

# A Case of Moschcowitz's Syndrome

Nora Kinsella  
St James's Hospital  
Dublin 8








ST. JAMES'S  
HOSPITAL

# Clinical Presentation

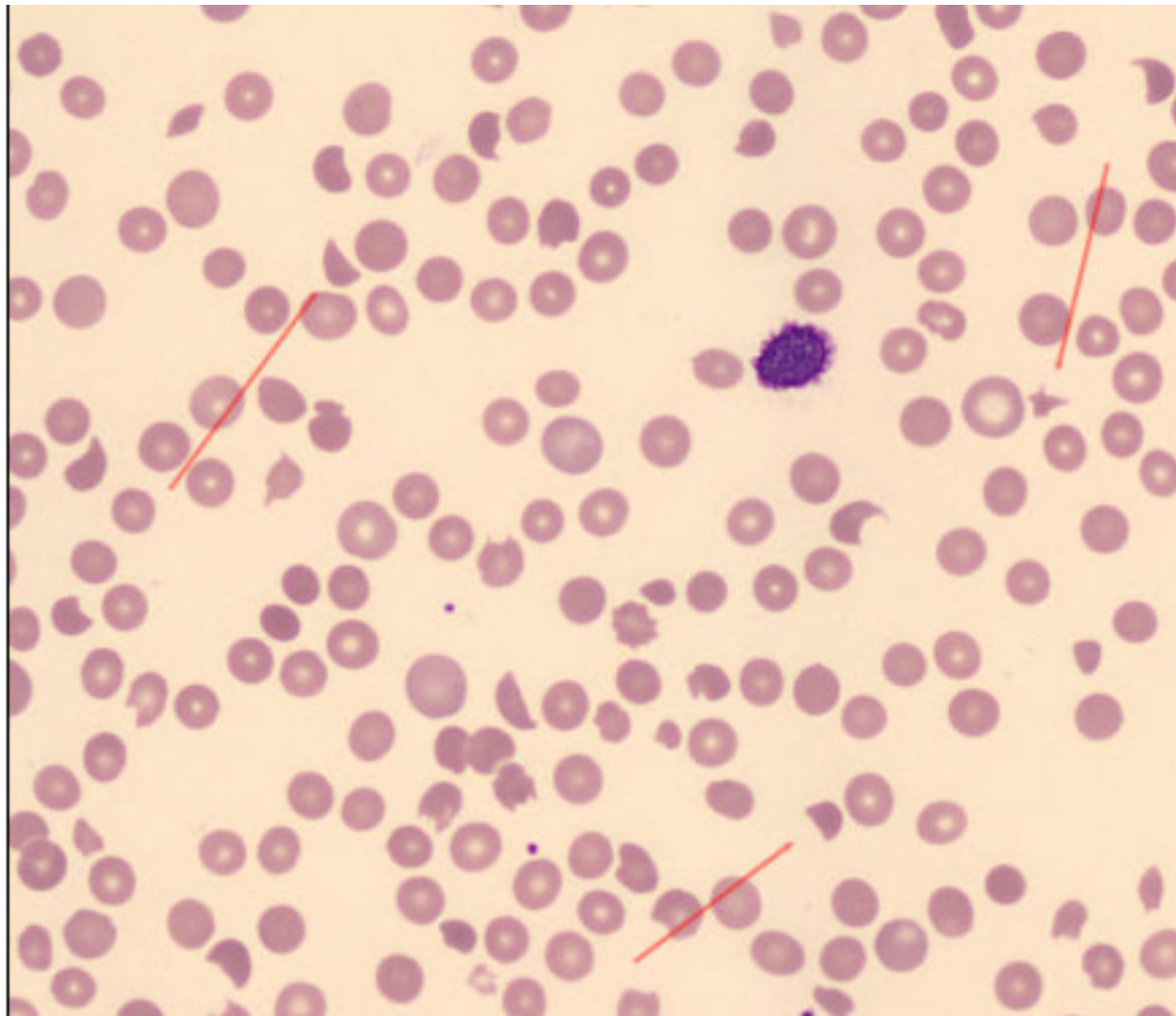
- 34 year old male presented in Emergency Department
- Generally unwell
- Petichiael rash on lower limbs
- Headache for past 2 days
- Nausea



