Coma And Thrombocytopenia In Kenya: Case Report
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Citation

Abstract

ANSWERS TO THE QUESTIONS AND DISCUSSION

1. WHAT COULD BE THE FINAL DIAGNOSIS?
Thrombotic thrombocytopenic purpura (TTP) and immune thrombocytopenic purpura (ITP) are uncommon multisystem disorders with increased platelet destruction. In ITP, an autoantibody (usually IgG) arises and interacts with the patient's own platelets. TTP is sometimes associated with predisposing conditions such as pregnancy, cancer, exposure to certain drugs, bone marrow transplantation and HIV-1 infection (1). It is a life-threatening multisystem disease characterized by thrombocytopenia, microangiopathic hemolytic anemia, fluctuating neurological signs, progressive renal failure, and fever (2, 3). Depressed consciousness can rapidly progress to coma and generalized seizures. In both, TTP and ITP, a main symptom is bleeding, which can include bruising (“ecchymosis”) and tiny red dots on the skin or mucous membranes (“petechiae”). In some instances bleeding from the nose, gums, digestive or urinary tracts may also occur. Rarely, bleeding within the brain occurs.

2. WHAT IS THE CAUSE OF SUCH A DISEASE?
Although the cause of thrombotic thrombocytopenic purpura is unknown, many drugs, including penicillin, antineoplastic chemotherapy agents, and oral contraceptives, have been associated with the syndrome (4). Quinine and quinine-containing beverages such as tonic water are other classic examples of drug-induced purpura. An abnormal interaction between the vascular endothelium and platelets which occurs in certain organs leads to thrombosis, endothelial proliferation, minimal inflammation and micro-angiopathic haemolysis (5). Recent studies suggest that endothelial cell perturbation and apoptosis caused by an as yet unknown plasma factor(s) may lead to the release of abnormal von Willebrand factor which facilitates the deposition of platelet microthrombi. (1). Histologically, there are widespread micro-thrombi and reactive endothelial proliferation. Thrombi consist of masses of platelets and entrapping erythrocytes and fibrin.

Its frequency is estimated to be only 3.7 cases per year per 1 million persons, with mortality rates ranging from 10% to 20% (4). Thrombocytopenic purpura is considered chronic when it has lasted more than 6 months. The onset of illness may be at any age. Adults more often have the chronic disorder and females are affected two to three times more than males. The onset of illness may be at any age. In most cases remissions can be attained, and cures are now common—although approximately one-half of the patients will relapse. While relapses are usually milder, they still carry a significant mortality and preventive therapies are not always effective (6). Idiopathic autoimmune thrombocytopenic purpura during childhood is usually self-limited.

3. WHAT ARE THE TREATMENT OPTIONS FOR THIS DISEASE?
Exchange transfusions of plasma or plasma-cryosupernatant remain the cornerstone of the treatment of TTP/ITP along with corticosteroids, platelet inhibitor drugs, vincristine and splenectomy.

If the doctor thinks a drug is the cause of the thrombocytopenia, standard treatment involves discontinuing the drug’s use. Infection, if present, is treated vigorously since control of the infection may result in a return of the platelet count to normal. The treatment of thrombocytopenic purpura is determined by the severity of the symptoms (6). In some cases, no therapy is needed. In most cases, drugs that alter the immune system’s attack on the platelet are prescribed. These include corticosteroids (i.e., prednisone) and/or intravenous infusions of immune...
globulin. Another treatment that usually results in an increased number of platelet is removal of the spleen, the organ that destroys antibody-coated platelet. Other drugs such as vincristine, azathioprine (Imuran), Danazol, cyclophosphamide, and cyclosporine are prescribed for patients only in the severe case where other treatments have not shown benefit since these drugs have potentially harmful side effects (6). The role of steroids, splenectomy, vincristine, and anti-platelet agents in the treatment of this disorder is controversial. Most studies using these agents also used many other different treatments and it is not clear what part of the clinical response could be attributed to these agents (6).

Plasmapheresis was developed as a therapeutic modality after it was observed that individuals with TTP receiving repeated whole blood transfusion underwent a remission. Subsequently, marked improvement was noted in some patients within hours following plasma exchange. Alternatively, some investigators have noted a response to plasma exchange in patients who have previously failed to respond to fresh frozen plasma. This has fueled the debate about whether the clinical manifestations of TTP result from a missing plasma factor that inhibits aggregation (which is replaced during plasma infusion) or a platelet aggregatory factor that is not normally present in plasma (which is removed during plasmapheresis) (7). A recent controlled trial of plasma exchange versus plasma infusion in patient with TTP of all origins, except HIV infection, demonstrated the superiority of plasma exchange, although proponents of plasma infusion argue that plasma exchange merely allows a greater volume of plasma to be infused.

Except in certain situations, (e.g., internal bleeding and preparation for surgery), platelet transfusions usually are not beneficial and, therefore, are seldom performed. Because all therapies can have risks, it is important that overtreatment (treatment based solely on platelet counts and not on symptoms) be avoided. In some instances lifestyle adjustments may be helpful for prevention of bleeding due to injury. These would include use of protective gear such as helmets and avoidance of contact sports in symptomatic patients or when platelet counts are less than 50,000 (6).

4. WHAT IS THE DIFFERENTIAL DIAGNOSIS?
A complete blood count should be done for diagnosis. A low platelet count will establish thrombocytopenia as the cause of purpura. The presence of schistocytes or fragmentocytes may confirm the diagnosis of thrombocytopenic purpura. Often the next procedure is a bone marrow examination to verify that there are adequate platelet-forming cells (megakaryocyte) in the marrow and to rule out other diseases such as metastatic cancer (cancer that has spread to the bone marrow) and leukemia cancer of the blood cells themselves). Another blood sample may be drawn to check for other conditions sometimes associated with thrombocytopenia such as lupus and infection (6).

Thrombocytopenic purpura may be confused with a variety of diseases including collagen vascular disease (such as systemic lupus erythematosus), lymphoproliferative disorders (such as chronic lymphocytic leukemia or non-Hodgkin’s lymphoma), and infections (particularly viral infections such as HIV, cytomegalovirus and mononucleosis) (6). These disorders can be ruled out by careful examination and the appropriate laboratory studies. A variety of diseases such as aplastic anemia, acute leukemia, etc. can cause thrombocytopenia. These can be easily ruled out by evaluation of the blood count and bone marrow (8). Certain drugs cause low platelet counts. The most common are quinine, quinidine, sulfia and sulfia-like drugs and heparin.

References
5. Charles L. Bennett, MD, PhD; Peter D. Weinberg, BS; Karine Rozenberg-Ben-Dror, PharmD; Paul R. Yarnold, PhD; Hau C. Kwaan, MD, PhD; and David Green, MD, PhD: Thrombotic Thrombocytopenic Purpura Associated with Ticlopidine; A Review of 60 Cases. Annals of Internal Medicine, 1 April 1998. 128:541-544. Available online at: http://www.acponline.org/journals/annals/01apr98/ticlopid.htm
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