A review of disseminated intravascular coagulation

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The author reviews the definition, causes, clinical signs and symptoms, laboratory diagnosis and treatment of disseminated intravascular coagulation. A review of the clotting mechanism is also presented.

In recent years there have been an increasing number of articles and studies on the topic of disseminated intravascular coagulation. It is not a newly found phenomenon. The syndrome was identified in general terms in a 1959 article by William Crosby. Numerous terms, including de-fibrination syndrome, diffuse intravascular coagulation, and consumptive coagulopathy have been used to describe this process. For the sake of clarity, it will be referred to here as disseminated intravascular coagulation (DIC).

A definition of DIC

Disseminated intravascular coagulation is a condition that presents as abnormally increased coagulation, resulting in capillary thrombus formation. The development of capillary thrombi leads to interference with perfusion. The result is focal hemorrhagic necrosis in organs such as the lung, liver, pancreas, bowel and/or kidney. Furthermore, increased coagulation leads to the depletion of the elements of the clotting mechanism, resulting in generalized hemorrhage. DIC also triggers fibrinolysis, leading to the destruction of existing clot and further compounding hemorrhage.

Review of clotting mechanism

To understand DIC, a review of the physiology of the clotting mechanism, hemostasis and appropriate pathophysiology is in order (see Figure 1).

When a blood vessel is damaged, the walls of the vessel constrict. Platelets adhere to the endothelium and react with collagen fibers, releasing ADP, serotonin and epinephrine. ADP causes adhesiveness with other platelets in the area, leading to the formation of a hemostatic platelet plug at the site or injury.

Blood clotting may be initiated by two mechanisms: the extrinsic system or the intrinsic system. DIC may trigger abnormal clotting by initiation of either system, depending on the underlying disease involved.

The extrinsic system is activated when tissue thromboplastin from damaged tissues reacts with clotting factor VII. Clotting factor VII then initiates subsequent reactions involving clotting factors V and X and calcium, to convert prothrombin to thrombin. The intrinsic system is activated when blood is exposed to the collagen fibers underlying the endothelium in blood vessels. As the hemostatic plug is formed, platelets are destroyed, releasing platelet factor III. Platelet factor III sets
off a series of reactions involving clotting factors V, VIII, IX, X, XI, and XII and calcium to produce thrombin from prothrombin.

The result is the same in both systems: thrombin converts fibrinogen to fibrin. The tough fibrin strands reinforce the weaker hemostatic platelet plug to create a clot in the injured area. To balance the clotting process, the activation of plasmin from plasminogen occurs. Plasmin's proteolytic action results in the destruction of fibrin (fibrinolysis) which acts as a natural preventive to pathologic deposits of fibrin.\(^7,^8\)

\**Diseases triggering DIC**

There are many disease processes that initiate DIC. Infectious states such as sepsis, gram-negative shock and viral infections can initiate DIC. In certain obstetric complications, including placenta previa, abruptio placenta, eclampsia, retained dead fetus and cesarean section, DIC may also occur.\(^6^\) Intravascular necrosis resulting from hemolytic transfusion reactions, certain venomous snake bites, and hypotonic hemolysis (intravascular hypotonic solution, transurethral prostatectomy), as well as neoplastic processes such as acute leukemia, lymphoma, and carcinoma may cause DIC.\(^5^\)

Autoimmune reactions such as drug reactions, renal homograft rejection and acute glomerulonephritis, as well as massive surgical insult such as pulmonary resection, repair of aortic aneurysm, multiple trauma, acute head injury,\(^10^\) and prolonged cardiopulmonary bypass have resulted in DIC. Many other varied disease states, such as heat stroke, massive burns, fat embolism and congenital cyanotic heart disease, have been implicated in DIC.

This list could be continued to include most disease states that result in massive tissue destruction or extensive damage of endothelial collagen fibers with exposure to foreign surfaces. Shock or other low perfusion states may complicate or intensify the DIC process.\(^9^\)

It is important to note that DIC is a symptom of an underlying disease process and not a primary disease in itself. Several etiologies may be present in the individual with DIC. When DIC occurs without an obvious source, a search should be made for occult disease.\(^9^\)

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**Figure 1**

*Blood clotting mechanism*

1. **Blood vessel damage**
   - Platelets + Collagen
   - Release of ADP, serotonin and epinephrine
   - More platelets
   - Hemostatic plug

2. **Vessel constriction**
   - Extrinsic system: Tissue thromboplastin, clotting factors VII, V, X and calcium
     - Collagen fibers + platelets
     - Platelet factor III
     - Clotting factors XII, XI, IX, VIII, V, X and calcium
     - Thrombin from prothrombin
     - Fibrin from fibrinogen

3. **Hemostatic platelet plug + fibrin**
   - Clot
Signs and symptoms

Of primary concern to the anesthetist is the potential DIC patient undergoing surgery. Physical signs and symptoms may alert the anesthetist to the process of DIC. Petechiae, excessive wound and venipuncture bleeding, acral (extremity) cyanosis and subcutaneous hematomas occurred in 16% of DIC patients studied by Minna, Robboy and Colman in 1974. The study further showed that 67% of DIC patients exhibited some type of skin lesion. In 32% of DIC cases, the skin lesion was the initial symptom.