# Laboratory Presentation

- Haemoglobin: 7.8 g/dl 
- Platelets:  $<10 \times 10^9/l$  
- WCC:  $10.0 \times 10^9/l$
- Retic: 8% 
- PT/APTT: Normal
- D-Dimer: 8,000 ng/ml 
- LDH : 6,000 IU/l 
- DCT : Negative

# Blood Film Picture



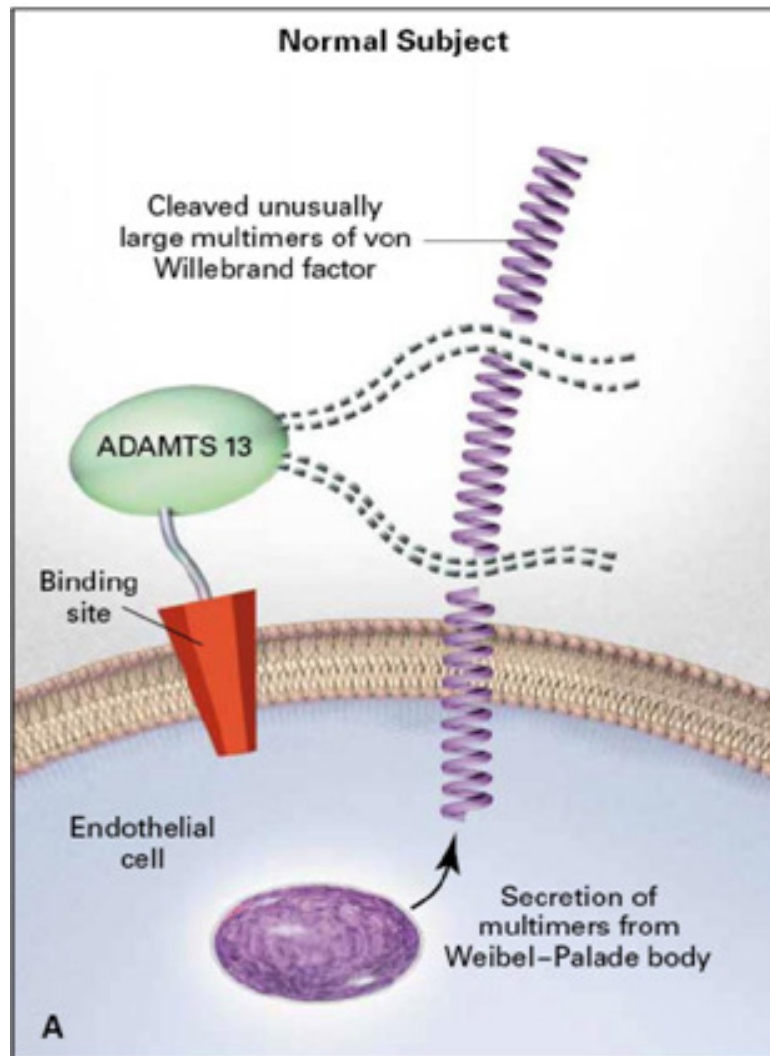
## Possible Diagnosis

ITP	Low Platelets	Normal Red Cells
AIHA	Normal Platelets	Damaged Red Cells
DIC	Low Platelets Coagulation Factors Consumed	Damaged Red Cells
TTP	Low Platelets Coagulation Factors Not Consumed	Damaged Red Cells

