

Primary Adrenal Insufficiency (Addison's Disease) Associated with Systemic Lupus Erythematosus: A Rare Occurrence

Okwuonu Chimezie Godswill, Ojeh-Oziegbe Odigie¹

Department of Internal Medicine, Federal Medical Center, Umuahia, Abia State, Nigeria, ¹Department of Internal Medicine, University of Benin Teaching Hospital, Benin city, Nigeria

Correspondence to:

Dr. Okwuonu Chimezie G,
Department of Internal Medicine,
Nephrology Unit, Federal Medical Center,
Umuahia, Abia State, Nigeria.
E-mail: getchimezie@yahoo.com

Date of Submission: Apr 30, 2014

Date of Acceptance: Aug 11, 2014

How to cite this article: Okwuonu CG, Ojeh-Oziegbe O. Primary Adrenal Insufficiency (Addison's Disease) Associated with Systemic Lupus Erythematosus: A Rare Occurrence. *Int J Prev Med* 2014;5:1324-27.

ABSTRACT

Coexistence of Addison's disease and systemic lupus erythematosus (SLE) is a rare occurrence with only few reported cases in the literature. We describe a 29-year-old woman who presented to us with clinical features of acute Addisonian crisis and SLE. Laboratory investigations were confirmatory of Addison's disease in a background of SLE. The patient made remarkable improvement on administration of steroids as replacement therapy for adrenal insufficiency and treatment of SLE. Clinicians need to have a high-index of suspicion of this possible coexistence in order to avoid the associated deleterious hemodynamic and metabolic consequences.

Keywords: Addison's disease, adrenocorticotrophic hormone, association, cortisol, systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage initially mediated by tissue-binding auto antibodies and immune complexes.^[1] Primary adrenal insufficiency (Addison's disease) is most commonly caused by autoimmune processes either as isolated autoimmune adrenalitis or as part of autoimmune polyglandular syndrome. Hence, autoimmune processes are common to both diseases and could account for any possible coexistence. Despite this, the association of primary adrenal insufficiency with SLE has rarely been reported. The objective of this report is to describe a case and review the published literature.

CASE REPORT

The index patient was a 29-year-old woman who presented with rashes on the face and dark discoloration of the palms and buccal mucosa of 5 months duration and postural dizziness of 3 days duration. There was also a history of vomiting, general body weakness, joint pains, painless oral ulcer, hair loss, progressive weight loss and color changes of fingers on exposure to cold. There was no history of frothiness of the urine, early morning facial puffiness, seizures, cough, severe

headache or head trauma. Last child birth was 11 months before onset of current problems. Past medical and drug history were not significant. Examination findings revealed a weak looking young lady, febrile to touch (axillary temperature 37.9°C), pale, dehydrated, anicteric, no peripheral lymphadenopathy nor body swelling. There was hyperpigmentation involving the palmar creases, knuckles of the hand and the buccal mucosa-worse on the sides of the mouth. An ulcer was noted on the buccal mucosa measuring 2 cm × 1 cm with erythematous edges, clean surface and nontender. There were hyperpigmented confluent macules on the malar area of the face extending to the nasal bridge. Pulse rate was 114 beats/min, low volume, thready; blood pressure was 110/80 mmHg supine. The patient was assisted to an erect position and the blood pressure measurement repeated after 2-3 min in this position. There was a postural drop in blood pressure to 85/60 mmHg. Other examination findings were unremarkable.

Laboratory investigations included a full blood count which revealed a normochromic normocytic anemia with a packed cell volume of 16%; white blood cell count of 2.5×10^6 cells/cm³ and platelet count of 23,000/ μ l (pancytopenia). Erythrocyte sedimentation rate was 115 mm 1st h. Chest X-ray was normal while tuberculin skin test was nonreactive. Serum electrolytes showed sodium = 121 mmol/L, potassium = 5.8 mmol/L, bicarbonate = 22 mmol/L, chloride = 130 mmol/L. Serum urea and creatinine were normal. Dipstick urinalysis result was negative for protein and blood, while urine microscopy was unremarkable.

Serology screening revealed positive titer of antinuclear antibodies (ANA) of 1:320 titers and presence of anti-double stranded DNA antibodies. Anti-adrenal antibody test was positive at 1 in 100 dilutions (normal value: Negative at 1 in 10 dilutions). Fasting blood sugar and thyroid function tests were normal.

A diagnosis of SLE with acute adrenal insufficiency was made. This was based on clinical features suggestive of adrenal insufficiency (fatigue, vomiting, hyperpigmentation of a frictional area-palm; and postural hypotension), arthritis, malar rash, oral ulcer and finding of leukopenia, thrombocytopenia, high titers of ANA and presence of anti-double stranded antibodies in a black woman of reproductive age.

