Disseminated intravascular coagulation (DIC) + Thrombotic microangiopathies (TTP+HUS)

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Disseminated intravascular coagulation (DIC)
Overview

• Systemic activation of coagulation

• Formation of thrombi throughout the microcirculation
  
  Consumption of platelets/coagulation factors + Fibrinolysis

• Severe bleeding (consumptive coagulopathy)
It is usually triggered by:

(1) the release of tissue factor or thromboplastic substances into the circulation (extrinsic pathway)

or

(2) widespread endothelial cell damage

or

(3) activation of intrinsic coagulation pathway
Thromboplastic substances, sources

- Placenta due to obstetric complications
  ...also there is shock, hypoxia & acidosis...endothelial injury

- Certain cancer cells...especially: -acute promyelocytic leukemia
  -adenocarcinoma

- Gram-negative and gram-positive sepsis (important causes of DIC):
  ...endotoxins or exotoxins stimulate the release of tissue factor from monocytes
  ...activated monocytes also secrete IL-1 & TNF...stimulate the expression of
  tissue factor on endothelial cells
  ...simultaneously decrease the
  expression of thrombomodulin
Widespread endothelial cell damage...can be produced by:

- The deposition of antigen-antibody complexes (e.g., in systemic lupus erythematosus)
- Temperature extremes (e.g., after heat stroke or burn injury)
- Infections (e.g., resulting from meningococci or rickettsiae)
- Systemic inflammatory response syndrome (SIRS)/septic shock

...DIC is a frequent complication of SIRS
Brain trauma, an important cause

• By the release of phospholipids and fat
  ...activation of intrinsic pathway
DIC, 2 consequences

- Widespread fibrin deposition and resultant obstruction
  - Ischemia & microinfarcts
  - Microangiopathic hemolytic anemia

- Superimposed bleeding tendency
  - ...due to:
    - platelet/clotting factors consumption
    - fibrinolytic pathway activation
DIC, morphology

- Microinfarcts and bleeds in any organ, especially:
  - the arterioles and capillaries of the kidneys, adrenals, brain, and heart

  Especially glomeruli

= Waterhouse-Friderichsen syndrome

...involvement of anterior pituitary after delivery
  = Sheehan postpartum pituitary necrosis

...also skin bleeds
DIC, lab investigations

• Thrombocytopenia

• Prolonged PT

• Prolonged PTT

• Increased fibrin split products
DIC, treatment

- Give anticoagulants (heparin) or coagulants (in fresh frozen plasma)
- Treat the underlying cause
Thrombotic microangiopathies (TTP & HUS)
• **TTP** = thrombotic thrombocytopenic purpura

• **HUS** = hemolytic uremic syndrome
**TTP**

- **Deficiency of the enzyme** ADAMTS13...inherited or acquired (autoantibodies)
  ...even in inherited, the onset is delayed until adolescence (we need triggers)

- **Defined by:**
  
  1- fever
  
  2- thrombocytopenia
  
  3- microangiopathic hemolytic anemia
  
  4- transient neurologic deficits
  
  5- renal failure
**HUS**

...the Shiga-like toxin...E.coli O157:H7
...or *Shigella*...etc.
...the toxin alters the endothelium in a way that increases platelet adhesion & aggregation

...also associated with:
  - microangiopathic hemolytic anemia
  - and
  - thrombocytopenia

...but: distinguished from TTP by:
  - the absence of neurologic symptoms
  - the dominance of acute renal failure
  - frequent occurrence in children

But sometimes:
  - TTP with less than 5 criteria
  - HUS with fever and neurologic symptoms
TTP & HUS

• Fundamental to both conditions:
  the widespread formation of platelet-rich thrombi in the microcirculation

...consumption leads to thrombocytopenia
...narrowing of blood vessels by platelet-rich thrombi results in a microangiopathic hemolytic anemia

• Normal PT & PTT
Both DIC and thrombotic microangiopathies:

- Microvascular occlusion

+ 

- Microangiopathic hemolytic anemia
Thank You