Refractory Anaemia Due to Cytomegalovirus (CMV) Infection in an Immunocompetent Adult.

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INTRODUCTION

The morbidity and mortality associated with cytomegalovirus (CMV) infection in immunocompromised patients (especially in HIV-infected patients and transplant recipients), as well as congenital CMV infection in babies acquired during passage through the birth canal of infected mothers are well known. While manifestations of CMV infection in immunocompromised hosts have been extensively reported in biomedical literature, those observed in immunocompetent patients have received comparatively little attention. We report a case of unusual presentation of persistent anemia and immunosuppression like features due to cytomegalovirus infection in an otherwise immunocompetent Nigerian adult.

CASE PRESENTATION

We reviewed a forty eight year old male civil servant with a one year history of progressive generalized body weakness with reduced exercise tolerance and pains and discomfort in the legs. The body weakness became worse in the last 2 months prior to presentation with an episode of a fainting on walking up a stairs, following which he was seen at a peripheral hospital. There had been episodes of fever, and body pains for which he was treated with antimalarials and antibiotics for a presumed diagnosis of typhoid fever. The patient admitted to some degree of weight loss in recent past which he attributed to pressure of work even though his appetite had been normal. He also developed mouth sores and odynophagia with whitish patches on the palate for which he was treated with antibiotics and antifungal. There was a history of epistaxis about two months prior to presentation which has since subsided. No history of cough, no history of jaundice, no episodes of haematuria or haemoglobinuria. There is no history of blood transfusion in the past, and patient is neither a known hypertensive nor diabetic. On exaimination, the patient was a middle aged man, mildly pale, anicteric with fair hydration status. There was no peripheral lymphadenopthy. Chest and CVS examination findings were unremarkable and there were no palpably enlarged organs in the abdomen. Following his first review at a private clinic in July 2008, he was commenced on double dose haematinics as a result of anaemia (Hb 8.4g/dl), repeat Hb check however remained low at about 9g/dl after two months on haematinics. He was subsequently requested to see a Haematologist. The preliminary investigations done was as follows; full blood count report: PCV -27% (Hb 9g/dl), WBC - Total: 6.8x 10^9/L; (differentials: N-62%, L-32%, E-6%), Platelet count: 110 x10^9/L; blood film report: significant rouleaux formation in the red cells with atypycal plasmacytoid lymphocytes cells and binucleated erythroid cells; erythrocyte sedimentation rate (ESR): 138mm in the first hour; reticulocyte count: <1 % ; direct Coombs test was negative; total and conjugated bilirubin levels were within normal range. Stool microscopy screen for ova of parasites was reported negative. The blood screen for HIV types 1 & 2 and Hepatitis B surface antigen was negative. A preliminary working diagnosis of refractory anaemia ?cause was made and he was scheduled to have a bone marrow investigation done, which he refused for personal reasons. He was thereafter continued on haematinics and symptomatic pain relief therapy. The anaemia persisted, fluctuating between 7g/dl and 9g/dl. He was however never transfusion dependent. He subsequently had a screening for CMV and was positive for CMV-IgM antibodies (ELISA) with raised anti-CMV IgG specific antibodies. He was then commenced on ganciclovir 5mg/kg bid for three weeks. His haemoglobin gradually increased and six weeks after therapy was 15g/dl which has been sustained. All clinical symptoms and signs have completely resolved. He has remained stable with normalization of the reticulocyte count, blood film appearance and the ESR. His clinical status has remained stable six months after therapy.

