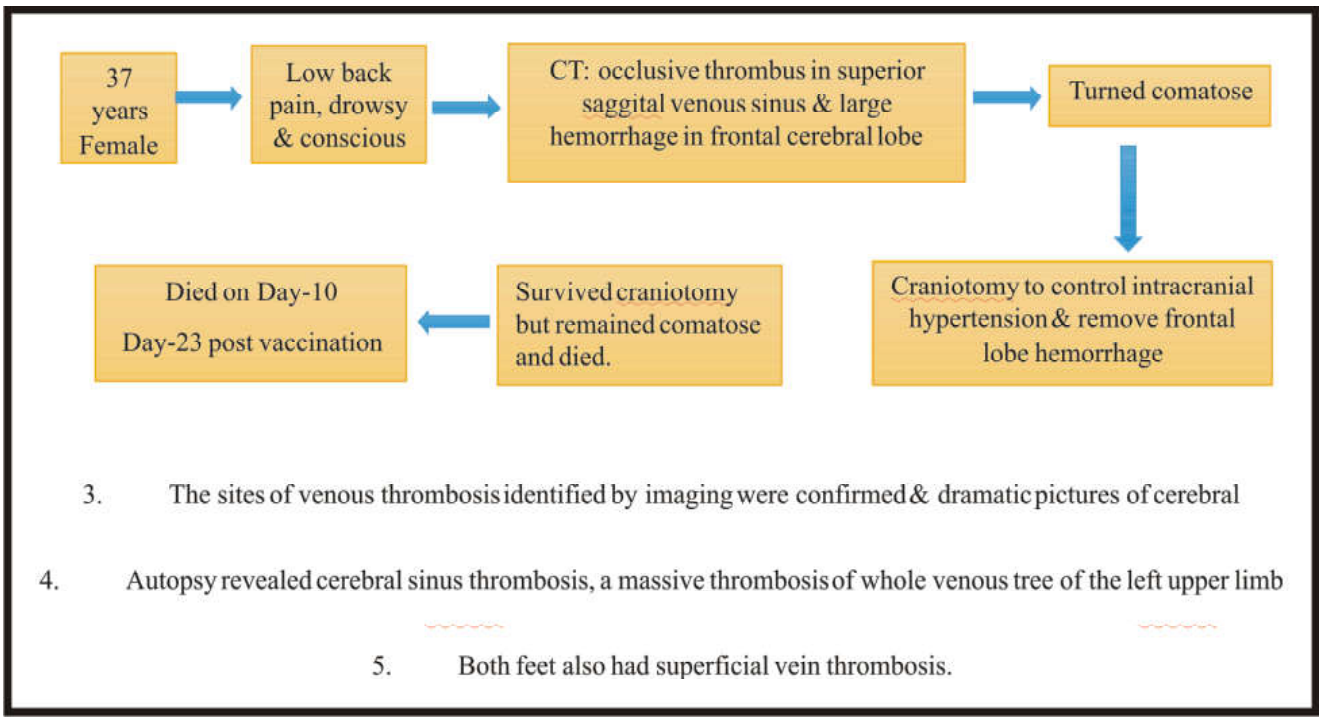


Fig. 4a and 4b: *Summary of autopsy findings in a case of VITT.*

A diagnosis of VITT is made with a positive PF4 ELISA in the clinical background of post-COVID-19 vaccine thrombosis and/or thrombocytopenia.

Imaging to confirm sites of thrombosis in the brain, thorax and abdomen may be done according to the clinical presentation of the patient.

Differential diagnosis

The other causes that have a similar presentation to VITT should be considered in patients presenting with thrombosis and thrombocytopenia following vaccination especially if the PF4 antibody is negative. The following conditions should be considered.

