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# Arterial and Venous Thrombosis following Vaccination against COVID-19 with Astra-Zeneca Vaccine Revealing Thrombophilia

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## Abstract

Vaccination against COVID-19 is the most recognised means of containing the pandemic. Vaccines are not without side effects, particularly vascular thrombosis. But before blaming the vaccines, a thorough assessment of thrombotic risk factors is necessary. We report a case of arterial and venous thrombosis after vaccination with AstraZeneca revealing an exaggeration of factor VIII in a 37-year-old female patient. The angioscanner showed a venous thrombosis of the right subclavian, a pulmonary embolism and the presence of a thrombus in the aorta. The biology was in favour of a high level of factor VIII. The patient was treated with an antivitamin K, and the clinical evolution was favourable.

## Keywords

Thrombophilia, Thrombosis, Vaccine, AstraZeneca

## 1. Introduction

SARS-CoV-2 is the virus responsible for the ongoing 2019 coronavirus pandemic (COVID-19). As of 21 February 2023, the COVID-19 pandemic has resulted in more than 700 million cases, more than 6 million deaths and more than 13 billion doses of vaccine administered worldwide [1]. In late 2020, the advent of vaccines against this respiratory syndrome brought new hope to the global fight against the COVID-19 pandemic [2]. Thrombotic adverse events attributable to these vaccines include venous thrombosis, thrombocytopenia and ischaemic stroke,

and have been reported in patients within days of their first vaccine dose [3]. Thrombosis, the obstruction of blood flow due to the formation of clots, may result in tissue anoxia and damage, and it is a major cause of morbidity and mortality in a wide range of arterial and venous diseases and patient populations [4].

Although there is a possible risk of arterial and venous thrombotic events with antiviral vaccinations, some people are genetically predisposed to thrombotic events and are commonly referred to as having hereditary thrombophilia or a hypercoagulable state [5]. In this case report, we present an illustrative case of a 37-year-old patient with elevated factor VIII levels causing arterial and venous thrombosis, for which the AstraZeneca vaccine was initially implicated.

## 2. Observation

A 37-year-old woman, a housewife living in Conakry, with no known history of cardiovascular disease, presented to a cardiology consultation with numbness and pain in the left upper limb that had been present for 2 days. The patient stated that she had received a dose of AstraZeneca one week before the onset of symptoms. The physical examination noted an absent pulse in the left thoracic limb; blood pressure asymmetry with figures of 120/80mmHg on the right, and impenetrable on the left, body temperature 36.4˚C, heart rate 67/min, respiratory rate 18/min and $SPO_2$ 95%. The rest of the physical examination was normal. The initial work-up showed a normal haemogram (Hb = 12.9 g/dl, WBC = 5710/$mm^3$, platelets = 315,000/$mm^3$), a PT of 69%, normal creatinine (7.48 mg/l), lipid profile was normal, CRP was 10 mg/l, liver and thyroid profiles were normal. Transthoracic echocardiography was normal. The arterial Doppler of the thoracic limbs was in favour of a damped, demodulated Doppler flow of the humeral, radial and ulnar arteries on the left. We ordered a thoracic angioscan, which concluded that there was venous thrombosis of the right subclavian vein (**Figure 1**), bilateral segmental and sub-segmental pulmonary embolism (**Figure 2**) and the presence of a thrombus in the aortic arch (**Figure 3**). The diagnosis of post-AstraZeneca arterial and venous thrombosis was made. Anticoagulation was initiated with Enoxaparin Sodium combined with Acenocoumarol, then Acenocoumarol alone with a target INR between 2 and 3.

To reinforce the hypothesis of post-vaccination thrombosis, further investigations were requested. These investigations showed an elevated factor VIII level of 384.20% (normal range 50% - 150%), which was confirmed on two further checks of the factor VIII balance at 3 month intervals. The patient was not taking Acenocumarol at the time of testing. The remaining tests are summarised in **Table 1**.

In view of these results it was decided to continue the anticoagulation for a long time. The pulmonary ventilation perfusion scan was not performed at the third month because it was not available in our country. The evolution was favourable during the first 6 months of follow-up, no recurrence of symptoms, no bleeding under VKA. The patient is currently living abroad.

