

Syndrome of thrombosis and thrombocytopenia, possibly occurring after coronavirus vaccination

Preliminary guidance on management. 2021.03.22 to be updated as further information comes to light

A rare syndrome of thrombosis (often cerebral venous sinus thrombosis) and thrombocytopenia is being noted and is highlighted as affecting patients all ages and both genders; at present there is no clear signal of what the risk factors are.

We are asking haematologists to be on alert for this syndrome, to understand how to make the diagnosis, to note the specifics of how to treat it. We further offer resource for expert advice. For patients presenting with acute thrombosis or new onset thrombocytopenia within 28 days of receiving COVID 19 vaccination, we are additionally asking clinicians to ensure that the online yellow card (link below) is completed - this will trigger a request from MHRA for further details. We would also be grateful for the Expert Haematology Panel to be informed of new cases and of their response to treatment, so that as much information as possible can be centrally collated.

The cases are unusual because despite thrombocytopenia, there is progressive thrombosis, primarily venous, with a high preponderance of cerebral venous sinus thrombosis but arterial events have also been noted.

Typical laboratory features include a platelet count $<150 \times 10^9/L$, very raised D Dimer levels above the level expected for VTE and inappropriately low fibrinogen.

Antibodies to platelet factor 4 (PF4) have been identified and so this has similarities to heparin-induced thrombocytopenia (HIT), but in the absence of patient exposure to heparin treatment. These antibodies are detected by ELISA HIT assay but not always by AccuStar.

While this is being further evaluated, we recommend these actions to be taken:

POSSIBLE CASE

Any patient presenting with acute thrombosis or new onset thrombocytopenia within 28 days of receiving COVID 19 vaccination

Investigations

1. Check a FBC-specifically to confirm thrombocytopenia $<150 \times 10^9/L$
2. Coagulation screen, including Clauss fibrinogen and D Dimers
3. Blood film to confirm true thrombocytopenia and identify alternative causes

UNLIKELY CASE

- Reduced platelet count without thrombosis with D dimer at or near normal and normal fibrinogen.
- Thrombosis with normal platelet count and D dimer <4000 and normal fibrinogen

PROBABLE CASE

- If D Dimers >4000
 4. Serum sample for PF4 antibody assay (HIT assay). Please see below *
 5. Serum sample to Colindale for Covid antibody testing and storage
 6. EDTA sample – to be stored locally until location of central lab is confirmed

Management of a suspected case – treat first while awaiting confirmatory diagnosis

1. AVOID platelet transfusions. Discuss any required interventions.
2. AVOID all forms of heparin including heparin-based flushes. (It is unknown whether heparin exacerbates the condition but until further data is clear, this is best avoided).
3. GIVE intravenous immunoglobulin 1g/kg (divided into two days if needed) and review clinical course. Further Ivlg may be required balancing bleeding and thrombotic risk.
4. ANTICOAGULATE with non-heparin-based therapies such as DOACs, argatroban, fondaparinux or danaparoid depending on the clinical picture.

5. Steroids and/or plasma exchange may also be considered.
6. Avoid thrombopoietin receptor agonists
7. Antiplatelet agents are not recommended based on current experience
8. If no overt thrombosis, but thrombocytopenia with raised D Dimer, thromboprophylaxis with non-heparin-based anticoagulants should be considered – balancing bleeding and thrombotic risk. DOAC, fondaparinux or danaparoid can be used.
9. Until further structures are in place, advice on management should be sought from the Expert Haematology Panel (for now please email sue.pavord@ouh.nhs.uk who will send the link to join the daily meeting)

CONFIRMED CASE

If PF4 antibodies positive by ELISA

Continue ongoing treatment as above

If negative, please discuss before changing treatment

*Samples:

Anti PF4 assays by ELISA based technique should be done locally or sent to Filton NHSBT.

HIT assay using Accustar have generally shown negative results and so cannot be relied upon.

Serum should also be sent to Colindale for Covid antibody test and storage:

For the attention of Kevin Brown
Virus Reference Department
National Infection Service
Public Health England
61 Colindale Avenue
London, NW9 5EQ

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950573/E59m_lab_request_form_vw_2289_01.pdf

Please use the code VATTS for easy identification.

EDTA – should be sent to Genomics England. Please store locally until this pathway is set up and consent procedures clear.

It is crucial that the online yellow card is completed and this will trigger a request from MHRA for further details.

<https://coronavirus-yellowcard.mhra.gov.uk/>

Those either affected by or under investigation for this entity as a potential complication of coronavirus vaccination should seek expert medical advice before getting the second dose of vaccine