VOLUME - 11, ISSUE - 06, JUNE - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Hematology

DISSEMINATED INTRAVASCULAR COAGULATION

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ABSTRACT Disseminated intravascular coagulation (DIC) is a hyperstimulation of proteins responsible for clotting, on injury the proteins migrate and stop bleeding, but when these proteins overact develops DIC. The DIC can cause microvascular thrombus leads to severe complications like tissue damage and organ failure. Various risk factor related to blood, malignant, vascular, obstetric, toxins, bacteria virus, transplant rejection. The present article describes the causes, risk, diagnosis and management of DIC.

KEYWORDS : Intravascular coagulation, Diagnosis of DIC

INTRODUCTION

Disseminated intravascular coagulation (DIC) is overactive of blood clot proteins that controls bleeding, then deposition of fibrin causes microvascular thrombosis and leads to organ failure.

A life threatening hemorrhage can precipitate on consumption of clotting factors and platelets in DIC. Fibrinolysis and activation of intravascular clot formation causes severe bleeding, henceforth patient with DIC are at risk of hemorrhage and thrombosis.[1,2,3]

Prevalence of DIC

1% of patients hospitalized develops DIC. DIC occurs to all age group.[2]

Risk factors for DI

- CThe DIC is not specific illness rather it is result of secondary effect of illness 4,5,
- 6A sepsis due to COVID can cause DIC
- Neurotrauma, organ destruction, malignancy, transfusion reactions can cause DIC
- Complication of obstetrics such as amniotic fluid embolism, abruption plancenta, hemolysis, raise in liver enzymes, low platelet HELLP syndrome and eclampia, retained dead fetus syndrome.[7,8]
- Vascular aneurysms, kasabach merritt syndrome
- Hepatic failure, toxic reaction like envenomation's, transplant rejection.
- Purpura fulminans, catastrophic antiphospholipid syndrome.
- Heat stroke and hyperthermia.
- Bateremia septic shock

Causes for DIC

- DIC is caused due to systemic inflammatory response, leads to activation of cytokines network leads to activation of coagulation and release or exposure of procoagulant materials.[9,10,11]
- Disease caused by bacteria, virus, fungal, parasitic infection.
- Malignancy disease relating to hematologic and metastatic
- Traumatic, myocardial infarction, ulceratis colitis, Crohn disease, sarcoidosis, aortic aneurysm giant hemangioma, acute renal allograft rejection, myeloproliferative syndrome, rheumatoid arthritis, Raynaud disease.[12]

Pathology of DIC

DIC is result of tissue factor mediated thrombin generation, dysfunctional coagulation mechanism, imbalance in thrombin generation, impaired fibrin removal and inflammatory activation.

Thrombin generation occur in 4-5 hours of bacterial infection, tissue factor get activated and circulate and disrupt endothelial, tissue damage, the tissue factor VIIA complex cleave fibrinogen to fibrin causing platelet aggregation.

Thrombin generation is regulated by multiple hemostatic mechanism, an intravascular coagulation commences the compensatory mechanism are incapacitated.

In patient with DIC plasma levels of thrombin, antithrombin are reduced due to continuous consumption of antithrombin in activation of coagulation, elastase produced by neutrophils, capillary leak of antithrombin, liver damage due to antithrombin leads to microvascular coagulation.[13]

The fibrinolysis is defective due to rapid release of fibrinolytic activity caused due to plasminogen activators from endothelial cells. The intravascular fibrin produce thrombin eliminated called fibrinolysis. During the maximum activation of coagulation fibrinolytic system is largely effected to close. The high level of tissue plasminogen activator antigen and decreased antiplasmin are observed in DIC.[14]

The fibrinogen play key in coagulation and hemostasis responsible to produce Von Willebrand factors, these factors are essential for platelet adhesion between surface, in case of DIC the vessel wall increases adhesion, impaired endothelial cell results in thrombin generation, results in increase platelet activation and fibrinogen to fibrin conversion.

