HYPEREOSINOPHILIC SYNDROME WITH SEVERE HYPOKALAEMIA IN A NIGERIAN WOMAN: a case report

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ABSTRACT

INTRODUCTION: Hypereosinophilic syndrome (HES) is a rare disorder. It is defined as eosinophilia of greater than1.5x10^9/L persisting for at least 6 months or death before 6 months without an identifiable cause and with eosinophil-mediated organ dysfunction. We present a rare case of hypereosinophilic syndrome with severe hypokalaemia in a Nigerian female patient.

CASE PRESENTATION: A 43year old food vendor referred to the Haematology Department, University College Hospital, Ibadan on account of a 6-week history of cough productive of mucoid, brownish, foul smelling sputum with associated breathlessness, high grade intermittent fever, and intense pruritus. She had accompanying non-projectile, non-bloody vomiting of recently ingested meals.

There was absolute eosinophilia of 83x10^9/L and bone marrow cytology revealed marked eosinophilia with blasts of less than 5%. She also had asymptomatic severe hypokalaemia (1.9mmol/l) likely due to vomiting and reduced dietary intake. The aetiology of the hypereosinophilia could not be ascertained. She was admitted and commenced on intranasal oxygen, Tabs Loratidine, intravenous hydration. The severe hypokalaemia was corrected with IV KCL over 48hours followed with the administration of slow K tablets 600mg tds. She also had tabs Hydroxyurea for cytoreduction and Allopurinol to prevent hyperuricaemia. She improved with the above line of management.

CONCLUSION: This appears to be the first reported case of HES with asymptomatic severe hypokalaemia in the literature. Being a rare disorder it could easily have been missed without a review of the peripheral blood film and marrow aspirate. This finding suggests a possible relationship between hypereosinophilia and hypokalemia which needs to be explored.

KEY WORDS: Hypereosinophilic syndrome, Eosinophilia, Bone marrow cytology, Hypokalemia, Hydroxyurea, Loratidine

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INTRODUCTION

Hypereosinophilic syndrome (HES) is a rare disorder. It is defined as eosinophil count of greater than 1.5x10^9/L persisting for at least 6 months, (or death before 6 months) without identifiable cause in the presence of eosinophil-mediated organ dysfunction.[1] Currently, HES is classified based on the aetiology, with the lymphocytic variant (L-HES) derived from monoclonal proliferation of T-lymphocytes and the myeloproliferative variant (M-HES) characterized by fusion genes arising from chromosomal aberrations.[2,3]

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Case presentation:
The patient is a 43-year-old food vendor referred to the Haematology Department of the University College Hospital, Ibadan on account of a 6-weeks history of cough that was productive of brownish, mucoid, foul smelling sputum and a week history of painful upper abdominal swelling. This was associated with breathlessness and high grade intermittent fever, significant weight loss, drenching night sweats and intense pruritus. She also had non-projectile, non-bloody vomiting of recently ingested meals.

The significant physical findings include widespread scratch marks/scars, generalized peripheral lymphadenopathy involving the left submandibular, left axillary and posterior cervical regions. The lymph nodes were firm and mobile. Abdomen was distended with right hypochondrial tenderness. There was hepatomegaly with a liver span of 19cm and a spleen of 12cm below the left costal margin with ascites demonstrable by shifting dullness. She was tachypnoeic with a respiratory rate of 30 cycles per minutes. There was equal chest expansion, percussion

was resonant and breath sounds were vesicular with few crepitations in the right lower zone. The cardiovascular system revealed a regular pulse of 120 beats per minute, and a normal blood pressure. Apex beat was at the 5th left intercostals space and mid-clavicular line. Normal heart sounds were heard. No abnormality was detected in the central nervous system.

The initial impression was a lymphopoliferative disorder and a superimposed bacterial pneumonia with differential diagnosis of disseminated Tuberculosis..

Full blood count done at presentation showed PCV 33%, WBC 97.6 x 10^9/L, Platelets 322 x 10^9/L. Peripheral blood film showed microcytes and mild hypochromia marked leucocytosis, predominance of matured eosinophils accounting for about 85% of the white cells. A left shift of neutrophils up to meta-myelocyte stage was noted and platelets were adequate. Bone marrow aspirate showed a hyercellular marrow with micronormoblastic erythropoiesis. There was marked increase in myeloid series with eosinophilic precursors accounting for at least 80% of the series. Eosinophilic blast was 3%, promyelocyte 6%, myelocyte 8%, metamyelocyte 10%, band forms 8%, mature eosinophil 50%, and neutrophil was 15%.

