IMJ Official Journal of the Irish Medical Organisation

Ir Med J; November-December 2023; Vol 116; No. 10; P880
14th December, 2023

Clots, Covid-19 and Cyberattacks – a case of Vaccine-Induced Immune Thrombotic Thrombocytopenia

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Abstract

We report the case of a 59-year-old male who experienced multiple acute arterial and venous thrombotic events culminating in a diagnosis of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). He was a non-smoker with hypertension and non-insulin dependent diabetes. He received the first dose of "Vaxzevria" ChAdOx1 nCov-19 vaccine (Oxford/AstraZeneca, Cambridge, United Kingdom) with no immediate side-effects. Twenty-four days later, he underwent the first revision stage for an infected total knee replacement (TKR). The pre-admission swab was negative for Covid-19 and he received prophylactic low molecular-weight heparin (LMWH) peri-operatively. A right basilic peripherally-inserted central catheter (PICC) was inserted to facilitate antibiotics between stages.

Day-13 post-revision TKR (Day-37 post-vaccine), his platelet count dropped to 138 $x10^9$/L. On day-14 he developed right upper limb swelling, dyspnoea and pleuritic chest pain, and was transferred to a tertiary centre for further management. His admission coincided with a nation-wide cyberattack on the information technology infrastructure of the public hospital network with severe disruption to radiology and laboratory reporting systems. Based on history and examination, the PICC was removed and therapeutic LMWH commenced for suspected right arm deep vein thrombosis. Confirmatory imaging was scheduled for next working day.

Three days later, he developed acute ischaemia of the right leg (Day-41 post vaccination). Examination revealed no palpable pulses with motor and sensory deficits. CT-Angiography demonstrated occlusive thrombus in the right common femoral and popliteal arteries. Based on examination and imaging, the patient was bolused with unfractionated heparin (UFH) and taken for an emergent femoral embolectomy. The evacuated thrombus was atypical and suspicious for malignant or marantic embolic tissue, though subsequent histology was unremarkable.

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Diagnosis and Treatment

The patient initially remained on UFH post-embolectomy. A CT-PA performed post-embolectomy confirmed a left-sided PE. An exhaustive embolic work-up was unremarkable. Considering the dual arterial and venous events, Haematology was consulted. Due to the cyberattack, historical results from the tertiary centre and referring hospital were inaccessible, and contemporary results were telephoned from the laboratory. VITT was initially considered but felt to be unlikely given the available information and the timeframe from vaccination to clot (>28 days), respectively. Haematology advised to switch UFH to LMWH, after which the platelet count remained low but stable with fibrinogen levels were normal.

Figure 1. *Atypical platelet-rich thrombus retrieved during the second embolectomy, of the same consistency as retrieved during the initial embolectomy*

Day-14 post embolectomy, while anti-coagulated with LMWH, the patient developed recurrent right acute limb ischaemia. Repeat CT-Angiogram confirmed fresh occlusive thrombus in the iliofemoral segment. UFH was restarted and a second emergent

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embolectomy was performed successfully with similar organised white fibrous material retrieved (**Figure 1**).

Post-operatively, UFH was switched back to LMWH due to ongoing thrombocytopenia and failure to achieve a therapeutic APTT. The atypical thrombotic material, recurrent arterial events while on therapeutic LMWH and persistently abnormal haematology laboratory values suggested a persistent coagulopathy (**Figure 2)**. Due to ongoing clinical concerns for HITT/VITT, intravenous Argatroban was commenced. Testing revealed positive Platelet factor-IV Induced Platelet Activation (PIPA) assays but negative Heparin-Induced Platelet Activation (HIPA) assays, consistent with VITT.