Additional patients with adenocarcinoma have predominant hyperfibrinolysis leads to DIC.[15]

The inflammatory and coagulation pathway stimulates hemostatic imbalance, hypercoagulable state produces DIC further, various factors such as thrombin, TF-VIIa complex activates the protein C and antithrombin leads worsen DIC to the patients.

Diagnosis of DIC

A clear history of risk factors associated with the DIC to be assessed.[16,17,18]

Observe for the clinical findings such as petechiae, ecchymosis, blood loss from venous line, the surgical site bleeding, drains, tracheostomies bleeding.

Observe for symptoms and signs following which physical examination of the patients for DIC.

A group of tests are essential to diagnose DIC moderate to severe disease diagnosis.

Patients with DIC exhibit prolong coagulation time, high level of fibrin degradation products,

Elevated D-dimer levels, peripheral smear,

Standardized test is platelet count, global clotting times, activated prothrombin tine, prothrombin time, one or two clotting factors and inhibitors, assay for D-dimer.

Specialized test molecular markers for activation of coagulation, fibrin formation sensitive assay for DIC.

Prothrombin activation fragments.

Serum level of thrombomodulin helps in identifying the multiple organ dysfunction syndrome.

International society on thrombosis and hemostasis ISTH developed scoring system called DIC scoring system

Clinical finding of DIC

- DIC exhibit petechiae on the soft palate, trunk and extremities
- Ecchymosis at venipuncture site
- Circulatory signs- subacute bleeding, diffused or localized thrombosis, cavities bleeding.
- Central nervous signs- altered consciousness, stupor
- Cardiovascular sign- hypotension, tachycardia, circulatory collapse.
- Respiratory sign- pleural friction rib, acute respiratory distress syndrome
- Gastrointestinal sign- hematemesis, hematochezia
- Genitourinary sign- azothemia, acidosis, hematuria, oliguria, metrorrhagia, uterine hemorrhage.
- Dermatological sign- petechiae, purpura, hemorrhagic bullae, acral cyanosis, purpura fulminans, localized infarction and gangrene, wound bleeding, deep subcutaneous hematomas, thrombosis.[19]

Complication due to DIC

- Acute kidney disease
- Respiratory, hepatic dysfunction
- Cardiac tamponade
- Hemothorax
- Intracerebral hematoma
- Gangrene, shock, loss of digits and death.[20]

Treatment of DIC

- Administration of blood components and coagulation factor
- Platelet transfusion is used for patients at risk of bleeding
- Coagulation factor replacement therapy include factor V, specific deficiencies such as fibrinogen corrected by fresh frozen plasma.
- Anticoagulants such as low molecular weight heparin is used in DIC, enoxaparin used in chronic DIC.
- Antithrombin therapy, tissue factor pathway inhibitors, recombinant thrombomodulin.
- Long term use of antiplatelet agents, subcutaneous heparin, low molecular weight heparin are used in chronic DIC.
- Commonly used drugs for management of DIC are heparin, antithrombin, recombinant human activated protein C, Drotecogin alfa.
- Blood components used in DIC are packed red blood cells, platelet, fresh frozen plasma, cryoprecipitate or fibrinogen concentrate, antifibrinolytic agents, aminocaproic acid, tranexamic acid are the drugs used in management of DIC.[21,22]