# Historical Perspective

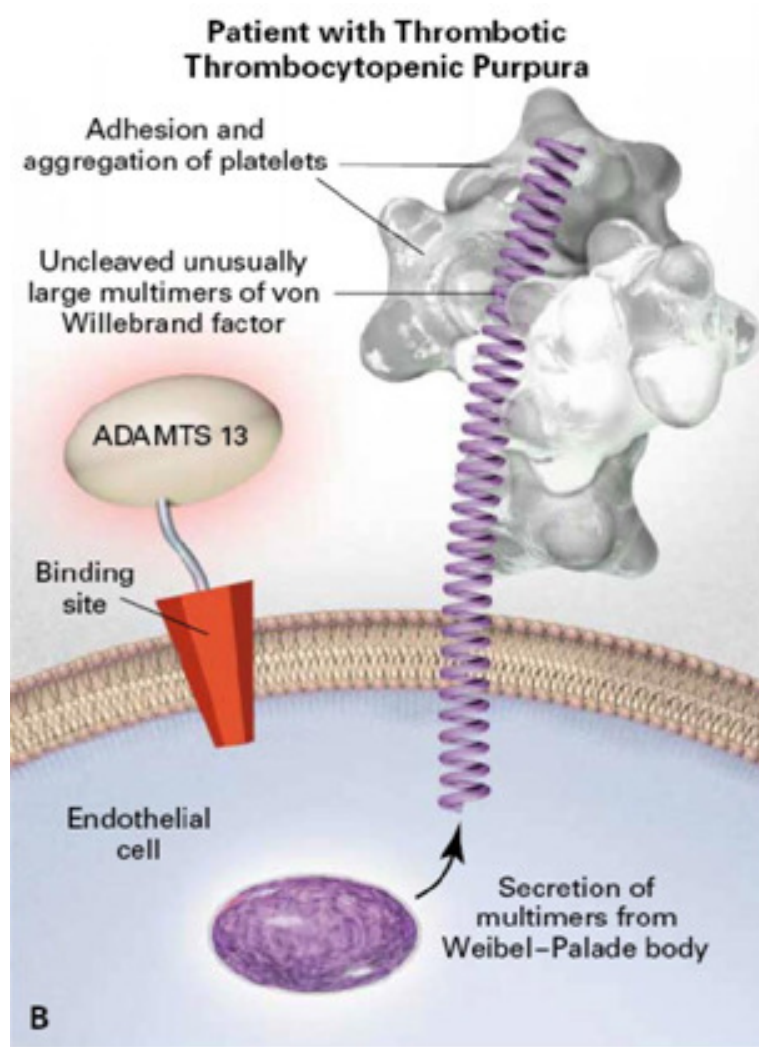
- Described by Dr Eli Moschcowitz in 1924 in a 16 year old girl with sudden onset of fever and haemolytic anaemia followed by rapid paralysis, coma and death. (Acquired TTP)
- A paediatric form of this condition was identified in the 1960's by Upshaw and Schulman. ( Congenital TTP)
- The pathogenesis was unclear but it was observed that plasma infusions improved the condition and platelet infusions caused deterioration of the condition
- Cause was not fully elucidated until 1996 when Furlan and Tsai identified a plasma protease that specifically cleaved VWF multimers .
- This protease was subsequently called ADAMTS-13

# How ADAMTS 13 works



- Von Willebrand factor is synthesised in Endothelial
- Stored in Weibel-Palade Bodies
- On stimulation, VWF is secreted as ultra large multimers which is extremely adhesive.
- Platelets will adhere to these UL-VWF
- ADAMTS 13 cleaves UL-VWF into smaller multimers and also from the surface of the endothelial.

