



DISSEMINATED

INTRAVASCULAR

COAGULATION

Epidemiology

The incidence of disseminated intravascular coagulation (DIC) is not known. Approximately 15 percent of septic patients may develop DIC.

Etiology and Pathogenesis

DIC represents systemic activation of the coagulation cascade. This leads to fibrin

deposition in the vasculature, which can cause organ ischemia and death. In addition, the consumption of platelets and coagulation factors can lead to bleeding. DIC occurs most commonly secondary to an underlying disorder .

□ Settings in Which Disseminated Intravascular Coagulation Can Occur

- · Sepsis
- · Trauma
- · Malignancy
- · Obstetric complication (amniotic fluid embolism, p
- · Vascular abnormalities
- · Hepatic failure
- · Immunologic reaction to drugs or toxins
- · Transfusion reactions
- · Transplant reaction
- · Protein C or S deficiency

In DIC, coagulation activation is a tissue factor-dependent (i.e., extrinsic or factor VIIa pathway). Inflammatory cytokines such as tumor necrosis factor- α promote damage to endothelial cells and activation of mononuclear cells. These cells then produce tissue factor, which binds to factor VIIa and activates downstream coagulation cascades. Thrombin generation is amplified by defective anticoagulant mechanisms and results in increased fibrin deposition. The fibrin that is generated fails to be degraded by the fibrinolytic system. In the healthy state, antithrombin regulates thrombin activity. In DIC, antithrombin levels are low due to continuous consumption, degradation by neutrophil elastase and impaired synthesis due to liver failure in some settings. Fibrinolysis is inhibited by plasminogen activator inhibitor type 1 (PAI-1). Studies show that individuals with high plasma levels of PAI-1 are at higher risk of mortality in DIC. This correlates with a mutation in PAI-1 that is associated with higher PAI-1 plasma concentrations. Thus, some individuals may be genetically predisposed to fatal outcomes from DIC due to a point mutation in PAI-1.

The infection most commonly associated with DIC is meningococcal sepsis. However, DIC has been reported after viral and other bacterial infections. Many recent reports suggest an emergence of sepsis due to staphylococcus, particularly those isolates containing exotoxins including staphylococcal enterotoxin serotypes B and C, TSS toxin-1, and Panton-Valentine leukocidin, a leukocyte toxin believed to be important in the pathophysiology of skin and soft-tissue infections and necrotizing pneumonia, as a factor in initiating DIC.

Clinical Findings

HISTORY

DIC is always secondary to an underlying condition or disorder and thus the patient generally first presents with the antecedent condition. Often, patients with DIC develop simultaneous bleeding, thrombosis, and multiorgan failure. The onset of DIC in the neonatal period is suggestive of protein C or S deficiency.

CUTANEOUS LESIONS

The most characteristic cutaneous finding in DIC is noninflammatory purpura with extensive microvascular occlusion referred to as purpura fulminans . Patients have diffuse bleeding, hemorrhagic necrosis of tissue, and skin necrosis . Patients with purpura fulminans may present with ischemic digits or extremities that, left untreated, can progress to gangrene.

RELATED PHYSICAL FINDINGS

In its most extreme form, patients with DIC develop the Waterhouse-Friderichsen syndrome, most commonly seen in meningococcal sepsis (see Chap. 180). This is a syndrome of multiorgan failure characterized by a petechiae or purpura, coagulopathy, cardiovascular collapse, and bilateral adrenal hemorrhage.

Laboratory Tests

DIC is characterized by laboratory evidence of massive activation of the coagulation cascade and the destruction of platelets. Platelet counts are generally less than 100,000. Because of the high conversion of fibrinogen to fibrin, soluble fibrin monomers and the D-dimer assay are usually elevated. The prothrombin time is usually prolonged to at least 1.2 times the upper limit of normal as well. Several scoring systems exist that assign numeric values to particular laboratory findings and allow the calculation of a single numeric score that is helpful in predicting the presence of and mortality from DIC as reviewed elsewhere.¹²

Differential Diagnosis

The differential diagnosis of DIC includes other conditions causing small and mid-size vessel thrombotic occlusions leading to organ failure and microangiopathic hemolysis. This includes thrombocytopenic thrombotic purpura, the hemolytic uremic syndrome, and the HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome seen in obstetric patients.

Complications

Complications of DIC include tissue necrosis and infection, often requiring amputation of limbs or digits, multiorgan failure (particularly the Waterhouse-Friderichsen syndrome), and death.

Prognosis and Clinical Course

The mortality risk is doubled in patients with DIC who are septic or have experienced trauma.

Treatment

Because DIC is always secondary to another condition, the most important factor in the management of DIC is treatment of the underlying cause. However, replacement of components consumed during DIC and inhibition of the coagulation cascade has an important role as well. Despite the conventional wisdom that replacement of platelets and coagulation factors in the patient with DIC adds “fuel to the fire,” more recent clinical trials have not shown this to be the case. These studies

have demonstrated a survival benefit to treating patients with DIC with low-dose heparin. Finally, activated protein C, which works by enhancing thrombomodulin activity, has been shown to significantly reduce mortality in patients with DIC.¹²

There is very little published experience regarding the treatment of the cutaneous necrosis seen in DIC. Skin necrosis secondary to DIC is similar to that seen in full thickness cutaneous burns. Possible excision of necrotic tissue and coverage with autografts, and/or amputation of extremities are treatment options.

Prevention

Most interventions in DIC are aimed at minimizing organ damage and bleeding. Prevention of DIC itself can be achieved by the prompt diagnosis and treatment of its causes, particularly sepsis.