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Drug-related hypersensitivity in a Nigerian woman on Antiretroviral Therapy: A Case Report

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Definition: Hypersensitivity to medication is a life-threatening reaction that results in a systemic illness that usually includes fever and maculopapular rash accompanied by constitutional symptoms (fatigue, malaise, myalgias and arthralgias), multivisceral involvement (lymphadenopathy, mucositis, pneumonitis, myocarditis, hepatitis, and nephritis), and haematologic abnormalities (atypical lymphocytosis and eosinophilia)[1]. Hypersensitivity is also known as *DRESS* (drug rash with eosinophilia and systemic symptoms) syndrome and *STEVEN JOHNSONS* syndrome.

Aetiologies: The aetiologies are multiple, diverse and include: aromatic anticonvalsivants (phenytoin, carbamazepine, and lamotrigine)[2], sulphonamides (sulphamethoxazole and dapsone)[3], Betalactam antibiotics (penicillins and cephalosporins)[4], antineoplastic agents (1-asparaginase and paclitaxel)[5], antipyretics (paracetamol)[6] and antirheumatic drugs (allopurinol, diclofenac, and fenoprofen)[7]. Antiretroviral agents reported to induce hypersensitivity reactions, include: Zidovudine[8], didanosine[9], Zakitabine[10], delavirdine[11], nevirapine[12], efavirenz[13], amprenavir[14] and abacavir[15]. Also some infectious agents have been reported to cause Stevens Johnson syndrome and they include herpes virus hominis and mycoplasma pneumoniae[16]. In 50% of the cases, no aetiologic agent is usually ascertained.

Pathology: The major pathologic change is an acute lymphohistiocytic inflammatory infiltrate around blood vessels and may include degenerative changes in the endothelial cells of the capillaries and marked papillary oedema. There is some evidence of an immune-complex aetiology with hypocomplementemic Vasculitis.

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Clinical Features:- Trimethoprim-Sulphamethoxazole causes rash and fever in up to 50% of HIV positive patients. The rash can be treated – limiting its severe form in up to 20% of HIV positive patients who receive it. Adverse reactions such as nausea may also occur. However, severe hypersensitivity with systemic manifestations have been noted in 8 case reports of HIV – positive patients who had a previous adverse reactions and who were rechallenged with trimethoprim-Sulphamethoxazole according to a review of the literature from 1994-1999[16]. Generally, the lesions occur in a characteristic symmetrical distribution all over the skin and mucous membranes. Oral lesions appear as blisters at first, then erosions of the buccal cavity, gums, and tongue. Often swelling and crusting of the lips are associated. The syndrome may also include severe toxaemia and prostration, high fever, cough and patchy inflammation of the lungs.

The skin lesions are often characterized by a vivid redness that gradually becomes duller, more indurated with development of centres that are pale or may have bullae. The efficacy of systemic corticosteroids has not been proved although this therapy is commonly used. The case of penicillins (ampiclox) hypersensitivity reactions among HIV-positive patients on antiretroviral therapy of Nevirapine, lamivudine and stavudine has not been reported in literature as far as we know. This first case among 550 patients taking antiretroviral therapy in Kano teaching hospital is therefore presented to you.

Case History

A case of a 26 year old Nigerian woman who had been in her usual state of good health until approximately 3 months earlier, when she developed sudden weight loss, malaise, anorexia, diarrhoea and fever lasting for 2 weeks. She admitted to have had repeated treatment for malaria and typhoid at a private hospital and was also screened and found positive for HIV antibodies for which she was referred to the STD/RetroViral Diseases clinic of this hospital. She had no cough or urinary symptoms. Her husband was a long distant driver and had died of AIDS about a year ago. She neither smokes nor drinks alcohol. She had no history of blood transfusion, traditional scarification nor surgery or any identifiable high risk behavior.
On examination, she was found to be emaciated (weight=48kg) and mildly dehydrated, febrile (T=38 degrees centrigrade), moderately pale with no jaundice. There were no palpable peripheral lymph nodes. There were no skin lesions and no oedema.

Her pulse rate was 90 beats per minute, regular and full volume; she had normal heart sounds and blood pressure. There were harsh breath sounds in the chest with no added sound. The abdomen was scaphoid, soft and non tender. No organ was palpable. Musculoskeletal system showed generalized wasting, with grade 4 power in both upper and lower limbs. She was well oriented in time, place and person.
Repeat HIV antibody test was done following counseling and consent of the patient. Full blood count showed a PCV of 26% and CD4 cell count was 190 cells/ml. Liver and renal function tests were within acceptable lower normal limits. Other tests are urinalysis, normal; stool microscopy, normal; pregnancy test, negative. A diagnosis of WHO stage 4 AIDS was made.

She was placed on 12 hourly Stavudine 30mg and Lamivudine 150 mg and a daily dose of Nervirapine 200mg (HAART) for 2 weeks. She was also asked to take oral rehydration therapy and lots of oral fluids as she could not afford admission. She reported 2 weeks later and had no complaints but for some weakness. Her HAART was continued with nervirapine changed to 12 hourly dosing. During the next few months she gained 7kg of weight and her PCV had appreciated to 32%. Several days later, she reported to the clinic with generalized itching following an injection of Ampiclox for her sore throat from a local chemist. Drug reaction was entertained and she was given antihistamine injection to continue with the tablets at home and was counseled to stop self medication. Two days later, she was admitted in the emergency room with exacerbated drug reaction. There was generalized macular rash, severe itching and peeling of skin and mucous membranes, she had associated fever, malaise and insomnia. A diagnosis of Steven Johnson's syndrome was made.

All medications were stopped. IV line was established and she was started on 50% Dextrose water 1 Liter to run 8 hourly and to alternate with Normal saline, a stat dose of 200mg IV hydrocortisone was given to be repeated whenever necessary. She did well over the next few days and was discharged home to be followed up in the clinic. She is currently doing well on her antiretroviral drugs with no further reaction.

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