# What happens in Acquired TTP

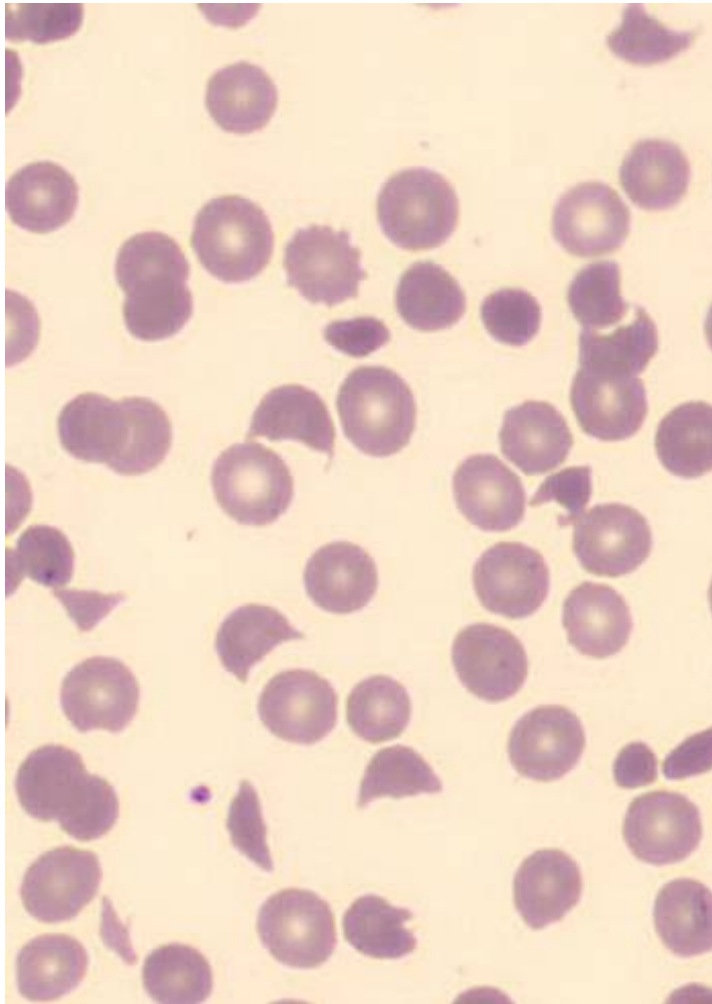


- ADAMTS<sub>13</sub> is inhibited by IgG autoantibodies.
- Highly adhesive UL VWF multimers are not cleaved and remain bound to the endothelial surface
- Platelets bind to the UL-VWF and form platelet thrombi

# What happens in TTP

- Wide-spread deposition of a platelet –rich thrombi in the microcirculation.
- Red blood cells passing the microscopic clots are subjected to shear stress which damages their membranes, leading to intravascular hemolysis and schistocyte formation
- Blocking of micro-blood vessels causes organ ischaemia and end organ damage (brain and kidneys)
- TTP typically presents abruptly
  - 1/3 of cases arise spontaneously
  - 2/3 of cases secondary to an underlying clinical condition
    - HIV, Disseminated Malignancy, Pregnancy, Viral or bacterial infection, drug treatments and auto-immune disorders

# Urgent Diagnosis



## 1. Thrombocytopenia

## 2. Evidence of MAHA

- Schistocytes
- Anaemia
- Reticulocytosis
- Increased LDH

(derived from both ischemic necrotic tissue and lysed red cells)

