Acute Dysautonomia: A Rare Cause of Mortality in AIDS Encephalopathy -A Case Report and Review of Literature

OR Obiako[1], SA Abubakar[2], JA Kehinde[3], E U Iwuozo[4], P Chukwuma[5], Ephraim Akase[6]

ABSTRACT

Introduction: Acute dysautonomia is a dysfunction of the autonomic system which can be caused by any diffuse systemic illness or a structural pathologic process of the brain

Aims and objectives: To describe the clinical presentation and outcome of acute dysautonomia on the background of AIDS encephalopathy. **Methods and material:** This is a hospital-based case report of acute dysautonomia in a 60 year old man who was diagnosed HIV-1 positive in 2001, but stopped his antiretroviral drugs in 2009 after 6 years of therapy. The patient presented with irrational behaviour and confusion of one year duration, generalised abdominal pains and constipation of 6 weeks duration, and labile blood pressures, pulses and temperatures few days prior to his demise. . He had no pre-morbid medical or psychiatric illness and neither smoked cigarette nor ingested alcohol. **Results:** At presentation, systemic examination was normal, except the central nervous system which revealed mini-mental score of 6/30 points and modified HIV dementia score of 5/12 points, necessitating a diagnosis of AIDS dementia complex. On the 14th day of admission, he developed acute autonomic syndrome and despite resuscitative measures, died of cardiac arrest within 48 hours. **Conclusion:** Acute dysautonomia is a rare complication of AIDS encephalopathy which has a fatal outcome.

Key-words: acute dysautonomia, AIDS dementia complex, HIV encephalopathy, hypothalamic atrophy

Neurology Unit, Department of Medicine, Ahmadu Bello University Teaching Hospital Shika Zaria.

Corresponding author mail: orobiako87@gmail.com

Conflict of interest: None declared

INTRODUCTION

Dysautonomia, also called autonomic syndrome, is the dysfunction of the autonomic system (ANS), which is composed of the enteric, parasympathetic and sympathetic systems [1]. Although rare, acute dysautonomia can be caused by any diffuse systemic illness affecting the nervous system or structural pathologic process of the brain [2.] Its presentation is usually complex and dramatic because of the arrays of symptoms and signs which

can result from damage to any or all of the components of the ANS. These features may include: total inability to sweat, dysrrhythmias, hypertensive or hypotensive emergencies, bladder atony, bloated painful abdomen, constipation or diarrhea, syncopal episodes and seizures. Acute renal failure may result from severe hypovolemic or hypotensive shock and, orthostatic hypotension may be of such a degree that the patient cannot sit upright without fainting [1].

This rare condition has been reported in patients with sepsis syndrome, diabetes mellitus, Guillain-Barré syndrome, Alzheimer's disease, Parkinson's disease, HIV/AIDS and other degenerative nervous diseases [3].

HIV encephalopathy (HE) is a recurrent brain disease resulting from damage to the brain by longstanding HIV infection. It is a spectrum of the infection manifesting in phases, the first being a self-limiting HIV meningoencephalitis which occurs during the acute HIV syndrome of sero-conversion phase. The second phase may present as subtle neurocognitive impairment with little or no functional impairment in activities of daily living (ADL) during the early to middle stages of the disease; while the final phase is known as the AIDS encephalopathy or AIDS-dementia complex (ADC) seen at the advanced stage of HIV [4].

The terminal features of ADC include severe psychomotor retardation, apraxia, paraparesis and akinetic mutism; and death may result from complications of autonomic dysfunction [5, 6]. Since the complex nature of both conditions (dysautonomia and HE) may pose tremendous diagnostic challenges to many health care professionals in resource-limited countries, we decided to report this case as our contribution to the body of knowledge of this clinical entity.

METHODS AND MATERIAL

Pino Oguche, 60 year old man presented to our hospital in June 2011 with 6 weeks history of generalised abdominal pain, constipation and confused behaviour. The abdominal pain was severe, non-colicky, and radiated to the back. There was associated constipation as he was passing pellets-like faeces once in 5-7 days. He was said be irritable, aggressive and behaving irrationally. He was withdrawn and kept to himself, having lost interest in personal hygiene, hobbies, family members, friends and meals. He was forgetful, misplacing objects and personal belongings, and was unable to recognise family members, friends and familiar surroundings. He had no history of

headache, convulsion, nausea, vomiting, jaundice, urinary or stool incontinence, and was not hypertensive or diabetic. He neither smoked cigarette nor ingested alcohol.

