***no patient handout*

Disseminated intravascular coagulation

Synopsis

AcuteDisseminated intravascular coagulation (DIC) is a complex disorder in which the clotting cascade is activated within blood vessels throughout the body. There is excessive and unregulated generation of thrombin, usually due to mechanical tissue or endothelial injury. Despite the systemic thrombosis taking place in the macro- and microvasculature, bleeding is also seen as fibrinolysis is activated and coagulation factors and platelets are depleted by the process. The combination of hemorrhage and thrombosis leads to inadequate tissue perfusion and infarction, often resulting in end-organ damage in severe and acute cases. DIC has no apparent age, race, or sex predilection.

DIC may be triggered by a variety of conditions, including trauma or burns, severe infections or sepsis, obstetrical complications, malignancies, severe snakebite reactions, and giant hemangiomas. Systemic signs and symptoms may include mental status changes, fever, dyspnea, hypotension, tachycardia, hematuria, and oliguria. Dermatologic signs include mucosal bleeding, retiform purpura, petechiae, and acral gangrene. In severe cases, fatality may occur rapidly. Complications from DIC include acute renal failure, severe hemorrhage in various locations (eg, cardiac tamponade, intracerebral hemorrhage, hemothorax), and gangrene.

DIC may be acute, chronic, or localized. Severe acute DIC is a medical emergency generally caused by trauma, malignancy, infection, or an obstetric emergency. It often presents with generalized bleeding and a shock-like picture (hypotension and tachycardia). Chronic DIC demonstrates subacute bleeding and diffuse thrombosis; its causes are often malignancies, other obstetrical complications, and autoimmune / inflammatory disorders. Many patients with low-grade chronic DIC can be managed on an outpatient basis. Localized DIC, as the name suggests, is confined to a specific body location. It is associated with giant hemangiomas (**Kasabach-Merritt syndrome**), aortic aneurysms, and hyperacute kidney transplant rejection.

Codes

ICD10CM:
D65 – Disseminated intravascular coagulation [defibrination syndrome]

SNOMEDCT:
67406007 – Disseminated intravascular coagulation

Look For

In the acute life-threatening form, look for extensive retiform purpura (purpura fulminans), necrosis, and gangrene extending symmetrically on the extremities and then body-wide over a period of a few days. There may be frank skin or wound bleeding and/or evidence of thrombosis.

In less acute forms, look for petechiae, acral cyanosis, palpable purpura, and bullae.

Diagnostic Pearls

The cutaneous signs can be localized to the buttocks and breasts.

Bleeding from 3 or more unrelated sites is suggestive of DIC.

Differential Diagnosis & Pitfalls

- **Coumadin (warfarin) necrosis**
- **Heparin necrosis**
- **Antiphospholipid antibody syndrome**
- **Recluse spider envenoming**
- **Acute meningococcemia**
- **Cryoglobulinemia**
- **Cryofibrinogenemia**
- **Necrotizing fasciitis**
- Large vessel **vasculitis**
- **Thrombotic thrombocytopenic purpura**
- Idiopathic **purpura fulminans**
- **Cocaine levamisole toxicity**
- Localized trauma

- Primary bone marrow failure – such as an infiltrative process or leukemia
- **HELLP syndrome** (hemolysis, elevated liver function tests, low platelets) in pregnant women
- Primary fibrinolysis

Best Tests

There is no single diagnostic test for DIC. A diagnosis of DIC may be suggested by the clinical picture, along with a falling platelet count, the presence of D-dimers and fibrin degradation products, and a prolonged prothrombin time (PT) and partial thromboplastin time (PTT). The most efficient tests for demonstrating excessive thrombin generation (essential to the underlying pathogenesis of DIC) are the D-dimer and protamine paracoagulation assays. The fibrinopeptide A and prothrombin fragment assays accomplish the same goal but are less universally available.

The following tests are often ordered in the workup of DIC. They are presented here with their common (abnormal) findings in this disease state:

- CBC with differential and smear – anemia with schistocytes, low platelets
- Prothrombin fragment 1 and 2 assays – abnormal levels
- D-dimer determination – elevated*
- Antithrombin III (ATIII) level – decreased
- Fibrin and fibrinogen degradation products – elevated
- Fibrinopeptide A – abnormal level
- Fibrinogen – decreased
- PT – variable, over half of patients with DIC have a prolonged value
- PTT – variable, over half of patients with DIC have a prolonged value
- Thrombin time – prolonged
- Protamine paracoagulation assay for fibrin monomer – positive
- Level of coagulation factors (especially factor V) – decreased
- Urinalysis – hematuria or hemoglobinuria
- Fecal occult blood test – positive

*D-dimer levels may be moderately elevated in patients who have had recent surgery or bleeding into tissues, or those who have cirrhosis or renal failure – interpret with caution.