## 3. Neurological Symptoms (60%)

## 4. Fever (20%)

## 5. Renal Impairment (45%)

# Treatment

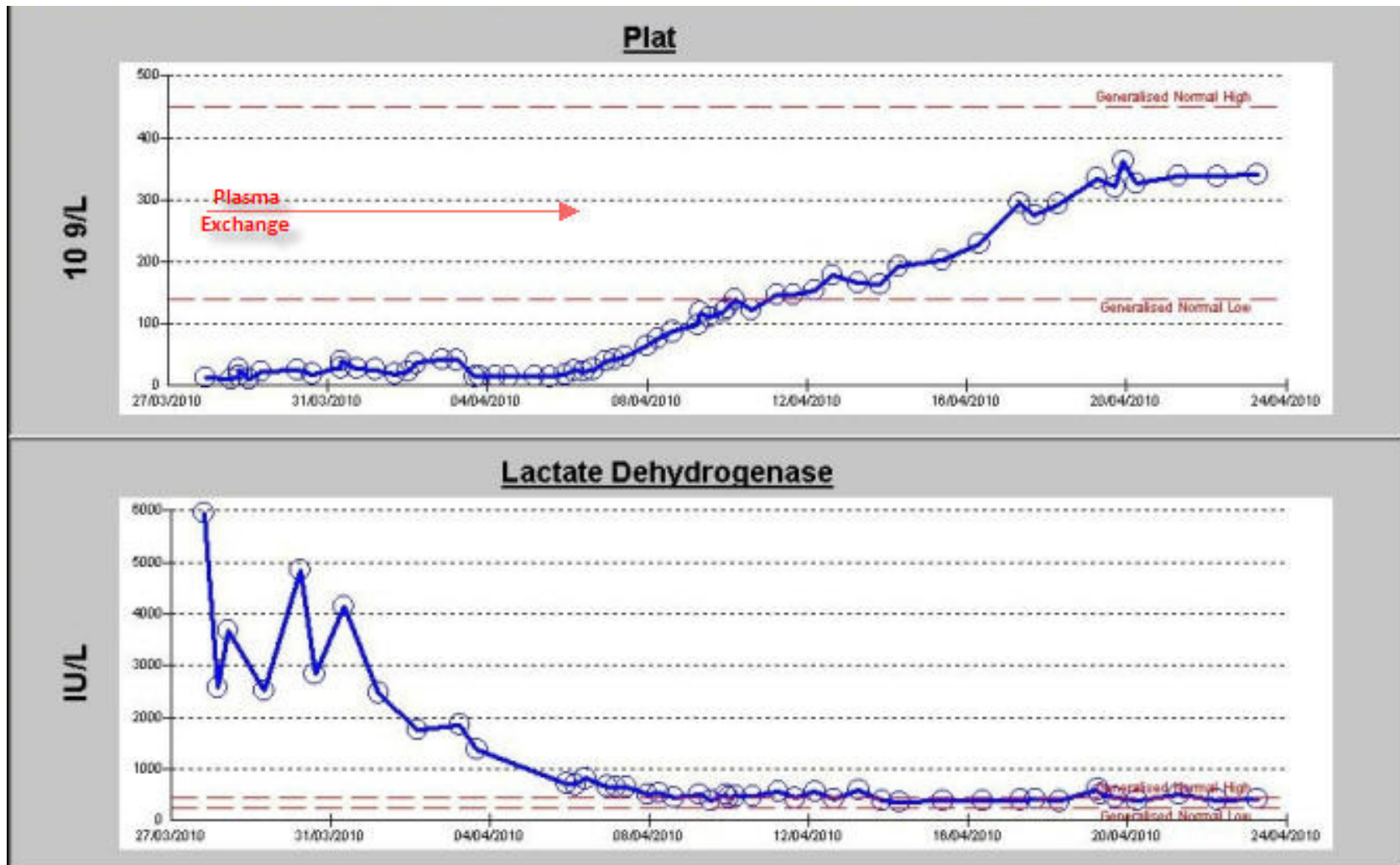
- Current therapy is based on support and plasmapheresis to reduce circulating antibodies against ADAMTS<sub>13</sub> and replenish blood levels of the protease.
- 16 units of Octaplas was replaced every day for 3 weeks

# Confirmatory Diagnosis

- ADAMTS-13 Activity <5%  
( Normal 55-160%)
- IgG anti ADAMTS-13 20 AU/ml  
(Normal <11 AU/ml)

(UCLH Haemostasis Research Unit)

# Progress over one month



# Summary

- Thrombotic thrombocytopenic purpura (TTP) is a life threatening illness whose mortality rate exceeds 90% in the absence of rapid appropriate treatment.
- Affects 4 / million
- May arise spontaneously or secondary to underlying condition
- Requires urgent diagnosis at clinical and laboratory level
- Laboratory Role is key
- Presence of profound thrombocytopenia and schistocytes
- Reduced ADAMTS 13 activity due to auto antibody results in high levels of highly adhesive VWF multimers.
- Platelets bind to the VWF multimers and form vaso-occlusive platelet-rich clots
- Ischaemia may result in end organ failure and death

# Thank You for Your Attention

## References

- Journal of Haemostasis & Thrombosis 2005;3: 1663-1675  
Thrombotic Thrombocytopenia Purpura
- [www.CTSJournal.com](http://www.CTSJournal.com). 2009. Thrombotic  
Micronangiopathies, :Multimers, Metalloprotease and  
Beyond
- Blood 2008;111: Page 3452-3457. ADAMTS 13 turns 3

# TTP and HUS

Very similar presentation and some researchers propose that they are viewed shared patho-physiology

- TTP is inhibition ADAMTS-13 which cleaves large VWF multimers.
- HUS is excessive production of large VWF multimers due to e-coli/shigella toxins
- ADAMTS-13 ( 13<sup>th</sup> member of a A Disintegrin And Metalloproteinase with ThromboSpondin)