He was diagnosed HIV-1 positive in 2001 and took antiretrovirals (zidovudine 300 mg + lamivudine 150 mg + nevirapine 200 mg BD) from 2004 to 2009. He decided to stop antiretroviral therapy in 2009 because he believed he had been cured of the HIV infection. In 2010, family members and his friends noticed progressive and gradual changes in his personality which they described as a change from previous 'normal' (sic) to 'antisocial', 'passive- aggressive', 'schizoid' and 'paranoid' personality (sic), although he had no pre-morbid or family history of psychiatric illness.

OBSERVATIONS AND RESULTS

On examination, he was afebrile (temperature of 36.9^0 C), anicteric, mildly dehydrated and pale. His chest was clear, and abdomen was scaphoid with normal liver size, impalpable spleen and kidneys. There was no ascites and abdominal sound was normal. Pulse rate (PR) and blood pressure (BP) were 78 beats per minute and 120/80 mmHg respectively and heart sounds were normal. He was conscious but confused with a Glasgow Coma Score of 14/15. There was no meningeal sign or cranial nerve palsy. He was incontinent of urine, in addition to contact allodynia, visual hallucinations, emotional lability and truncal ataxia. Digital rectal examination yielded hard pellets of faeces.

Mini-mental examination yielded a score of 6 out of a maximum of 30 points as follows: orientation=1/10, registration of names of 3 objects within 5 minutes = 3/3, recall of names of 3 objects after 5 minutes= 0/3, language=2/4, attention=0/4, calculation=0/6. Neuropsychiatric screening with the modified HIV dementia scale yielded a score of 5 out of a maximum of 12 points thus: registration/ recall=3/6, psychomotor speed (finger tapping test)= 1/2 (he had bradykinesia), construction ability= 0/2 (apraxia), concentration= 1/2.Sensory perceptions could not be tested because of cognitive deficits. Results of relevant laboratory investigations were as follows: cerebrospinal fluid (CSF) = unremarkable; hemoglobin= 12g/dl; platelet counts= 250 x 10^9/l; toxic neutrophilia and relative lymphopenia; CD4+ = 106 cell count/ µl; plasma HIV load = 1.6 x 10^6 copies/ml; brain MRI = generalized cerebral atrophy, hypothalamic atrophy and ventriculomegaly, no evidence of cerebral oedema / space occupying lesion/

hematoma or infarct (figures 1 and 2 below); random blood sugar = 5.4 mmol/l; electrolytes and urea= normal; fluid cultures were negative. Serology was negative for syphilis and toxoplasma antibodies respectively.

Based on above clinical features and laboratory results, a diagnosis of AIDS encephalopathy was made and patient was admitted for rehydration and rehabilitation. He was given normal saline and his rectum was evacuated both manually and with soap enema. Within 48 hours the abdominal symptoms resolved. A week later he developed paraparesis (lower limbs muscle power of 3/5), but remained conscious and confused. Two weeks later (i.e. 8th week of current illness), he developed sudden, unpredictable and irregular extremes of temperatures (as low as 34.2 ^{0} C, and as high as 42.8 ^{0} C); extremes of pulse rates (as low as 40/min, and as high as 160/min); extreme of blood pressure (as low as 40/0 mmHg, and as high as 250/ 140 mmHg); extremes of random plasma glucose (as low as 1.6 mmol/l and as high as 24.8 mmol/l). His conscious level also fell rapidly from the previous GCS of 14/15 to 3/5.

At this point, we made a diagnosis of acute dysautonomia complicating ADC and he was managed symptomatically and conservatively as outlined below:

a. Nasogastric tube was inserted for feeding and oral drug administration.
b. Hypotensive shock was managed with intravenous infusion of 250 g dextran 40 in normal saline alternated with 1000 milliliters (mls) of normal saline 8 hourly; intravenous hydrocortisone 100 mg given 8 hourly for 24 hours, and then replaced with dexamethasone 16 mg 8 hourly.
c. Severe hypertension was managed with slow infusion of hydralazine 20 -50 mg diluted in 500 mls of normal saline 12 hourly.
d. Blood glucose dysregulations was managed with 20 I.U soluble insulin in 1000 mls of 5% glucose infusions 8 hourly.
e. Hypothermia was managed with warm water bath and thick blanket clothing.
f. Hyperthermia was controlled with tepid sponging and exposure to air-conditioner and/or electric fan.
g. Continuous cardio-respiratory system monitoring in the intensive care unit was done.

h. Continuous nursing care was ensured.

In spite of above resuscitative measures, patient's condition continued to deteriorate and he died of sudden cardiac arrest within 48 hours of coma.

