British Journal of Bio-Medical Research Vol.01, Issue 04, Pg.217-222, September-October 2017

Available Online at http://www.bjbmr.org

BRITISH JOURNAL OF BIO-MEDICAL RESEARCH

Cross Ref DOI: https://doi.org/10.24942/bjbmr.2017.165 Volume 01, Issue 04, Sept-October 2017

ISSN:2456-9739

Review Article

Thrombotic Microangiopathic Haemolytic Anaemia: A Pathologic Abnormality Associated with Diverse Clinical Syndromes

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ARTICLE INFO

Article History:
Received on 07th Sept 2017
Peer Reviewed on 21st Sept 2017
Revised on 16th October 2017
Published on 29th October 2017

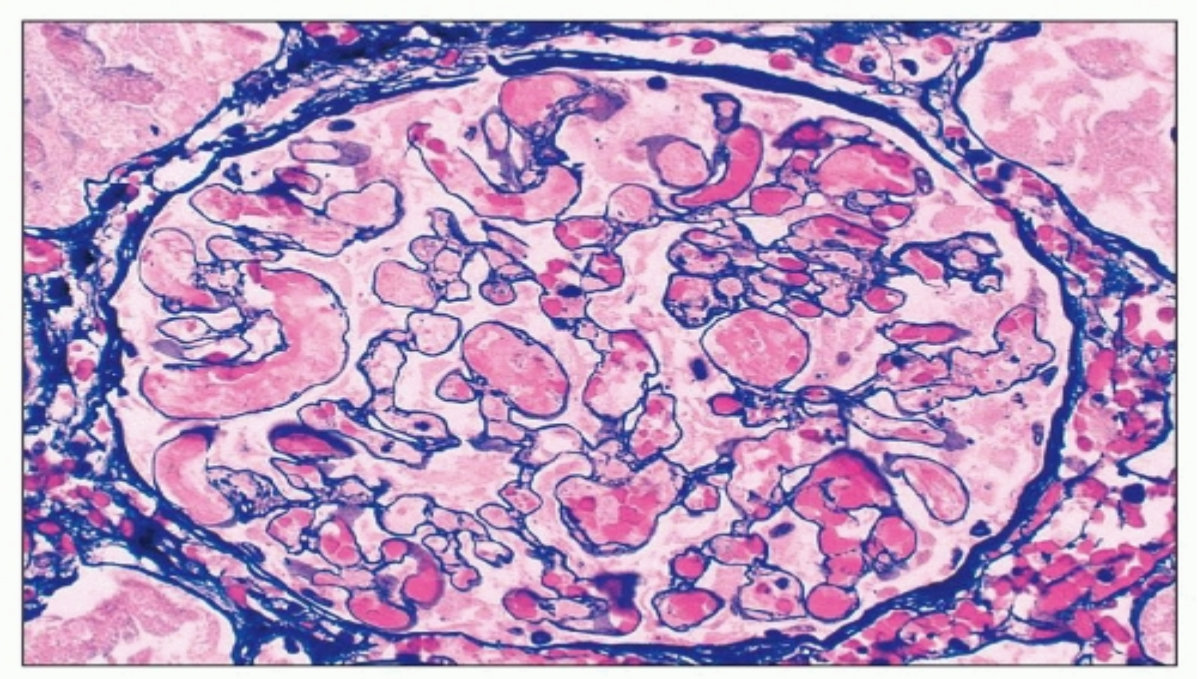
Keywords:
Bone marrow infiltration, Microangiopathic Anemia, Thrombotic microangiopathy, Thrombotic Thrombocytopenic Purpura.

ABSTRACT

A pathological process of microvascular thrombosis, microangiopathic hemolytic anemia and thrombocytopenia, with ischemia and infraction, affecting particularly kidney and brain is Thrombotic microangiopathy (TMA). Disseminated intravascular coagulation (DIC) is caused by severe infectious disease and systemic inflammatory syndrome (SIRS). Thrombotic microangiopathy (TMA) a rare but devastating disease, also known as microangiopathic hemolytic anemia (MAHA) in combination with thrombocytopenia and signs of organ damage. These pathological features are included in different clinical syndromes, such as hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), and HELLP syndrome in pregnancy. Now comes to secondary TMA which can be triggered by many factors such as various drug, bone marrow transplantation, infections and malignant diseases.