REFERENCES

1. Levi M, ten Cate H, Bauer KA, van der Poll T, Edgington TS, Büller HR, et al. Inhibition of endotoxin-induced activation of coagulation and fibrinolysis by pentoxifylline or by a monoclonal anti-tissue factor antibody in chimpanzees. J Clin Invest. 1994 Jan. 93(1):114-20.
2. Carey MJ, Rodgers GM. Disseminated intravascular coagulation: clinical and laboratory aspects. Am J Hematol. 1998 Sep. 59(1):65-73.
3. Mesters RM, Mannucci PM, Coppola R, Keller T, Ostermann H, Kienast J. Factor VIIa and antithrombin III activity during severe sepsis and septic shock in neutropenic patients. Blood. 1996 Aug 1. 88(3):881-6.
4. Nawroth PP, Stern DM. Modulation of endothelial cell hemostatic properties by tumor necrosis factor. J Exp Med. 1986 Mar 1. 163(3):740-5.
5. Novotny WF, Brown SG, Miletich JP, Rader DJ, Broze GJ Jr. Plasma antigen levels of the lipoprotein-associated coagulation inhibitor in patient samples. Blood. 1991 Jul 15. 78(2):387-93.
6. Biemond BJ, Levi M, Ten Cate H, Van der Poll T, Büller HR, Hack CE, et al. Plasminogen activator and plasminogen activator inhibitor I release during experimental endotoxaemia in chimpanzees: effect of interventions in the cytokine and coagulation cascades. Clin Sci (Lond). 1995 May. 88(5):587-94.
7. van Hinsbergh VW, Kooistra T, van den Berg EA, Princen HM, Fiers W, Emeis JJ. Tumor necrosis factor increases the production of plasminogen activator inhibitor in human endothelial cells in vitro and in rats in vivo. Blood. 1988 Nov. 72(5):1467-73.
8. Mesters RM, Flörke N, Ostermann H, Kienast J. Increase of plasminogen activator inhibitor levels predicts outcome of leukocytopenic patients with sepsis. Thromb Haemost. 1996 Jun. 75(6):902-7.
9. Asakura H, Ontachi Y, Mizutani T, Kato M, Saito M, Kumabashiri I, et al. An enhanced fibrinolysis prevents the development of multiple organ failure in disseminated intravascular coagulation in spite of much activation of blood coagulation. Crit Care Med. 2001 Jun. 29(6):1164-8.
10. Levi M. Disseminated intravascular coagulation in cancer patients. Best Pract Res Clin Haematol. 2009 Mar. 22(1):129-36.
11. Levi M, van der Poll T, Büller HR. Bidirectional relation between inflammation and coagulation. Circulation. 2004 Jun 8. 109(22):2698-704.
12. Altieri DC. Molecular cloning of effector cell protease receptor-1, a novel cell surface receptor for the protease factor Xa. J Biol Chem. 1994 Feb 4. 269(5):3139-42.
13. Camerer E, Huang W, Coughlin SR. Tissue factor- and factor X-dependent activation of protease-activated receptor 2 by factor VIIa. Proc Natl Acad Sci U S A. 2000 May 9. 97(10):5255-60.
14. Erez O, Mastrolia SA, Thachil J. Disseminated intravascular coagulation in pregnancy: insights in pathophysiology, diagnosis and management. Am J Obstet Gynecol. 2015 Oct. 213 (4):452-463.
15. [Guideline] Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. Br J Haematol. 2009 Apr. 145(1):24-33.
16. Sohn CH, Kim SR, Kim YJ, Seo DW, Ahn S, Lee YS, et al. Disseminated Intravascular Coagulation in Emergency Department Patients With Primary Postpartum Hemorrhage. Shock. 2017 Sep. 48 (3):329-332.
17. Matsuda T. Clinical aspects of DIC--disseminated intravascular coagulation. Pol J Pharmacol. 1996 Jan-Feb. 48(1):73-5
18. Levi M, de Jonge E, van der Poll T. New treatment strategies for disseminated intravascular coagulation based on current understanding of the pathophysiology. Ann Med. 2004. 36(1):41-9.
19. Iba T, Levi M, Levy JH. Sepsis-Induced Coagulopathy and Disseminated Intravascular Coagulation. Semin Thromb Hemost. 2020 Feb. 46 (1):89-95.
20. Asakura H, Ogawa H. COVID-19-associated coagulopathy and disseminated intravascular coagulation. Int J Hematol. 2020 Nov 7
21. Branson HE, Katz J, Marble R, Griffin JH. Inherited protein C deficiency and coumarin-responsive chronic relapsing purpura fulminans in a newborn infant. Lancet. 1983 Nov 19. 2(8360):1165-8.
22. Yuen P, Cheung A, Lin HJ, Ho F, Mimuro J, Yoshida N, et al. Purpura fulminans in a Chinese boy with congenital protein C deficiency. Pediatrics. 1986 May. 77(5):670-6.