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Pernicious Anaemia Masquerading as Addison's Disease in an HIV-Infected Woman

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Abstract

Pernicious anaemia is a manifestation rarely reported in HIV-infected patients. We report a case of a 35-year-old female with well-controlled HIV-infection, who presented with skin hyperpigmentation, pancytopenia and productive cough which mimick Addison's disease. All the clinical symptoms, signs and laboratory findings improved after initiating Vitamin B-12 injections. We highlight the need for low threshold to rule out Vitamin B-12 deficiency in patients presenting with symptoms and signs involving multiple body systems.

Keywords: *HIV, Pernicious anaemia, Pancytopenia, Productive cough, Hyperpigmentation*

Case Report

A 35-year-old female presented to our tertiary hospital with one-year history of hyperpigmentation that involved the feet, palms and the tongue. This was accompanied by history of productive cough with yellowish sputum and significant weight loss for 6 months, loose motions, vomiting, amenorrhoea and dizziness for 4 months. She is HIV-positive on antiretroviral therapy (ART) for the past 10 years. She has no history of either opportunistic infections or hospitalizations. Her CD4 count at presentation was 513 cells/mm^3 with undetectable viral load. She has been on first line ART regimen according to Botswana HIV Treatment guideline of 2016 (1), i.e., Tenofovir, Emtricitabine and Dolutegravir (DTG). She denied history of either use of any over the counter medications or being on corticosteroids. She eats beef and other dairy products. On examination, she was cachexic (weight 39.2kg), severely pale on the conjunctiva, hypotensive with blood pressure of 97/68mmHg and tachycardia of 122 beats/minute. There was hyperpigmentation over the soles, palms and some dark patches on the tongue without characteristic beefy tongue (Figure 1). The rest of the systemic examination was unremarkable. Her full blood picture revealed pancytopenia with WBC of 2.2 $x10^9$/L (4-10), haemoglobin of 6.7g/dl (12-15), platelet count of 135 x 10^9/L (150-400) and raised mean corpuscular volume (MCV) of 107fl (83-101). Serum cortisol, blood sugar, electrolytes, liver and renal function tests, chest x-ray, abdominal-pelvic ultrasound and stool examination were all normal. Sputum for acid-fast bacilli and geneXpert were negative. Serum folate was normal at 23.40 mmol/L, whereas Vitamin B12 was low at <109pmol/l (138-652) with a positive intrinsic factor antibody test at 109.12 AU/mL (Negative=0.93 to < 1.20). Based on the investigations; a diagnosis of pernicious anaemia was made, and the patient was started on intramuscular injections of cyanocobalamin 1000mcg daily for 7 days, followed by 1000mcg weekly for one month, then 1000mcg monthly life-long. She was reviewed after three months with remarkable improvement in all the

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symptoms and signs including productive cough, which had resolved completely. There was no skin hyperpigmentation (Figure 1) and she had gained 12kg at 6 months visit; full blood picture indices had resolved back to normal. Follow up Vitamin B12 level done four months after initiating intramuscular injections of cyanocobalamin was 758pmol/l. She was reviewed six monthly for the next 18 months with neither recurrence of hyperpigmentation nor constitutional symptoms.