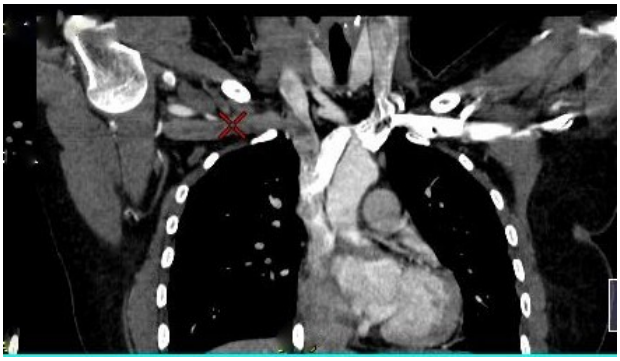


**Figure 1.** Coronal section showing thrombosis of the right subclavian vein (red cross).

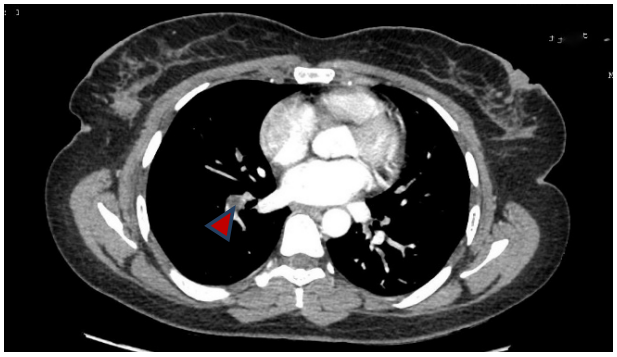
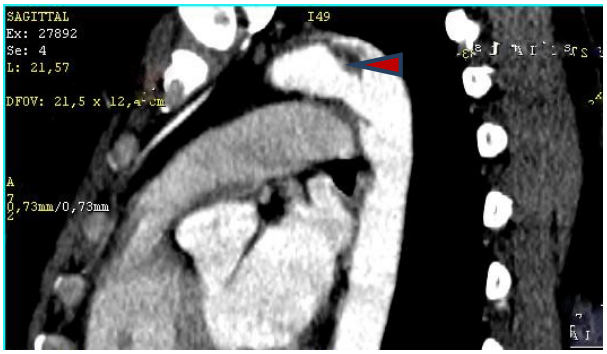
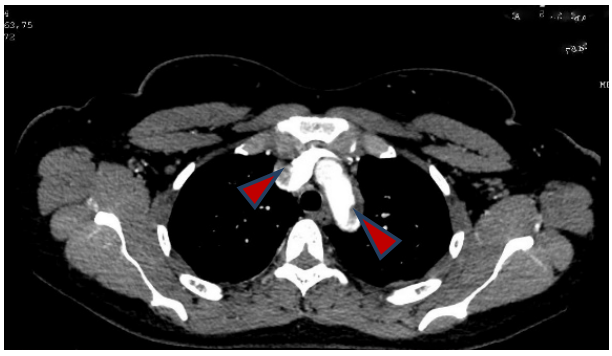


**Figure 2.** Axial section showing sub-segmental pulmonary embolism (red triangle).




(a)



(b)

**Figure 3.** (a) Sagittal section showing thrombus in the aortic arch (red triangle); (b) Axial section showing thrombus in the aorta (red triangle).

**Table 1.** Summary of biological tests.

| TEST | RESULT | STANDARD |
|---|---|---|
| FIBRINEMIA | 4.09 | 2 - 5 |
| HEMOCYSTEIN | 11.88 | >15 |
| ACTIVE PROTEIN C | 130 | 64 - 164 |
| FREE PROTEIN S | 82 | 54 - 103 |
| ANTITHROMBINE | 93 | 66 - 124 |
| AC ANTI-NUCLEAR | NEGATIF | NEGATIIF |
| AC ANTI CARDIOLIPIN IgG | <20 | <20 |
| AC ANTI CARDIOLIPIN IgG | <20 | <20 |
| FACTOR II MUTATION | Absence of mutation | Absence of mutation |
| **FACTOR III** | **384.20** | **50 - 150** |

## 3. Discussion

Vaccination against coronavirus 2019 (COVID-19) is the most effective way to control and mitigate the ongoing pandemic [6].

As of 20 August 2021, more than 4.89 billion doses of various COVID-19 vaccines have been administered worldwide and more than 40 candidate vaccines are in human trials [7].

Yet there is varying degrees of hesitancy, fear and anxiety about the perceived risk of vaccination. This fear is partly justified by the risk of thrombosis that may occur after vaccination [2] [8].

However, some individuals are genetically predisposed to thrombotic events and are commonly referred to as having a hereditary thrombophilia or hypercoagulable state [4]. This is the case for factor VIII [9] [10] [11].

The Leiden Thrombophilia Study (LETS) was the first to report an association between high plasma Factor VIII levels and thromboembolic disease [12].

A high prevalence of Factor VIII: C levels in patients with Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE) has subsequently been confirmed in a number of cohort and case-control studies [10].

Factor VIII is a plasma sialoglycoprotein that plays an essential role in normal haemostasis by acting as a critical cofactor for the serine protease, activated Factor IX (FIXa). For many years it has been recognised that FVIII deficiency in haemophilia A patients leads to significant bleeding. In recent years, there has been increasing evidence to suggest that the reverse is also true, as high plasma FVIII levels may be a clinically important risk factor for thrombosis [10].

This case highlights the possible role of factor VIII in the etiology of arterial and venous thrombosis. Other cases have been reported of acute coronary syndrome associated with elevated factor VIII in patients with no other known cardiovascular risk factors or significant underlying atheromatous disease [13].

In addition to being a prevalent risk factor for first thrombosis, elevated plasma FVIII levels are also associated with a significant increased risk of developing

recurrent thrombotic events [10].

The regulation of plasma factor VIII levels is complex and involves both genetic and acquired factors. Levels are higher in women and people with blood types other than O, high body mass index, diabetes or hypertriglyceridaemia as well as in other situations including pregnancy, surgery, chronic inflammation, cancer, liver disease, hyperthyroidism, intravascular haemolysis and renal disease [14]. Apart from female gender, no other clinical situation was found in our patient.

Previous population studies have shown that plasma FVIII levels are influenced by ethnicity, with significantly higher levels in African Americans than in Caucasians. The biological mechanisms underlying this observation have not been clearly defined, but are probably partly related to the higher prevalence of blood group O in the Caucasian population [15] [16].

The duration of oral anticoagulation affects the risk of thrombosis recurrence. Thus, the identification of a prothrombotic risk factor such as factor III implies lifelong anticoagulation; this is a major clinical decision that influences all aspects of the patient's life [17] [18].

The evolution under anticoagulation was favourable in our patient.

## 4. Conclusion

The risk of thrombosis following the injection of AstraZeneca's vaccine is a reality, but it is important to realize that there are genetic abnormalities that compromise hemostasis and may predispose to thromboembolic events. Among these abnormalities, the high level of factor VIII is an independent risk factor for thrombosis, with a greater impact on venous thrombosis than on arterial thrombosis. In all cases of thrombosis, an exhaustive etiological search is required.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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