1. Heparin-induced thrombocytopenia: Classically presents following exposure to heparin and the thrombocytopenia resolves following cessation of heparin.
2. Immune thrombocytopenia: Not associated with thrombosis. Coagulation profile remains unaltered.
3. Thrombotic thrombocytopenic purpura: Presents with thrombocytopenia and microvascular thrombosis with

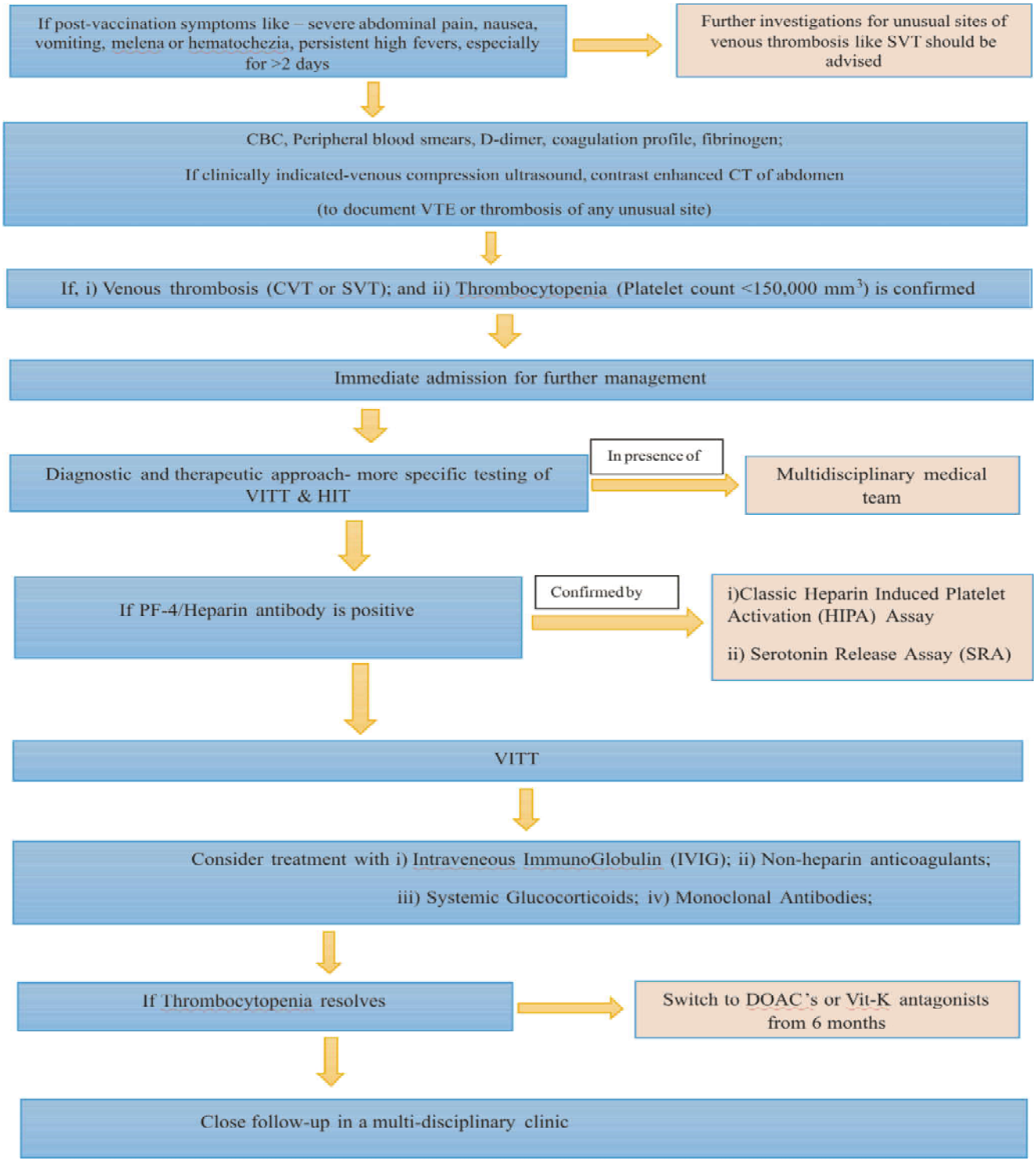


Fig. 5: *Overview of management in VITT.*

neurologic/kidney/cardiac involvement. Coagulation profile remain normal.

