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Case Report

Unveiling the uncommon autoimmune insights: systemic lupus erythematosus and Addison's disease

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ABSTRACT

Systemic lupus erythematosus (SLE) has been on the rise with the availability of easily accessible diagnostic modalities and prompt treatment. This autoimmune disease encompasses a wide range of clinical features, hinting at multisystem involvement. SLE manifesting as adrenal insufficiency has been reported in the literature as a rare occurrence. We describe one such uncommon case of an 18-year-old girl who presented with adrenal crisis. The clinical complexity of her presentation led to a comprehensive clinical and laboratory evaluation. An ANA-immunoblot revealed the underlying causative factor, SLE. She was started on parenteral therapy with steroids and showed a remarkable recovery. This case emphasizes the diverse presentations of SLE and the need to maintain a high index of suspicion when dealing with such peculiar cases. Early diagnosis and quick initiation of therapy are crucial in managing SLE effectively. Increased awareness among healthcare professionals is also essential to improve patient outcomes. This case highlights the importance of considering SLE in differential diagnoses, even in uncommon presentations, to ensure timely and appropriate treatment. With improved diagnostic capabilities, more cases like this can be identified and managed successfully.

Keywords: Addison's disease, Autoimmune disease, Systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematous (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. Rare causes include haemorrhage, infection malignant infiltration and TB (leading cause in India).[1] 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

An 18-year-old female patient, resident of nearby district reported to medicine casualty of tertiary care centre with complaints of fever, generalized weakness, abdominal pain and multiple episodes of vomiting since, 1 month, aggravated since, 5 days and altered sensorium since, 1 day. History of joint pain on and off since, 1 month along with hyperpigmentation of face. Retrospectively, we were able to elicit that she had experienced loss of libido and significant weight loss for 3 months prior to her presentation. On presentation, patient was drowsy, her

blood pressure was 80/60 mmHg, pulse rate was 70/min and her laboratory glucose was 56 mg/dl. Bilateral plantar reflexes were flexors and all DTRs were within normal limits in all four limbs with power of 5/5. Rest of systemic examination was within normal limits. No history of fever, diarrhea, vomiting, seizures, focal neurological deficit, trauma, any drug intake. No neck rigidity or any sign of meningeal irritation was present. She received two doses of 50 ml 50% dextrose intravenously, which restored his blood glucose to 153 mg/dl, with a marginal improvement in her level of consciousness. Then patient was immediately shifted to MICU where further investigations were done and Inj. Hydrocortisone were started as per advised from endocrinologist. Patient gradually improved over time and was discharged on hydrocortisone and fludrocortisone replacement therapy.

The patient was followed up for six months, with visits scheduled bi-monthly. At each follow-up visit patient reported progressive improvement in symptoms. The patient adhered well to the treatment regimen with no significant issues with compliance and this contributed significantly to the successful outcome. After six months of follow up, the patient shows significant improvement and is nearly back to pre-condition functional status.

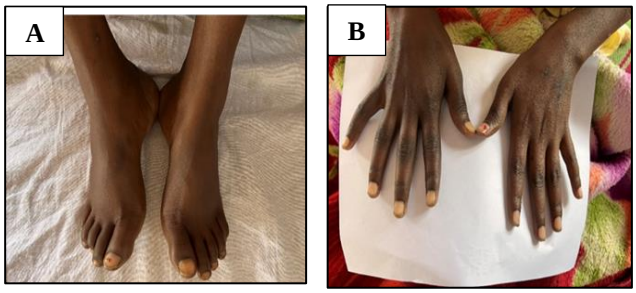

Figure 1 (A and B): Hyperpigmentation of sun exposed areas (hands and feet).

Figure 2 (A and B): Pigmentation of gums and palate.

Lab investigation

The patient's investigation results are as follows: Hemoglobin is 8 g/dl, WBC count is 11,200/cm^2, and platelet count is 150,000/cm^2. Total protein is measured at 6.1 g/dl, total bilirubin at 0.3 mg/dl, alkaline phosphatase at 49 U/l, aspartate transaminase at 29 U/l, and alanine transaminase at 13 U/l. Urea levels are 12 mg/dl, creatinine is 0.5 mg/dl, and the 8 am serum cortisol is 7.80 mcg/dl. Plasma ACTH is significantly elevated at >1250 pg/ml. The ANA test is positive with a titer of 1:1000, showing a cytoplasmic speckled pattern. Sodium levels are recorded as 116, 117, 119, and 128 mmol/l measured serially, while potassium is 5.2 mmol/l. HbA1c is 8.4%, free T3 is 1.79 pg/ml, free T4 is 1.41 ng/dl, and serum TSH is 0.256 uIU/ml. The erythrocyte sedimentation rate (ESR) is 20 mm in the first hour, and C-reactive protein (CRP) is 0.7. Rheumatoid factor (RA) is negative, sickling test is positive, and the lipid profile is within normal limits.