A variety of other tests will likely be needed based on the underlying pathogenesis and the need to monitor for end-organ damage, and may include electrolytes, tests of liver and renal function, cultures, and a chest x-ray or other imaging. Repeat determinations of platelet counts, fibrinogen, and the PT and PTT are often necessary.

Management Pearls

Patients with acute DIC should be managed in the intensive care unit by a team of specialists including intensivists, hematologists, and/or blood bank / transfusion personnel.

Maximize supportive measures and treatment of the underlying disease process (antibiotics for sepsis, etc). Pay close attention to electrolyte balance, gas exchange, and volume status. Monitor and treat for shock, and perform replacement therapy for consumed platelets, fibrinogen, plasma, etc, as needed, based on the clinical scenario.

Therapy

In addition to treating the inciting process and maximum supportive measures, blood product replacement therapy should be considered in patients that are actively bleeding and for whom an invasive procedure is planned.

- Platelets – The goal is to maintain the count at 20-30 x 10^9/L (higher if a procedure is planned). Each unit should raise the count 6-8 x 10^9/L. Check platelet counts 30-60 minutes post-transfusion and every 6 hours after that.
- Cryoprecipitate – Given to maintain a plasma fibrinogen over 100 mg/dL. Give 1-4 units/10 kg. Repeat the fibrinogen level 30-60 minutes post-transfusion and every 6 hours subsequently.
- Fresh frozen plasma (FFP) – Given when significant bleeding is associated with a prolonged PT and PTT, with the goal of reducing these values. Administer 10-15 mL/kg of FFP. Monitor the PT and PTT every 6 hours.

Transfusions may be required up to every 8 hours. They may be discontinued when bleeding or other symptoms have been controlled and parameters have stabilized and/or normalized.

If the laboratory parameters fail to respond to transfusions and bleeding persists, consider concurrent heparin infusion. Heparin treatment should also be considered in patients in which the thromboembolic manifestations predominate, such as those with tumor-associated chronic DIC. The use of heparin in many clinical scenarios remains controversial, however, and specialty consultation should be sought in making this treatment decision. A suggested initial bolus is 80 units/kg IV followed by an infusion of 18 units/kg/hour. The use of heparin requires the ongoing monitoring of coagulation parameters. Subcutaneous injections and low-molecular-weight

heparins (enoxaparin, dalteparin) have been used in select clinical instances such as cases of chronic malignancy-associated DIC and Trousseau syndrome.

Antithrombin concentrate and activated protein C have also been used as adjuncts in the treatment of DIC. Antithrombin may be most helpful in patients with DIC who are resistant to heparin or who have hepatic insufficiency (a common regimen consists of a loading dose of 100 units/kg over 3 hours, then a continuous infusion of 100 units/kg/day). Activated protein C may be beneficial in patients with severe sepsis and DIC. The dose is 24 µg/kg/hour by continuous IV infusion over 96 hours.

In general, fibrinolysis inhibitors such as aminocaproic or tranexamic acid should not be used in DIC. Certain exceptions include when intense primary fibrinogenolysis can be demonstrated, such as in cases of prostate cancer, Kasabach-Merritt syndrome, and acute promyelocytic leukemia, and in patients who continue to bleed despite aggressive hematostatic factor replacement and heparin infusion.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
abacavir	1
acenocoumarol	1
alemtuzumab	1
Alkylating agent	2
Antiarrhythmic	2
Anticoagulant	3

Medication	Citations
Anticonvulsant	2
Antimalarials	2
Antimetabolite	2
Antimycobacterial	6
Antiparasitic	1
Antiretroviral	1
aprotinin bovine	1
aspirin	3
BRAF kinase inhibitor	1
clofibrate	1
Coumadin	1
dextran	1
disopyramide	1

Medication	Citations
fludarabine	1
fondaparinux	1
gefitinib	1
gemcitabine	1
hydroxyethyl starch	2
ifosfamide	1
lamotrigine	2
Monoclonal antibody	1
non-NRTI antiretroviral	1
NSAID	3
oxaliplatin	1
propylthiouracil	1
quinine	5

Medication	Citations
rifampin	6
Salicylates	3
sunitinib	1
thalidomide	1
Tyrosine kinase inhibitor	1
valproate	1
vemurafenib	1
zomepirac	2