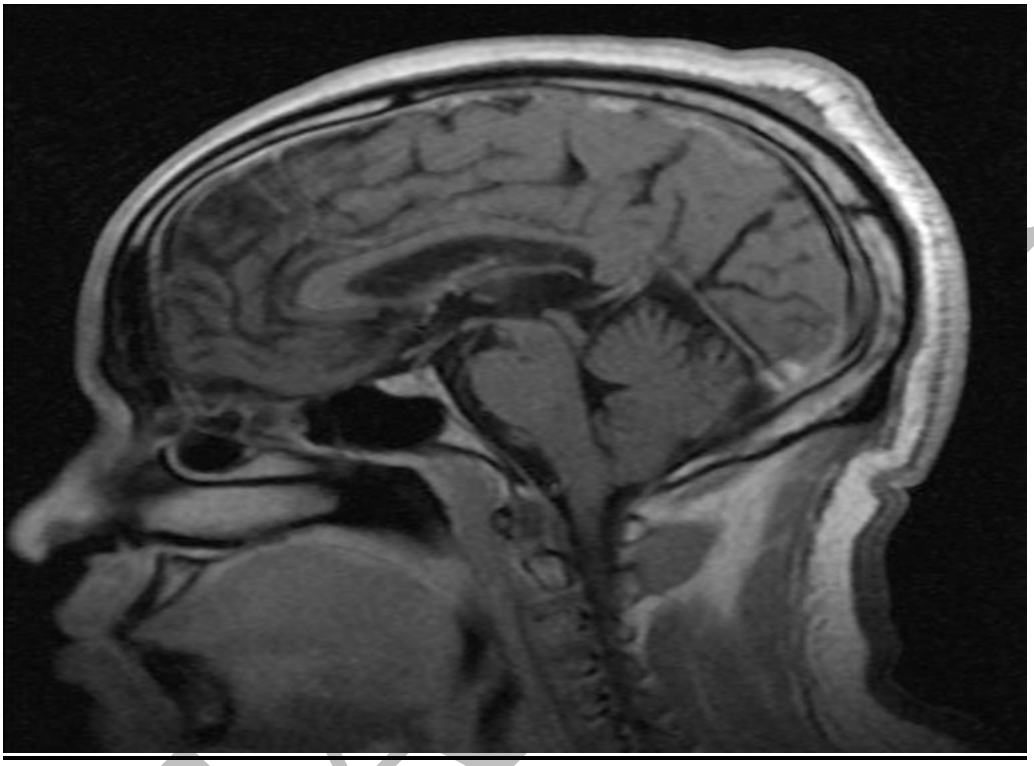

Figure 1: Sagittal view of brain MRI showing generalised cerebral and hypothalamic atrophy

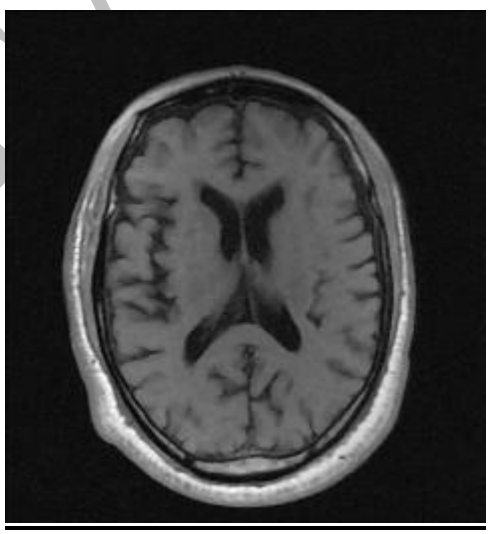

Figure 2: Transverse view of brain MRI showing generalised cerebral and ventriculomegaly

DISCUSSION

The ANS is involved in the function of virtually every organ system in the body, being composed of the sympathetic, parasympathetic, and enteric nervous systems, which together maintained internal homeostasis by modulating the involuntary motor activities of the viscera (cardio-respiratory organs, gastrointestinal and genitourinary tracts), the smooth muscles of the vasculature, and the exocrine glands [7]. The sympathetic nervous system helps control the reaction of the body to stress. It is a freeze, fright and flight system. The parasympathetic system works to conserve the body's resources and to restore equilibrium to the resting state, while the enteric system controls the function of the gut. In this way the ANS regulates heart rate, blood pressure, fluid and electrolyte balance, body temperature, sweating, digestive tract peristalsis, penile erection and ejaculation; through tonic, reflex, and adaptive integration of hormonal, immune-modulatory, and pain controlling responses to internal and external environmental challenges [8].

The clinical manifestations of autonomic dysfunction can thus be quite diverse and complex in nature, and the syndromes are so sudden in onset that patients and relations can usually relate the exact day symptoms first began. They can also be rapid in progression because of severe and widespread failure of both the sympathetic and parasympathetic systems, and mild to moderate alteration of enteric functions. Patients may suddenly lose the ability to sweat, complain of nausea, vomiting, abdominal bloating and pain. Constipation may alternate with diarrhea and the heart rate may become irregular or remain fixed at a particular rate, with associated chronotropic incompetence. The pupils are often dilated and poorly reactive to light, and some patient may suffer from a combination of supine hypertension and upright hypotension [9].