DISCUSSION

Cytomegalovirus is a herpesvirus which belongs to the same class of viruses as the Ebstein Barr virus (EBV), the viral agent of infectious mononucleosis. Cytomegalovirus (CMV) can cause severe disease in immunocompromised patients, either via reactivation of latent CMV infection or via acquisition of primary CMV infection. Clinical syndromes that may be observed in this setting include encephalitis, pneumonitis, hepatitis, uveitis, retinitis, colitis, and graft rejection. Furthermore, CMV infection affecting the human embryo, a host with immature immunologic responses, is often associated with serious complications, such as microcephaly, mental retardation, spastic paralysis, hepatosplenomegaly, anaemia, thrombocytopenia,

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deafness, and optic nerve atrophy leading to blindness. In immunocompetent patients, primary CMV infection typically runs an undifferentiated viral syndrome, or is manifested by a mononucleosis-like syndrome. Infections in the immunocompetent and immunosupressed are not rare; the seroprevalence for CMV worldwide ranges from -60%-100%.[1] In Nigeria a study at the Jos University Teaching Hospital reported the seroprevalence of prospective blood donors for CMV as 92%[2]. Symptomatic CMV infection in immunocompetent hosts has traditionally been considered to have a benign, self-limited course. However, in the medical literature there is considerable number of reports of severe clinical manifestations of CMV infection in immunocompetent patients, and in recent years, the severity of CMV infection in immunocompetent hosts leading to multi-organ infection with severe life threatening courses is gaining significant attention. [3] The primary infection is usually subclinical in nearly 90% of immunocompetent adults, although it is severe with a mortality rate of 10% in immunocompromised patients. [4] The commonest modes of transmission are through blood transfusion and sexual contact. Documented systemic involvement in CMV infection of immunocompetent hosts include the central nervous system (CNS) in which it can cause encephalitis and Guillan-Barre like syndrome, gastrointestinal tract (GIT), ocular, respiratory (pulmonary) and haematological disorders. Haematological disorders resulting from CMV infection in immunocompetent individual include: symptomatic thrombocytopenia, haemolytic anaemia, disseminated intravascular coagulation, myelodysplastic changes, pancytopenia, and splenic rupture.[3] There is a diversity of symptoms, including fatigue, fever, abdominal or chest pain, headache, pain in the extremities, numbness of the hands, darkening of urine due to the presence of haemoglobin, epistaxis, easy bruising, purpura, increased incidence of infections, jaundice, and systolic ejection murmur due to anaemia.[3] The suppression of haematopoiesis that is associated with CMV infection may be due to direct inhibition by the virus of progenitor haematopoietic cell growth, as well as to stromal cell dysfunction, or to effects of inhibitory cytokines produced by CMV infected leukocytes. [3,5] Furthermore, the detection of specific antibodies, [5] and of other immunological abnormalities in CMV - infected patients with haemolysis or myelodysplasia indicates a probable immune-mediated mechanism responsible for these manifestations. [5,6]

Our patient, an otherwise immunocompetent healthy adult developed progressive worsening anaemia which became symptomatic. Significantly he with fatigue, non specific body weakness, anaemia, epistaxis and myelodysplastic changes in the blood film. Severe haemolysis is a rare, but potentially life-threatening, complication of cytomegalovirus (CMV) infection which may occur in immunocompetent adults. [7] Treatment with steroids or immunoglobulins, or even splenectomy, may be justified when an autoimmune mechanism can be identified as the cause of the anaemia. The direct Coombs test was negative in this patient. Even though Coombs negative haemolytic anaemia has been reported in literature in association with anaemia of CMV, [7] the presence of binucleated erythroid cells in the peripheral blood film however suggests some degree of myelodysplasia as a possible cause of the refractory anaemia. Although bone marrow aspiration cytology was most desirable in this patient, it was not done due to the patient's refusal of the investigation. The presence of IgM and IgG anti CMV antibodies in the patient gave an index of suspicion that CMV could be responsible for the plethora of signs and symptoms that the patient presented with. The patient responded well to the antiviral (ganciclovir), and has since remained clinically stable. While CMV diagnostic kits are not generally available in many hospitals in the country, this case may be an indication that its availability may improve the diagnostic capabilities of our hospitals in unraveling some unusual cases. In addition, a high index of suspicion is required to make the diagnosis in such instances.

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