Various organ dysfunctions may be demonstrated in patients with DIC. Although cardiac dysfunction is often present in DIC patients, its etiology is usually related to the disease process involved rather than directly to DIC. Pulmonary dysfunction, such as dyspnea, cyanosis with high FIO₂ requirement, rales, wheezing and pleural friction rubs are signs of acute respiratory failure and may be related to DIC. The 1979 study of DIC by Mant and King relates respiratory failure to the underlying disease process.¹

Renal dysfunction manifested as oliguria was attributed to DIC by Gotta, et al. in 1975.² Generally, however, it is acknowledged that renal dysfunction, like cardiac dysfunction, is caused by the underlying disease process rather than DIC. The most significant finding available to the anesthetist is unexplained or inappropriate oozing or hemorrhage.¹,³

Laboratory diagnosis

The physical signs and symptoms of DIC present an equivocal picture at best. The best course of action for the anesthetist to follow in the suspected DIC patient is to correlate physical findings with more definitive laboratory findings. The three hematological laboratory tests most useful in the identification of DIC are the platelet count, prothrombin time and fibrinogen level.

The platelet count falls as disseminated coagulation occurs. The platelet count usually drop below 150,000/mm³ as the process develops (a normal platelet count is 200,000 to 350,000/mm³). While a low platelet count can be an indication of DIC, it alone cannot be used to diagnose DIC.

Prothrombin time becomes prolonged in DIC. A more than 5 second prolongation or a time greater than 15 seconds (a normal prothrombin time is 10 to 12.5 seconds) may be an indication of DIC.

Fibrinogen levels of less than 150 mg/dl occur in DIC (a normal fibrinogen level is 150 to 350 mg/dl). It is necessary to view fibrinogen levels in light of the underlying disease. The level of fibrinogen will be increased in sepsis; thus the decrease seen in DIC may not fall below normal levels. These levels are very helpful in identification of DIC in patients with acute trauma with no underlying sepsis.

The simultaneous changes of these tests as just described are strongly diagnostic of DIC. Other useful tests, including partial thromboplastin time, bleeding time, and thrombin time, are all usually prolonged in the presence of DIC.

Fibrin split products also may be diagnostic of DIC. The presence of a significant level of fibrin split products indicates that fibrinolysis has been triggered in response to abnormal fibrin deposition. Fibrinolysis, however, is not triggered until organ anoxia due to fibrin deposits occurs. Therefore, the elevation of fibrin split products occurs only after the DIC has progressed for a significant length of time. A normal fibrin split product level is 0 to 10 µg/ml; in DIC it may rise to 80 to 100 µg/ml or more.³,⁶,⁸,¹¹

Treatment

The treatment of DIC is an area surrounded by controversy. Heparin therapy has been advocated by some authorities for the treatment of DIC. A course of heparin therapy can be initiated with an intravenous dose of 50 to 100 units per kilogram of patient weight. Heparin therapy can be maintained by a continuous intravenous heparin infusion of 10 to 15 units per kilogram per hour.¹²,¹³

Most authorities use heparin therapy only if the underlying cause will take a prolonged time to correct or cannot be corrected. Heparin acts by inhibiting the coagulation system, and as a result blocks the action by thrombin, resulting in the termination of DIC.³ However, Mant and King summarize in their 1979 study that “heparin is seldom useful and often causes increased hemorrhage.”¹⁴

Clotting factor levels will usually increase within three doses (eight hours) of heparin, although this depends on the response of the underlying condition to therapy. Replacement of the decreased clotting factors with fresh frozen plasma or replacement of other specific clotting factors is contraindicated until heparin therapy is begun or the underlying disease process corrected. The reason for this is that the administration of clotting factors in the face of untreated DIC will only fuel the process further.¹⁴ Ω-Aminocaproic acid appears to have little use in the treatment of DIC and may increase the adverse effects of DIC by interfering with fibrinolysis.³ The best treatment of
DIC is the removal or repair of the underlying disease process.

Evaluation of the response to therapy is based on improvement of clinical and laboratory findings. Clinically, if bleeding and acral cyanosis decrease, a conclusion can be drawn. Laboratory findings indicative of improvement include a return to normal or more than a 5-second fall in the prothrombin time, a greater than 50,000/mm³ rise in the platelet count (or a 100% rise if the platelet count is less than 50,000/mm³). No change or deterioration of laboratory values indicates poor response to therapy.9

The role of the anesthetist

The role of the anesthetist in managing patients with DIC is an important one. It is necessary for the anesthetist to be able to identify those patients most likely to be at risk of developing DIC during their intraoperative course. It is essential that the anesthetist understand the process of DIC and be able to relate this process to the events of the normal clotting mechanism. He should be able to identify DIC patients by the use of appropriate clinical findings, and be able to utilize the appropriate laboratory tests to verify the presence of DIC. The anesthetist should also be familiar with the treatment of DIC in order to assist with the therapy during the time the patient is under the anesthetist's care.

Intraoperatively, the anesthetist must communicate appropriate physical symptoms and laboratory abnormalities to the operative team for prompt treatment and/or further referral. Close communication with blood bank personnel will aid in maintaining a prompt flow of needed blood products. The anesthetist must also work closely with laboratory personnel and consulting physicians to coordinate proper monitoring of appropriate tests and treatment regimens during surgery.

DIC is a devastating process with an associated high rate of mortality. The ability of the patient to survive an episode of DIC is in part based on the prompt recognition and treatment of the process. As an integral member of the surgical care team, the anesthetist can greatly assist in this process.

REFERENCES


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