Dysautonomia can be quite difficult to treat and prognosis depends on the underlying disease. In ADC it runs a rapid course with a mean of 3-6 weeks, particularly in the absence of antiretroviral therapy (ART). In a study of 329 HIV+ patients who had CD4+ cell count of less than 200 /µl, ADC was an independent predictor of time to death, particularly in patients with poor medication adherence. Rapid loss of consciousness may result from cerebral hypoxia and death can occur from pneumonia, acute respiratory failure, or sudden cardiopulmonary arrest [10].

ADC encompasses 3 entities (cognitive deficits, behavioral changes, and motor abnormalities), and affected patients may manifest all or some of the abnormalities. Cognitive deficits are exhibited as inattention, impaired concentration, forgetfulness, slowed verbal response and blunted affect mimicking depression. Motor abnormalities occur in the form of difficulty with fine movements such as doing up buttons, putting on shoes or brushing teeth and difficulty walking. Behavioural abnormalities include decreased libido, sleep disturbances, psychosis with mania and depression [11].

To confirm the clinical impression of both dysautonomia and ADC, a detailed history and physical examination (including a concise neurologic examination) has greater diagnostic yield than multiple tests. Laboratory examinations should be obtained in a careful and directed manner, based upon history and physical findings. The hypothalamus which is the centre for ANS control may be affected in ADC, but it is usually not accessible to direct measurement. Thus one must rely on the responses of various organ systems to physiologic or pharmacologic challenges to the hypothalamic-pituitary-adrenal axis. A number of other autonomic tests are also available [12].

Pharmacotherapy should be used cautiously and should be tailored to fit the needs of the patient based on the type of autonomic disorder being treated, as well as coexisting symptoms and conditions. Unfortunately, virtually any drug used in treatment can worsen symptoms [13]. In order to ameliorate this management dilemma, the physician should discuss the prognosis with patient and/or relatives and desist from giving them unrealistic expectations.

REFERENCES

1. Low P, McLeod J. Autonomic neuropathies. In: Low P. Clinical Autonomic Disorders. Lippincott-Raven Publishers. Philadelphia 1997, pp. 463-486.
2. Low PA, Suarez GA, Benarroch EE. Clinical autonomic disorders: Classification and clinical evaluation in Clinical Autonomic Disorders 2nd ed. Low P (ed) Lippincott-Raven Publishers, Philadelphia. 1997, pp.3-12.
3. Passant V, Warkentin S, Karlson et al. Orthostatic hypotension in organic dementia: Relationship between blood pressure, cortical blood flow, and symptoms.*ClinAuton Res*

1996; 6:29-36.

4. Bouwman FH, Skolasky RL, Hes D, Selnes OA, Glass JD, Nance-Sproson TE, et al. Variable progression of HIV-associated dementia. Neurology 1998; 50: 1814-20.
5. Navia BA. Clinical and biological features of the AIDS dementia complex. Neuroimaging Clin N Am. Aug 1997; 7 (3): 581-92
6. Ances BM, Ellis RJ. Dementia and neurocognitive disorders due to HIV-1 infection. Semin Neurol. Feb 2007; 27 (1): 86-92.
7. Robertson D, Polinsky R (eds). A Primer on the Autonomic Nervous System. Academic Press, San Diego CA 1996.
8. Benarroch E. The central autonomic network: Functional organization, dysfunction and perspective. *Mayo Clinic Proc*1993; 68:988-1001.
9. Benarroch EE. The Central autonomic network in Clinical Autonomic Disorders 2nd ed. Low P (ed) Lippincott-Raven Publishers, Philadelphia 1997; pp.17-22.
10. Sevigny JJ, Albert SM, McDermott MP. An evaluation of neurocognitive status and markers of immune activation as predictors of time to death in advanced HIV infection. Arch Neurol. 2007; 64 (1): 97-102.
11. Price RW, Brew BJ. The AIDS dementia complex. J Infect Dis. Nov 1998; 158 (5): 1078-83.
12. Mathias CJ. The classification and nomenclature of autonomic disorders: Ending chaos, restoring conflict, and hopefully achieving clarity. ClinAuton Res 1995; 5:307-310.
13. Tierney LM, McPhee SJ, Papadakis MA. In: Current Medical Diagnosis and Treatment 2007 (Current Medical Diagnosis and Treatment). McGraw-Hill Professional. p. 1010. ISBN 0-07-147247-9.