Management consisted of admission and rehydration with normal saline, glucocorticoid replacement with bolus dose of 200 mg hydrocortisone, then 100 mg 12 hourly. Mineralocorticoid replacement was initiated on the 3rd day on admission with 100 μ g of IV fludrocortisone. The patient made remarkable improvement on 2nd day of admission as evidenced by resolution of fever, postural dizziness and hypotension.

An abdominal computed tomography (CT)-scan done on 4th day on admission showed bilateral adrenal atrophy but was negative for hemorrhage, infiltration or masses. Baseline early morning cortisol assay was 95 nmol/L (normal value: 140-550 nmol/L). An adrenocorticotropic hormone (ACTH) stimulation test was done by intravenous administration of 0.25 mg of cosyntropin. Blood samples were collected at baseline, 30 and 60 minutes time to assay cortisol levels. There was a rise of plasma cortisol to only 101 nmol/L after 60 minutes. Based on the results the diagnosis of adrenal insufficiency was established. Serum ACTH and renin levels were requested for. Plasma renin level was 5.2 ng/ml/h (normal value: 0.2-3.3 ng/ml/h) while serum ACTH was 101 pg/ml (normal value: 9-52 pg/ml). This confirmed the diagnosis of primary adrenal insufficiency (Addison's disease).

Oral steroid was commenced with prednisolone at 1 mg/kg/day in two divided doses. Laboratory investigations were repeated after 1 week on admission and showed normalization of the electrolyte parameter; though patient still had mild anemia. Ten days on admission, the rashes and hyperpigmentation were resolving, the oral ulcer showed marked healing. She was discharged after 16 days on admission with satisfactory improvement in clinical condition. She was placed on hematinics and tapered dose of oral steroids. She was referred to the clinic for outpatient follow-up.

DISCUSSION

Systemic lupus erythematosus is a systemic disease characterized by immunologic abnormalities with pathologic changes mediated by tissue-binding autoantibodies and immune complexes.^[1] It affects a number of organs and systems and clinical manifestations are heterogeneous. Ninety percent

of patients at diagnosis are women of childbearing years; people of all genders, ages, and ethnic groups are susceptible.^[1] Interactions between susceptibility genes and environmental factors result in abnormal immune responses, which underlies the pathogenesis of the disease.^[2]

The diagnosis of SLE is based on characteristic clinical features and auto antibodies. The American College of Rheumatologists (ACR) enumerated a criteria for the diagnosis of SLE.^[3] These include malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, hematologic disorder, neurologic disorder, immunologic disorder, and Presence of antinuclear antibody. If four or more of these criteria, well documented, are present at any time in a patient's history, the diagnosis is likely to be SLE (specificity is 95%; sensitivity is 75%).

Primary adrenal insufficiency (Addison's disease) develops as a result of bilateral adrenal cortex destruction.^[4] Damage to the adrenal cortex results in decreased production of adrenocortical hormones, with inadequate cortisol and aldosterone. Autoimmune factors are responsible for the destruction of the adrenal glands in most cases, but infection (such as tuberculosis) hemorrhage, adrenal vein thrombosis, and carcinoma are also known to be the cause of a significant number of cases. Symptoms of the disease can be difficult to recognize in some patients. It may only be detected when Addisonian crisis occurs, precipitated by physiologically stressful events (e.g. infection or surgery) in the life of the patient. Clinical features of Addisonian crisis include postural dizziness, craving for salt; abdominal pain, severe vomiting and diarrhea; dehydration; and loss of consciousness. Hyperpigmentation of the skin and mucous membranes often precedes all other symptoms by months to years. Addison's disease can be associated with various diverse autoimmune conditions such as autoimmune thyroid disease, vitiligo, premature ovarian failure, type 1 diabetes and pernicious anemia.

There is a subnormal response to ACTH stimulation in a patient with hypocortisolism, which may be primary (Addison disease) or secondary (due to pituitary or hypothalamic disease). This can be distinguished by checking serum ACTH level; the level will be elevated in Addison disease.

The index patient had features of SLE (six ACR criteria-malar rash, oral ulcer [Figure 1], arthritis, hematologic disorder, immunologic disorder [anti-double stranded DNA antibody] and ANA), and presented to us with features of adrenal insufficiency-fatigue, vomiting, hyperpigmentation of frictional areas-palm, knuckles and buccal mucosa; postural hypotension, hyponatremia and hyperkalemia.