Other investigations done were ESR 10mm/hr (Westergren), biochemistry revealed marked hypokalaemia 1.9mmol/L (normal 3.5-5.0 mg/dL). Other parameters were within the reference intervals. See table 1. Stool microscopy did not show ova, cyst or trophozoite of parasites. HIV and HBsAg screening by ELISA was non-reactive. Sputum microscopy and culture was negative. Fine needle aspiration and cytology (FNAC) of submental and left axillary lymph nodes was reported as acute on chronic lymphadenitis. Chest radiograph revealed multiple patchy opacities with background nodularities with some coalescing seen in both lung fields suggesting infiltration of the lungs by the eosinophilic cells. The heart was not enlarged. Echocardiograph was normal. ECG revealed sinus tachycardia and normal morphology.

The diagnosis of Hypereosinophilc syndrome was considered because of the marked eosinophilia, organ dysfunctions (pulmonary infiltrates and skin) even though there was no previous FBC done. It was obvious that the problem had been present for more than 6 months as evidenced by the abdominopelvic ultrasound done 6months earlier which showed hepatomegaly with liver span of 15cm, Lymph node enlargement along the abdominal aorta, iliac vessels and the hilar area of the spleen. The lymph nodes were about 2-4cm in diameter. No other abnormalities were detected in the other organs.

Urgent correction of severe hypokalemia was commenced with IV potassium chloride (KCL) 20mmol in normal saline 8 hourly over 48hrs and maintained on oral Slow K 600mg tds until potassium normalized. The serial plasma Potassium done during potassium correction was 1.9, 2.8, and 4.1 mg/dL on days 1, 8, and 14 respectively. On day 5 of admission, her respiratory rate was noted to be 36/min and she decompensated in room air, Oxygen saturation (SaO_2) was 79%. However her symptoms improved on intranasal oxygen, Loratidine 10mg PO daily, Hydroxyurea 1g PO twice daily which were added to the intravenous ceftriaxone 1g twice daily she had been commenced on since admission. She also had tabs Allupurinol 100mg three times daily and intravenous hydration to prevent tumour lysis symdrome. Twenty-one days after the patient was admitted, she was discharged having made sustained clinical improvement and SaO_2 was 90-91% in ambient air. However, the patient was lost to follow-up.

Table 1: Summary of full blood count (FBC) and Electrolytes

Tests	**Normal range***	**Day 1**	**Day12**	**Day 16**	**Day 21**
FBC					
PCV (%)	36-48	33	34	33	30
WBC Totalx10^9cells/L	4-11	97.6	60.3	40.9	71.4
Neutrophils (%)	45-75	15	25	ND	30
Lymphocytes (%)	20-50	-	20	ND	30
Monocytes (%)	2-10	-	02	ND	01
Eosinophils (%)	1-4	85	55	ND	28
Basophils (%)	0-1	-	01	ND	01
Plateletsx10^9cells/L	150-400	322,	297	344	203
Electrolytes		**Day 1**	**Day 7**	**Day8**	**Day 14**
Na^+ (mmol/L)	130-145	133	ND	ND	ND
K^+ (mmol/L)	3.5-5	1.9	2.7	2.8	4.1
Cl^- (mmol/L)	95-110	89	ND	ND	ND
HCO^-_3(mmol/L)	20-30	26	ND	ND	ND
Urea (mg/dl)	15-45	13	ND	ND	13
Cr (mg/dl)	0.5-1.5	0.6	ND	ND	0.3

* Normal range for an adult female; ND- Not done.