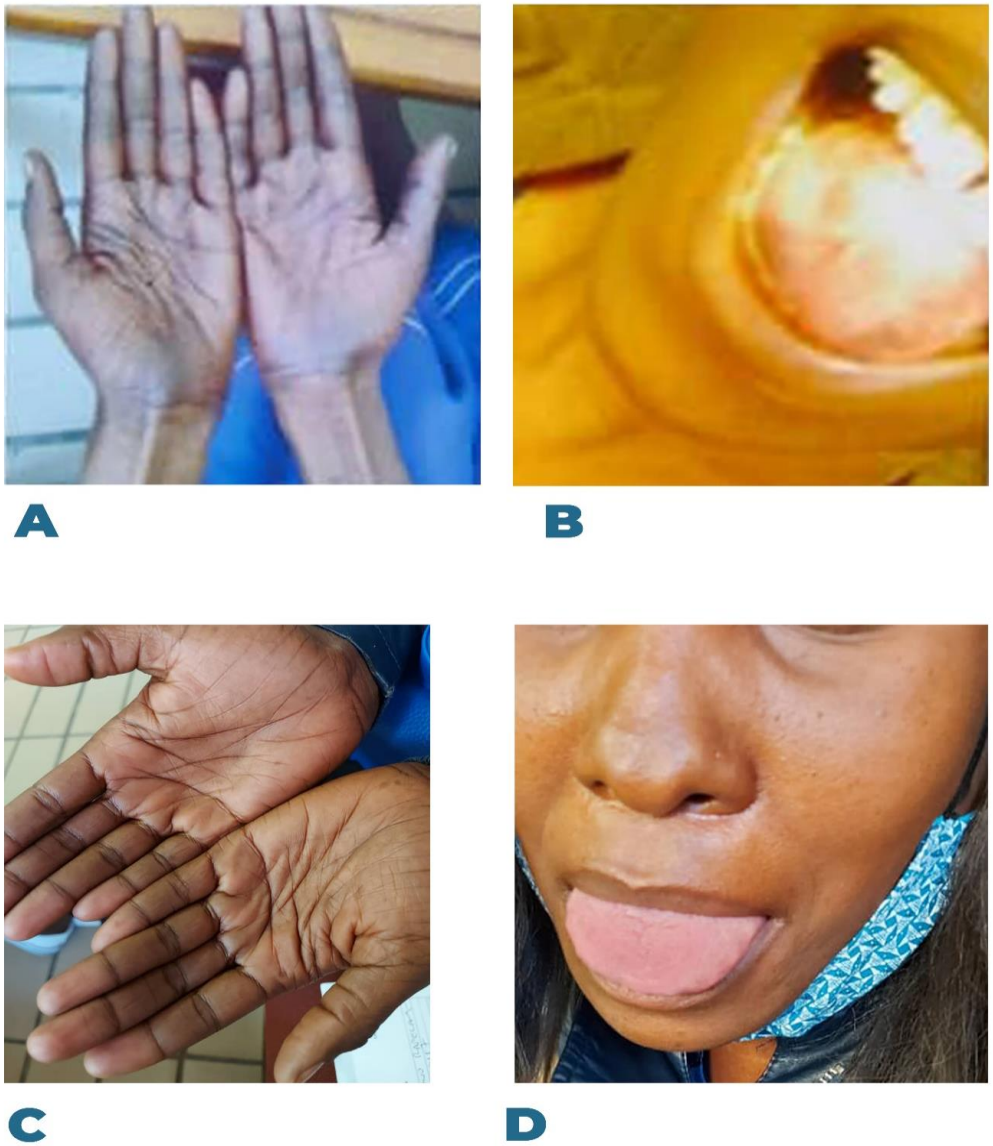

Figure 1. Images A and B showing hyperpigmentation and pallor of palms and tongue respectively before treatment, whereas C and D shows the palms and tongue three months after treatment

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Discussion

Pernicious anaemia is the most common cause of Vitamin B-12 deficiency accounting for over 90% of cases (2); however, it is a rare cause of Vitamin B-12 deficiency among HIV-infected patients (2). With diverse causes of anaemia in people living with HIVAIDS (PLWHA) such as HIV virus itself, poor diet, antiretroviral medications and secondary infections such as tuberculosis; autoimmune causes such as pernicious anaemia are rarely considered (3).

HIV infection is known to be one of the triggers of autoimmunity leading to autoimmune diseases such as pernicious anaemia (4). Immune dysregulation occurring in HIV infection results in increased numbers of autoreactive CD4 T-lymphocytes that infiltrate the gastric parietal cells in pernicious anaemia and promoting local cytotoxicity and B-cell autoimmune activation; both of which lead to autoimmune gastritis (5) . Patients with declined immunity as indicated with low CD4 count usually do not present with autoimmune disease as the latter remain occult (6). Our patient was on long term HAART therapy with CD4 of 513cells/mm^3 at the time of presentation; hence, mostly likely pernicious anaemia was unmasked as a result of improvement of immune status and immune dysregulation (5, 7).

Our patient presented with pancytopenia and macrocytic anaemia in the full blood picture which warranted ruling out Vitamin B12 deficiency (8). She also presented with skin hyperpigmentation that involved the palms, plantar and tongue. Hyperpigmentation is rarely seen in Vitamin B-12 deficiency and clinically mimics Addison's disease (8), making it necessary to rule out the latter in the differential diagnosis. All the symptoms and signs resolved upon initiating intramuscular Vitamin B-12 injections and have not recurred even after more than 2 years of follow-up.

Chronic cough has been previously documented among patients with Vitamin B12 deficiency. The explanation for the chronic cough is due to Vitamin B12 sensory neuropathy and autonomic nervous system dysfunction, leading to laryngeal hyperresponsiveness and increased levels of nerve growth factor (NGF) in the pharynx (9, 10),

Because delayed diagnosis of Vitamin B-12 deficiency can result in irreversible neurological manifestations (11), it is imperative that clinicians have a low threshold to rule out Vitamin B-12 deficiency whenever attending patients with non-specific symptoms and signs including unexplained chronic cough (9); as the diagnosis will help to avoid the worse scenario. Follow up of patients with pernicious anaemia should bear in mind that; other autoimmune diseases

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such as type 1 diabetes mellitus, hypoparathyroidism, Addison's disease, Graves' disease may co-exist or appear later (12).

Conclusion

Vitamin B-12 deficiency may lead into cutaneous manifestations coupled with pancytopenia and other non-specific symptoms and signs. Early treatment of Vitamin B-12 deficiency is paramount to avoid debilitating irreversible neurological manifestations.

Declaration of conflicting interests

The author(s) declare no potential conflicts of interest with respect to this case report, authorship, and/or publication of this article.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors. Written consent for publication was obtained from the patient.

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