The etiology of adrenal insufficiency in SLE is unknown, but proposed mechanisms may be adrenal vascular thrombosis and infarction, hemorrhage due to antiphospholipid syndrome,^[5] vasculitis^[6] and a direct organ specific autoimmune insult.^[7]

Association of both diseases has been reported in the literature in only few cases. Mamun *et al.* described an 18-year-old girl who presented with low grade fever, malar rash, discoid rashes over the trunk, anorexia and abdominal pain. She was found to be febrile with postural hypotension, hyperpigmentation of the palmar creases and painless oral ulcers. Laboratory findings showed positive ANA and anti-dsDNA antibodies, normal IgG cardiolipin, low hemoglobin and bilateral adrenal cortical atrophy on abdominal CT-scan. The patient improved remarkably on treatment with oral prednisolone.^[8] Da Costa *et al.* reported a case of 44-year-old patient found with photodermatitis, nephropathy, and pancytopenia with positive ANA and anti-ds DNA. There was associated weight loss of 6 kg in 2 months, weakness and diarrhea. The patient had adrenal failure diagnosed by hypernatremia, relapsing fever, and low baseline cortisol and impaired response to ACTH stimulation. The patient's condition significantly improved under steroid therapy.^[9] Bhat *et al.* recently reported a 20-year-old female who presented in an acute hypoadrenal state with a finding of anti-adrenal antibodies. She was found to have SLE with renal involvement, was successfully



Figure 1: Pictures of the index patient revealing the facial rashes and the oral ulcers

managed with steroids and improved clinically.^[10] Together with previous case reports on this rare association,^[11,12] this points to the need for increased suspicion of adrenal insufficiency in patients with SLE with systemic complaints. Addison's disease is nonspecific in clinical presentation but potentially fatal in its outcome.

Clinical suspicion should be high when SLE patients present with features such as abdominal pain, fever, falling hemoglobin, electrolyte changes and marked postural hypotension.^[7] However, it is worth noting that clinical features of SLE may obscure signs of adrenal insufficiency.

CONCLUSIONS

Although occurrence of adrenal insufficiency in SLE is rare there is need for proper evaluation of patients with SLE to identify this rare, but potentially devastating association.

REFERENCES

- Hahn BH. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al.*, editors. Systemic Lupus Erythematosus. Harrison's Principles of Internal Medicine. 18th ed. USA: Mc Graw-Hill Companies; 2012.
- Rahman A, Isenberg DA. Systemic lupus erythematosus. N Engl J Med 2008;358:929-39.
- American College of Rheumatology Criteria for Classification of Systemic Lupus Erythematosus; 1997. Available from: <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0041704/>. [Last accessed 2014 Apr 04].
- Longmore M, Wilkinson IB, Davidson EH, Foulkes A, Mafi AR. Addison's disease (adrenal insufficiency). Oxford Handbook of Clinical Medicine. 8th ed. New York: Oxford University Press; 2010.
- Lenaerts J, Vanneste S, Knockaert D, Arnout J, Vermynen J. SLE and acute Addisonian crisis due to bilateral adrenal hemorrhage: Association with the antiphospholipid syndrome. Clin Exp Rheumatol 1991;9:407-9.
- Kuster GM, Merlo CM. An uncommon case of lupus. Schweiz Med Wochenschr 1999;129:961-5.
- Koren S, Hanly JG. Adrenal failure in systemic lupus erythematosus. J Rheumatol 1997;24:1410-2.
- Mamun AA, Islam S, Rashid AK, Ahasan HA. Co-existence of systemic lupus erythematosus and Addison's disease. Pak J Med Sci 2006;22:74-7.
- Da Costa GM, Forga Llenas L, Martínez Bruna MS, Orta Martiartu M. Adrenal hemorrhage linked to systemic lupus erythematosus associated with the antiphospholipid syndrome. Rev Clin Esp 1992;191:54-5.
- Bhat R, Khan I, Mir T, Khan I, Wani M. Systemic lupus erythematosus presenting as acute adrenal insufficiency: A rare clinical presentation. Ann Med Health Sci Res 2014;4:140-2.
- Eichner HL, Schambelan M, Biglieri EG. Systemic lupus erythematosus with adrenal insufficiency. Am J Med 1973;55:700-5.
- Jakobsen AS, Cvitanich VB, Kirkegaard BC. Acute Addisonian crisis in a patient with systemic lupus erythematosus and secondary antiphospholipid syndrome. Ugeskr Laeger 2007;169:2224-5.

Source of Support: Nil, **Conflict of Interest:** None declared.