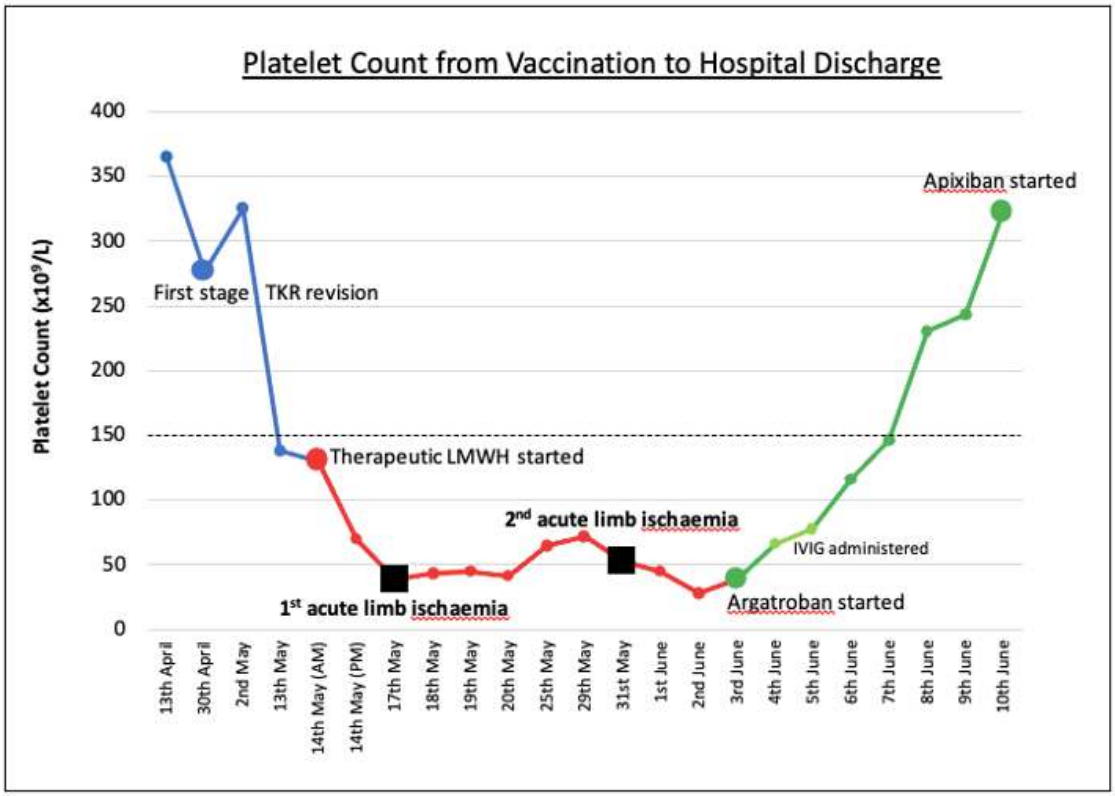

Figure 2. *Graphical representation of platelet count over hospital admission with major venous and arterial events highlighted. The blue line represents time on prophylactic LMWH, the red line represents time on therapeutic LMWH +/- UFH and the green line represents time on Argatroban. NB: timeline compressed for ease of viewing, x-axis intervals are not consistently fixed at 24 hours*

As VITT was confirmed, Factor Xa assays were not determined necessary. Intravenous immunoglobulin was given as per the National Coagulation Centre. Five days later, the

platelet count recovered and Argatroban was switched to Apixaban. The patient was discharged home with no outstanding vascular concerns.

Discussion

The prothrombotic nature of the novel coronavirus SARS-CoV-2 (Covid-19) virus has been widely documented, particularly the high incidence of acute arterial events in patients with active Covid-19 infection (1, 2). The AstraZeneca™ vaccine has also been linked to higher than anticipated rates of venous thromboembolism (3). Since public vaccination policies were introduced worldwide to combat Covid-19, a number of adverse arterial events relating to thrombocytopenia and thrombosis post-vaccination have been reported(4). This new syndrome was named VITT, immunologically similar to Autoimmune Heparin-Induced Thrombocytopenia (5, 6). Similar to HITT, avoiding heparin was essential, and intravenous immunoglobin and anticoagulation with direct thrombin inhibitors became the mainstay of treatment as clinician's experience with VITT evolved(7, 8).

The Covid-19 pandemic created a unique situation whereby clinicians were constantly adapting to new information as the global medical community gathered data on the virus. At the time of this case, the limited reports on VITT outlined common features: patients typically present 4-28 days after an adenoviral-based Covid-19 vaccine, have laboratory findings consistent with a consumptive coagulopathy (thrombocytopenia, raised D-dimer, low fibrinogen) and thrombosis (9). Notably, the majority of scant published reports on arterial events secondary to VITT occurred within the twenty-eight timeframe, as such this case represents an important contribution to the literature documenting an exception (10-13). As this patient had their first arterial event 41 days post-vaccine, VITT was initially considered but deemed unlikely. Xie et al reported a similar case, whereby a patient underwent revascularisation for acute limb ischaemia with peri-operative UFH, as was standard practice for vascular surgeons; a second arterial event five days later prompted further examination of the case and the ultimate diagnosis of VITT.

This case has further novelty as it describes the impact of a cyberattack on Irish healthcare at a granular level. The previously published literature detailed the disturbance to large registries and clinical trial infrastructure but not on individual patient care(14, 15). As laboratory data was critical to this case, the lack of readily available contemporary and historical blood results may have delayed the recognition of concerning trends in the coagulation profile, and ultimately, the diagnosis of VITT. A survey of Irish hospital laboratories reported a significant decrease in sample volume during this period and significantly impacted communication systems. When it came to flagging critical results to the

clinical teams, 21% of laboratories had no access to a phoneline in the lab, 33% reported difficulties in contacting the requesting doctor and 91% had no email access. This case demonstrates the importance of developing contingency plans for medical data communication in the case of disrupted laboratory interface systems.

Surgeons practicing in a post-Covid landscape where patients receive ongoing booster vaccinations must remain cognizant of these rare aetiologies for limb ischaemia and the different anti-coagulation requirements. Furthermore, with electronic medical records becoming the more prevalent, hospitals must have robust contingency plans for maintaining access to patient information in case of cyberattack.

Declarations of Conflicts of Interest:
None declared.

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