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Vaccine-Induced Thrombotic Thrombocytopenia: Insights from Blood Smear

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Vaccine-induced thrombotic thrombocytopenia (VITT) is a thrombotic complication mimicking heparin-induced thrombocytopenia. This very rare but severe thrombotic complication occurs postvaccination against SARS-Cov-2 (severe acute respiratory syndrome coronavirus-2). Diagnosis of VITT remains challenging, but a current consensus report suggests a 10-point guideline for early detection of VITT, which should be confirmed by platelet factor-4 (PF-4) immunoassays. The latter is considered to be the most reliable diagnostic test. We observed platelet aggregates and increased platelet volume in patients with VITT in routine blood smear analyses. These routine blood analytic findings may—together with the clinical presentation—support and speed up the diagnosis of VITT, and may be of particular importance in low-income countries with limited access to PF-4 immunoassays.

Discussion

Two patients (patient 1: age 25; patient 2: age 28, female) were hospitalized on day 7 and 14, respectively, postvaccination (first dose, ChAdOx1nCov-19) with symptoms like nausea, dizziness, and headache. Negative coronavirus disease 2019 (COVID-19) RT-PCR (reverse transcription polymerase chain reaction) excluded SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2). Laboratory results showed platelet count of 75/nL (patient 1) and 76/nL (patient 2), whereas the D-dimer level was 30.65 and 34.62 mg/L, respectively. Computed tomography showed transversal sinus thrombosis.

Blood counts revealed thrombocytopenia in both patients (►**Fig. 1**). In routine blood smears aggregated (A–D; dotted arrows, platelet aggregates) and enlarged platelets (C, D, solid arrows; May–Grünwald Giemsa stain; scale bar 50 µm) were readily detectable upon hospitalization. Increased platelet volume was confirmed by impedance measurement (E, F; PLT histograms; LD = lower discriminator; UD = upper discriminator).

The patients received intravenous argatroban and 2 g/kg immunoglobulin on days 3 and 4 (patient 1) or on day 1 and 2 (patient 2) posthospitalization. Within 6 to 9 days, the platelet changes normalized (G–K).

These cases are suggestive of vaccine-induced immune thrombotic thrombocytopenia (VITT)[1]. VITT is a rare but severe clotting and thrombocytopenia syndrome occurring postvaccination, initially reported in individuals receiving the ChAdOx1nCov-19 AstraZeneca vaccine and later also with the Johnson & Johnson vaccine. It is characterized by thrombosis, thrombocytopenia, and a positive platelet factor 4 (PF4)–heparin ELISA (enzyme-linked immunosorbent assay) and platelet activation assays. In addition to vaccination, early diagnosis of patients at risk of disease worsening or complication thereof and anticipating medical care is an important part for the management of the COVID-19 pandemic.[2] The consensus remains that the benefits of vaccination outweigh the risks. To reduce vaccine hesitancy, a tracking algorithm for vaccinated patients based on a 10-point guideline has been proposed,[3] including anti-PF4 antibody testing and confirmation by PIPA testing. Our findings, made by routine blood smear analyses, may be a first and easily accessible diagnostic step aiding in the identification of patients with VITT and supporting its timely diagnosis. These insights may be particularly helpful in low-resource countries where anti-PF4 antibody tests are not readily available.

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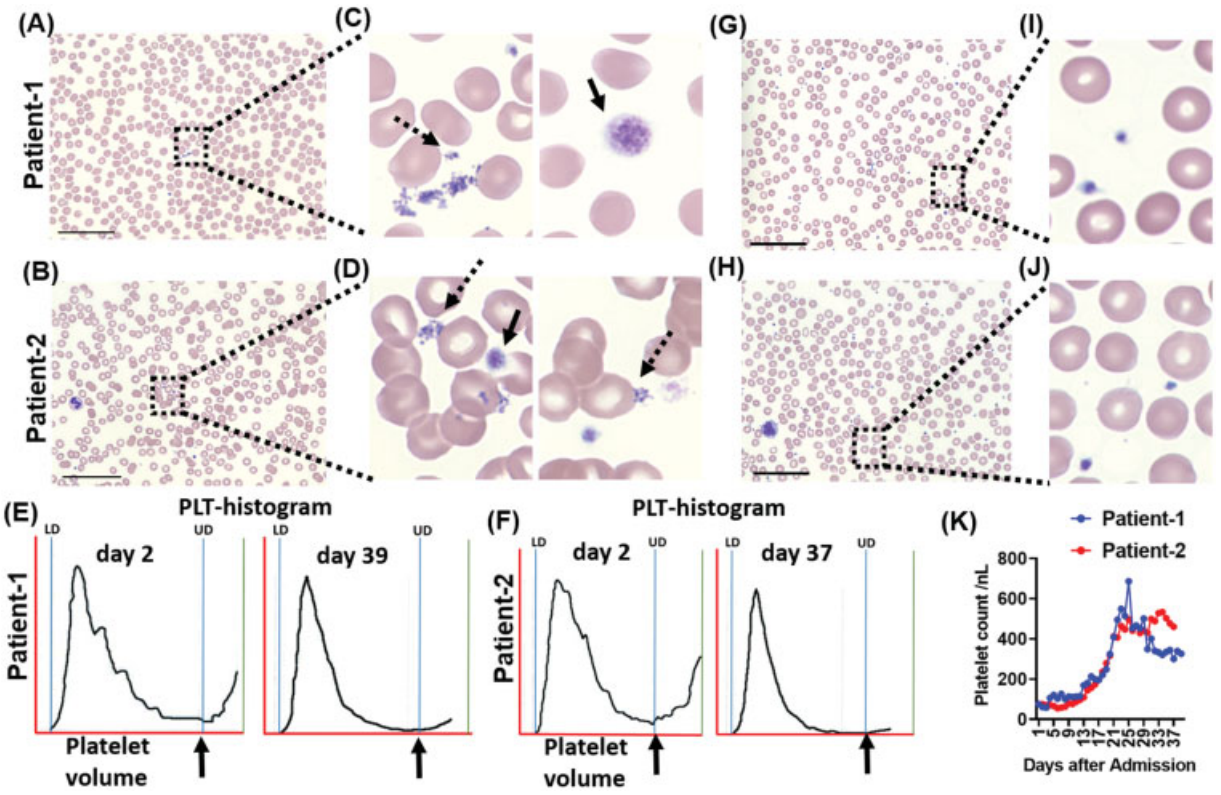

Fig.1 May–Grünwald stained blood smear analysis (**A–J**, microscopic analysis) from two patients with reduced platelet counts (**K**) suggestive of VITT. Enlarged platelets (C, D, *solid arrows*) were detectable and their reactive volume change was observed by impedance technology; (E, F) platelet histograms.

A limitation of our finding is that it is not pathognomonic for VITT, but rather depicts a general immunogenic reaction, such as in heparin-induced thrombocytopenia. Yet, in the context of a typical clinical presentation and a history of COVID-19 vaccination, these findings, reduced platelet count in combination with platelet aggregates and an enlarged platelet volume, which can be obtained from a routine blood test, support the diagnosis of VITT. Such findings warrant further diagnostic and clinical work-up.

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Conflict of Interest
None declared.

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