INTRODUCTION:

A microangiopathic hemolytic anemia with elevation of lactate dehydrogenate and negative direct Comb's test thrombotic occlusion of the microvasculature leading to fragmentation of red blood cells and profound thrombocytopenia, are the results from which cause thrombotic microangiopathy results from and. Due to one disease entity, the constellation of clinical and laboratory cannot be find; rather, it represents a variety of underlying diagnoses[1-3]. Diseases like Kasbah-Merritt phenomenon and stem cell transplantation which can be congenital or acquired, bacterial infections, medications, vascular or endothelial pathology are the major disease entities of TTP/HUS. Some of the major causes of thrombotic microangiopathy (TMA) is a term that describes pathological findings of microangiopathic hemolytic anemia (MAHA), thrombocytopenia and microvascular thrombi. Formation of fibrin- and platelet-rich thrombi in microcirculation results in the beginning of TMA process. Due to optical treatment TMA, be identified quickly. Ischemia in brain is caused due to systemic microvascular aggregation of platelets[4-5]. Platelet –fibrin thrombi predominately include renal circulation in hemolytic –uremic syndrome(HUS). Adult with major central neurological involvement are labeled as TTP. HUS and TTP, their essential diagnostic criteria are same. Autoimmune disease characterized by vascular thrombosis, pregnancy complications ,or both due to antiphospholipid antibodies is antiphospholipid syndrome(APS) disease. Protein that interact with phospholipids in APS is due to pathogenic autoantibodies[6].



Source: https://abdominalkey.com/thrombotic-microangiopathies-2/

THROMBOTIC THROMBOCYTOPENIC PURPURA

The pentad of microangiopathic thrombocytopenia, hemolytic anemia, fever, renal compromise and neurological is known as Thrombotic thrombocytopenic purpura (TTP)[7-8]. The prevalence and diversity of the disease has been increased due to diagnosis of thrombocytopenia and microangiopathic anemia, with or without ischemic organ damage, and not attributable to an alternate recognizable cause. Some entities like vacuities, infection, pregnancy, mediation or

development of post-stem cell transplant take place in the term TTP (or secondary TTP) has also been used to refer to microangiopathic hemolytic anemia[9].

HEMOLYTIC UREMIC SYNDROME

The most common subtype of HUS is Diarrhea-associated HUS (D+HUS). Most commonly caused by infection with Shiga-toxin producing Escherichia coli O157 (STEC) and usually caused in children. The mean incidence of HUS in children under 18 years of age ranges from 0.28 to 0.71 cases per 100,000 persons. The disease has been reported between 0.85 and 1.87 cases per 100,000 children that is more common in those <5 years of age[10-11]. Common cause of acute renal failure in children in the USA is due to D+HUS. Mortality ranges with the highest mortality in those >60 years of age from 1 to 33%.

Microangiopathic hemolytic anemia and thrombocytopenia characterized with Hemolytic uremic syndrome (HUS) with accompanying renal impairment. There is three subtypes division: first is congenital HUS (which has also been referred to as atypical) and pneumococcal (also known as atypical or diarrhea negative) HUS and then diarrhea-associated HUS (D+HUS), these three entities share clinical features, pathogenesis and the underlying epidemiology, and treatment are markedly different.[12] Spectrum of thrombotic microangiopathy referred to term HUS caused by medications or associated with pregnancy or other clinical conditions.