4. COVID-19 infection: This must be ruled-out in all cases of VITT as the COVID-19 infection itself can cause thrombosis and thrombocytopenia. VITT causes thrombosis in cerebral and splanchnic circulation commonly while COVID-19 involves the pulmonary veins and the deep veins of the lower limb.
5. Other causes of thrombocytopenia like sepsis, splenomegaly and inherited disorders.
6. Other causes of thrombosis like oral contraceptive pills, cancer, pregnancy, surgery and trauma.

Treatment

There is no specific therapy that is efficacious for the management of VITT. For effective therapy, it is crucial to assess the phenotype, risk factors, natural history, early detection, and management of VITT[10]. Clinicians should be familiar and vigilant in creating awareness among colleagues regarding the triggers of VITT along with the clinical signs and laboratory investigations[18]. Treatment options may include Monoclonal antibodies (Rituximab, Eculizumab); Direct thrombin inhibitors (Bivalirudin, Argatroban, Dabigatran); Direct Factor Xa inhibitors (Rivaroxaban, Apixaban, Edoxaban); Indirect Factor Xa inhibitors (Fondaparinux); Steroids (Prednisolone, Methyl-prednisolone, Dexamethasone)[13].

A life-saving approach could be early administration of high dose Intravenous immunoglobulin in addition to non-heparin anticoagulation which may help in the interruption of thrombosis cascade. All patients of VITT should be offered high-dose IVIG unless contraindicated. The recommended dose is 1gm/kg intravenously once a day for 2 days. It acts by promoting autoantibody binding to cellular receptors and thereby blocking platelet activation. It is crucial to monitor the platelet count during hospitalisation and after discharge as thrombocytopenia can occur even after the course of IVIG is completed.

In a Canadian study, three patients with VITT were administered high dose IVIG and dramatic improvement in thrombocytopenia was noted[21]. Another study on VITT patients with thrombotic manifestations also concurred with the Canadian study.

IVIG not only halted the platelet activation but also prevents occurrence of new thrombosis or worsening of progressive thrombus[22].

Anticoagulation is the mainstay of treatment in VITT. Even cerebral venous thrombosis (CVT) associated with haemorrhage is not a contraindication to anticoagulation as this finding is attributable to increased venous "back pressure" and often resolves rapidly with anticoagulation. Anticoagulation is also indicated in patients with VITT without thrombosis and patients with strong clinical suspicion of VITT who are awaiting laboratory confirmation[20.] Anticoagulation is a challenging task as most of the reported deaths among the patients with VITT were due to intracerebral haemorrhage. Fig. 5 presents an overview to the approach and management of VITT.

Steroids are used as second-line drugs in the management of VITT. Steroids are thought to counter the synthesis of new antibodies thereby interrupting the platelet activation and the resulting thrombosis. Despite this hypothesis, there are no large studies to corroborate the benefits of steroids in VITT. There is only some limited data available in this regard from its use in specific cases only. There is more benefit of steroid when use concurrently with IVIG. In the study by Schulz *et al*, 80% (4 out of 5) were treated with IVIG and steroids. Among the treated patients, half of them succumbed to VITT despite treatment. In another study by George *et al*, there was a better response to treatment with IVIG and steroids reported. As these studies have reported the use corticosteroids with IVIG, the stand alone benefit of steroids in VITT is still uncertain.

Platelet transfusions should be minimised (except in cases of critical bleeding tendencies) in VITT as it can trigger further platelet activation[1]. There is no role for aspirin in the treatment of VITT as it has no function in the prevention of platelet activation due to PF4 antibody.

The natural history of the antibody is not known. Hence, such cases require close follow-up with clinical and laboratory parameters for risk of recurrent thrombocytopenia.