DISCUSSION:

We report a case of a middle age female food vendor with hypereosinophilic syndrome (HES) and severe hypokalemia. HES is a rare disorder which peaks at about 20 to 50 years with a male: female ratio of 9: 1. The clinical features of generalized lymphadenopathy, hepatosplenomegaly, would suggest the diagnosis of a lymphoproliferative disorder with B-symptoms i.e.

significant weight loss and high grade fever with possible pulmonary infiltration. This diagnosis was not supported by the findings of the FNAC. The diagnosis of acute on chronic adenitis reported by the FNAC, when seen in HES, is suggestive of the lymphocytic variant (L-HES).[4] The diagnosis of HES was more likely with the marked hypereosinophilia of 85% of the total WBCs (Absolute eosinophil count of $83x10^9$cells / L). Other diagnostic criteria in keeping with HES were the marked pruritus and lung dysfunction probably resulting from lung infiltration by the eosinophils. Also there was no other identifiable cause of the hypereosinophilia in this patient. A common aetiology of hypereosinophilia in the tropics is helminthes which was negative in this patient (5). The screening for disseminated Tuberculosis was negative. The hepatosplenomegaly seen in this patient is not uncommon in HES. It is seen in about 50% of cases (1, 6). Chronic eosinophilic leukaemia could present in a similar fashion but was ruled out by the peripheral blood and bone marrow morphology which showed myeloblast of less than 5%. This case buttresses the relevance of morphologic examination in this age of molecular diagnosis. In the past, due to the overlap between these two entities, the incidence of HES was underreported.[1]

The diagnosis and the variant of HES would have been further characterized but for the unavailability of facility for routine immunophenotyping in our centre. The immunophenotypes for the L-HES include CD3-CD4+, CD3+CD4-CD8-,CD4+CD7-, CD16+CD56+ and the Myloproliferatve variants(M-HES) have the fusion genes PDGFRa, PDGFRb, and FGFR1 originating from a chromosomal translocation in 4q12, 5q33, and 8p11, respectively (2,3).This underscores the need for routine molecular diagnostic methods and immunophenotyping in the diagnosis of haematological malignancy

Asymptomatic severe hypokalaemia was detected and the patient responded to correction to both parenteral and oral potassium supplements. The aetiology of the severe hypokalaemia was not obvious but vomiting and reduced dietary intake would have contributed. Vomiting and hypokalaemia have a complex pathogenesis. Vomiting may have led to dehydration, hypovolemia and hypokalaemia. In such instances, there is accompanying metabolic alkalosis which was absent in our patient. There was no evidence of a renal disease or cardiac dysfunction that could have accounted for the hypokalaemia. The plasma potassium normalized around day 14 of admission with significant clinical improvement. The release of K+ following cell lysis by the high dose hydroxyurea might have contributed to this response.

A literature search did not reveal any report of HES with hypokalaemia. The patient deteriorated despite the use of parenteral 3rd generation cephalosporin and intranasal oxygen for the presumed superimposed pyogenic pneumonia. However, there was significant clinical improvement after commencement of antihistamine and hydroxyurea. Hydroxyurea instead of a glucocorticoid was used in her case because of the marked eosinophilia, hypokalaemia and multi organ dysfuctions.7 There was subsequent reduction in the absolute eosinophilia. The proliferation and destruction of eosinophils is associated with marked increase in the levels of numerous cytokines (TNF-α, IL-5, IL-10, eotaxin-3, IL-10 etc) which would have worsened the breathlessness and subsequent reduction in oxygen saturation.[4,8,9] The breathlessness and pruritus abated with the use of antihistamine and hydroxyurea and the patient was discharged in a stable clinical state to be followed up at the outpatient clinic. The patient was lost to follow up as it is with many patients in this environment. Most patients only present in relapse or for other complaints. Even though, the prognosis of HES is known to be good with a 5 year survival of 80%, marked splenomegaly as seen in this patient could worsen the prognosis. Other bad prognostic factors are increased blasts, multilineage dysplasia and increasing white cell counts.[1,6,7]

CONCLUSION AND RECOMMENDATION:

This case of HES with asymptomatic severe hypokalaemia in a female patient has not been reported in the literature. It is a rare disorder which could easily be missed but was diagnosed with the aid of peripheral blood and bone marrow aspirate review. The finding points that there is a possible relationship between hypereosinophilia and hypokalaemia which needs to be confirmed by other cases. The reasons for patients being lost to follow up would include the relatively high cost of care in a tertiary hospital which are borne out of pocket and illiteracy. We therefore recommend that the National Health Insurance Scheme (NHIS) should be scaled up to include the treatment of cancers. This would facilitate prompt hospital presentation, diagnosis, treatment and compliance with follow up appointments.

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