Thrombo-Guide
vom Labor zur Diagnose

Heparin-PF4 Antibodies
Heparin-Induced Thrombocytopenia (HIT)
Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT)

Description and Clinical Significance

Antibodies against platelet factor 4 (PF4) can trigger several severe conditions. PF4 is a tetrameric protein released from activated platelets. It binds strongly to heparin and heparinoids and inactivates them. This alters the conformation of PF4, and the resulting neo-antigens can act immunogenically. Autoantibodies against PF4 can induce PF4 complexes, further activate platelets, and thus have a strong thrombogenic effect. This can lead to extensive, life-threatening thrombosis and coagulation disorders.

Heparin-induced thrombocytopenia (HIT) is the most frequent condition caused by PF4 antibodies, but it remains a very rare phenomenon overall. In affected patients, a sharp drop in platelet counts and the occurrence of thrombosis manifest during the second week of heparin therapy. This occurs almost exclusively with unfractionated heparin given at high intravenous doses in acute-phase situations (infections, inflammation, surgical interventions, intensive care therapy). With low-molecular-weight heparins or subcutaneous administration, HIT is very rare.

Vaccine-induced immune thrombotic thrombocytopenia (VITT) occurred very rarely approx. 2 weeks after vaccination against SARS-CoV2 using adenoviral vector-based vaccines. In this condition, viral particles bind to PF4, and this complex acts immunogenically. Clinically, patients developed thrombocytopenia, extensive thrombosis, fibrinogen depletion, and very high D-dimer values. However, this vaccine is no longer available.

Nevertheless, similar clinical presentations have been described, extremely rarely, following **adenovirus infections**.

Autoimmune forms of PF4 antibodies without prior patient contact with heparin are also extremely rare.

Diagnostics

The determination of heparin-PF4 antibodies can be performed using immunological methods. ELISA-based methods are preferred because rapid tests fail to detect VITT. The result is usually reported as optical density. The higher the value, the more likely the diagnosis of HIT. Since clinically irrelevant, non-coagulation-activating HIT antibodies occur in many individuals (estimated 80% false-positive results), the analysis should only be requested when there is high clinical suspicion and after estimating the pretest probability using the 4T score.

4T Score

The 4T score serves to estimate the pretest probability of the presence of HIT. With a score

below 4, HIT is highly unlikely; immunological testing should be omitted, and heparin should be continued. The score encompasses the severity, timing, and potential causes of thrombocytopenia, as well as the presence of thrombosis. The calculation is performed here: https://www.mdcalc.com/calc/1787/4ts-score-heparin-induced-thrombocytopenia

Therapeutic Options

HIT: Discontinue heparin; initiate therapeutic anticoagulation with non-heparin anticoagulants (argatroban, danaparoid, fondaparinux, DOACs). DO NOT transfuse platelet concentrates.
VITT: High-dose intravenous immunoglobulins (IVIG), fibrinogen concentrate, therapeutic anticoagulation with non-heparin anticoagulants (argatroban, danaparoid, fondaparinux, DOACs). DO NOT transfuse platelet concentrates.

References

- Thomas L, Labor und Diagnose, 2023, Release 5: https://www.labor-und-diagnose.de/index.html
- Parameterkatalog des Klinischen Instituts für Labormedizin, Med.Univ.Wien und AKH Wien: https://www.akhwien.at/default.aspx?pid=3982
- Leistungsverzeichnis der Klinischen Chemie, Univ.Klinikum Ulm: https://www.uniklinik-ulm.de/zentrale-einrichtung-klinische-chemie/leistungsverzeichnis.html
- Greinacher A, Warkentin TE. Thrombotic anti-PF4 immune disorders: HIT, VITT, and beyond. Hematology Am Soc Hematol Educ Program. 2023 Dec 8;2023(1):1-10. doi: 10.1182/hematology.2023000503. PMID: 38066843; PMCID: PMC10727100. (https://pmc.ncbi.nlm.nih.gov/articles/PMC10727100/)
- Müller L, Gebicka P, Handtke S, Schönborn L, Thiele T. Advances in our understanding of anti-PF4 related immunothrombosis. Front Immunol. 2026 Jan 21;16:1724207. doi: 10.3389/fimmu.2025.1724207. PMID: 41646984; PMCID: PMC12867913. (https://pmc.ncbi.nlm.nih.gov/articles/PMC12867913/)