Therapeutic plasma exchange (TPE) and immunosuppression can be considered for refractory VITT or with associated complications such as cerebral vein thrombosis (CVT) or multiple thromboses with evidence of excessive platelet activation (platelet count <30,000/microL)[23].

Prevention

Though the pathophysiology of VITT leads to thrombosis, there have not been any reports of VITT in individuals with HIT or thrombosis caused by another risk factor. Also, the mechanism of VITT differs from HIT (due to different PF4 epitope) and other types of thrombosis (which have different mechanisms). Hence there is no recommendation at present for patients with history of thrombosis to avoid adenoviral vaccines.

Individuals who have received the first dose of adenoviral vaccine without any VITT related complications can take the second booster without hesitation. According to a review based on data from the AstraZeneca database from Europe and UK, it was noted that there were 399 cases of VITT following the first dose but only 13 after the second-dose. This shows the sharp decline in the incidence of cases following the second-dose. Thus, it is advisable for individuals to take the second-dose as they can avail the full benefit of the superior efficacy of this vaccine on completion of the booster dose[24].

Keeping this in mind, UK has maintained that the second vaccination must be given to all patients who have received the first-dose of the AstraZeneca vaccine without any complications. However, in Germany, France and Canada the authorities have restricted the use of the AstraZeneca vaccine to patients older than 60 years, 55 years and 40 years respectively.

VITT and booster dose

In the event of VITT, a booster or annual vaccination (usually advised to protect from COVID-19 and emerging variants) comes into question. Should patients who have had VITT after the first- or second-dose of COVID-19 consider taking a booster dose?

The Centre for Disease Control (CDC) recommends repeat immunisation with the same vaccine in the absence of any VITT event with the first vaccine. However, those who developed VITT from an adeno-virus mediated vaccine can be switched to an mRNA-based vaccine for the second dose. There has also been a recommendation to consider non adeno-virus mediated vaccines as boosters.

Despite sparse evidence, several countries have recommended a "heterologous prime boost regimen" where the second-dose or booster dose is replaced by an mRNA based vaccine when the first vaccination has been done using the AstraZeneca vaccine.

Presently, there is no data available on booster dose for COVID-19 in patients with VITT.

Implications and Conclusion

Although we do see cases of venous and arterial thrombosis in clinical practice, we need to be aware of its presentation following vaccination. We should be aware about the recent literature and guidelines about the diagnosis and management of VITT as it will help us narrow down the differential diagnosis for arterial and venous thrombosis and thereby aid in tackling this emerging problem more efficiently. Hence, details of vaccinations and predisposing risk factors such as hormone therapy/oral contraceptive use must be actively sought for such cases as they will guide the clinician to make a correct and timely diagnosis. Prodoromal symptoms like lethargy, prolonged fever and headache must not be neglected following vaccination.

Treatment in VITT is wrought with hurdles such as bleeding which is challenging due to the competing goals of halting the bleed and preventing thrombus. The significance of PF4 assays in the management of VITT is also unclear. The cornerstone of treatment remains anticoagulation. The duration of anticoagulation is decided along the same lines as for HITT. VITT with thrombosis will warrant anticoagulation for 3 months (after normalisation of platelet counts) while VITT without thrombosis requires anticoagulation until 4 to 6 weeks after normalisation of platelet counts. Newer oral anticoagulants are preferred during the period of thrombocytopenia over vitamin K antagonists like Warfarin.

This review concluded that VITT has become an important differential diagnosis to consider in the light of the current pandemic, especially to avoid a battery of unnecessary investigations to prove aetiology. Also, diagnosing VITT also restricts the duration of anticoagulation to 3 months which otherwise would have been indefinite (if aetiology remains unproven). With this review we have attempted to demystify the prejudices and myths associated with VITT and to present it as a new and treatable condition in the post-vaccination period.

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Regarding Updating the Address/Mobile No/Email-ID

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