TRANSPLANT-ASSOCIATED MAHA:

Approximately 14% with the majority of the patients having no systemic manifestation of TMA was observed with renal transplants with an incidence. If diseased person is treated and get Living Donor Liver Transplant (LDLT) they will have developed TMA with an incidence of approximately 5% and at a median interval of 18 days following transplant. Drugs used for Graft Versus Host Disease (GVHD), mainly FK506 and cyclosporine or with other GVHD prophylaxis are another major factor in the development of TMA. High-dose chemotherapy for antilogous stem cell transplant (ASCT), conditioning regimen for allergenic stem cell transplant, total body irradiation, and use of immune suppressive therapy are the factors that can contribute to this condition[13]. Complication of bone marrow transplantation, both antilogous and allergenic with variable incidence rates ranging from 0 to 74% depending on the diagnostic criteria used to make the diagnosis can be described as Microangiopathic hemolytic anemia (MAHA), also called post-transplant thrombotic microangiopathy (TA-TMA)It is also a well-known complication following solid organ transplants, such as kidney transplants, with a variable time from transplant to diagnosis and could be due to viral infections, arise de novo, or be related to the use of calcineurin inhibitors, mainly the micro emulsion form of cyclosporine[14-15].

PREGNANCY-ASSOCIATED MAHA

Pregnancy-associated microangiopathy has been reported in the first trimester of pregnancy typically occur during late pregnancy, with continuous plasma therapy throughout the pregnancy in which case the patient was managed very intensely. Without any complications both mother and fetus survived. In many cases, we did not find any gender or race predilection that was associated with pregnancy-associated microangiopathy, as well as with hematopoietic stem cell tragus.Pregnancy-associated thrombotic microangiopathy a serious disorder cause due to the deposition of fibrin and platelet thrombi in the microcirculation of the placenta that is associated with significant maternal and perinatal morbidity and mortality,. It has been reported to occur in 1: 25,000–1: 100,000 pregnancies. Pregnancy can exacerbate the recurrence of an existent condition or can precipitate the disease for the first time[16].

PATHOGENESIS

Malignancy associated TMA may be triggered by chemotherapeutic agents

(mitomycin C and gemcitabine). However, the occurrence of HUS/TTP in the absence of these agents suggests that some cases result from a paraneoplastic phenomenon. Radiation exposure and opportunistic infections such as cytomegalovirus infection contribute to the difficulty of assigning a cause. The pathogenesis of malignancy associated TMA is multifactorial. ADAMTS13 levels in malignancy range from undetectable to normal[17]. Microvascular tumor emboli, monocyte procoagulants, tumor procoagulants and impaired fibrinolysis may also be implicated.

TREATMENT:

In this review the mortality rate of the subset of patients treated with plasmapheresis or plasma exchange was 31.9%, compared with 44.4% in a group not treated with plasmapheresis or plasma exchange. The most frequent choices of therapy are Plasma exchanges, prednisone, and cyclophosphamide[18-19]. There is no established guideline for the treatment of SLE-TMA.It is not as effective as in TTP, while plasmapheresis may reduce the mortality rate in SLE-TMA where the mortality rate in treated patients is <10%. There is no standard of care because of the limited number of reported cases of APLS-TMA[20].

CONCLUSION:

Several conditions that are associated with TMA are Hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP). Distinguishing HUS from TTP is not always possible unless there are specific causes, such as Shiga toxin, Streptococcus pneumoniae, or a specific molecular defect such as factor H or ADAMTS13 deficiency. The discovery of association of the ADAMTS13 enzyme's level, one of the newer advancements in the management of this disorder and activity with TTP that has led to earlier and improved detection rate which was translated to better survival. This review describes the forms of HUS/TTP that are not related to Shiga toxin, pneumococcal infection, genetic causes, or ADAMTS13 deficiency. Conditions include HUS/TTP associated with autoimmune disorders, human immunodeficiency virus (HIV) infection, transplantation, malignancy, and medications.

No specific therapy can be claimed to cure this group of disorders; however, few interventions have been proven to be helpful (and even lifesaving) in some disorders such as the use of plasma infusion and plasma exchange in the management of TTP.

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How to cite this article:
Bhawna Gondwal. ***Thrombotic Microangiopathic Haemolytic Anaemia: A Pathologic Abnormality Associated with Diverse Clinical Syndromes.*** **Br J Bio Med Res , Vol.01, Issue 04, Pg.217-222, September-October 2017.**
ISSN:2456-9739 Cross Ref DOI : https://doi.org/10.24942/bjbmr.2017.165

Source of Support: Nil **Conflict of Interest:** None declared.