DISCUSSION

This case report highlights many important aspects of adrenal insufficiency and crisis with background of SLE. Addison's disease is a relatively rare condition with an annual incidence of 4 million in the western population.[1] It can be very difficult to diagnose and easily missed due to its presentation with non-specific symptoms. The delay in diagnosis is not uncommon and patients can be seen by various healthcare professionals and hence a high index of suspicion is must. The wide variety in symptoms means that the diagnosis can be attributed to other conditions and the more cardinal features such as skin or mucous membrane pigmentation may be missed although these may not always be present. Clinical and laboratory features suggesting adrenal crisis are dehydration, hypotension, shock out of proportion to severity of current illness, nausea and vomiting, acute abdomen, unexplained fever and hypoglycemia, hyponatremia, hyperkalemia, azotemia, hypercalcemia or eosinophilia.[11] The association between AI and SLE, however, has not been analyzed so far, mainly because coexistence of SLE and AI is rare and only a few cases have been reported until now.[8]

The mechanism of this association is unknown but it is proposed that common autoimmune mechanisms or vasculitis may provoke AI in SLE patients. Overall, the 10-year survival rate of patients with SLE is reported to be approximately 90%, but no information exists regarding survival rate of SLE with concomitant AI.[7] For any patient with confirmed cortisol deficiency, a stepwise approach is followed to determine the etiology beginning with whether the adrenal insufficiency is primary (due to adrenal gland dysfunction) or central (i.e., secondary or tertiary due to dysfunction of the pituitary gland or hypothalamus, respectively). In patients with confirmed cortisol deficiency, an early morning (by 8 AM) plasma ACTH (prior to initiation of glucocorticoid replacement therapy) can help distinguish between primary and central adrenal insufficiency. It should be interpreted with a concurrently measured serum cortisol level. An elevated ACTH level indicates primary adrenal insufficiency, whereas a low or inappropriately normal

value indicates central (i.e., secondary or tertiary) adrenal insufficiency. An ACTH level in the upper half of the reference range is indeterminate and requires additional evaluation with measurement of serum electrolytes and plasma renin and aldosterone levels. A low plasma aldosterone level with an elevated renin level is consistent with primary adrenal insufficiency, a condition that results in mineralocorticoid as well as cortisol deficiency. In the early evolution of primary adrenal insufficiency due to autoimmune adrenalitis, mineralocorticoid deficiency may be more pronounced than cortisol deficiency and therefore precede overt elevation in ACTH.[1,9] For most patients, we first measure antibodies to 21-hydroxylase to assess for autoimmune adrenal insufficiency and for those who test negative can be evaluated with plasma levels of very long chain fatty acids (VLCFAs) and contrast-enhanced CT scan of the abdomen/pelvis. For patients with evidence of infectious, hemorrhagic, metastatic, or infiltrative adrenal disease, the underlying cause should be identified and treated appropriately. Adrenal crisis is a life-threatening emergency that requires immediate treatment.

Table 1: Conditions associated with Addisons disease and autoimmune polyglandular syndrome APS Type 1 and 2.

Addisons Disease	APS1	APS2
Condition associated Thyroid disease, Coeliac disease pernicious anaemia, Type 1 DM, Gonadal failure, Vitiligo, alopecia, myasthenia gravis.	Main: Addisons disease, Hypoparathyroidism, Chronic candidiasis. Other: Gonadal failure hepatitis, pernicious anaemia, Type 1 DM, Thyroid disease, Hypopituitarism.	Main: Addisons disease, Type 1 DM, Autoimmune thyroid disease. Other: Gonadal failure, vitiligo, pernicious anaemia, arthritis, diabetes insipidus.

Treatment must be initiated promptly for all patients with suspected adrenal crisis and should never be delayed for diagnostic testing. Patients with adrenal crisis require fluid resuscitation. We administer isotonic fluid, typically saline (0.9% saline solution or 5% dextrose in 0.9% saline) to correct hypovolemia and hyponatremia. Dextrose-containing fluids help correct confirmed or suspected hypoglycemia. A rapid infusion of 1 over the first hour and typically give at least 2 to 3 within the first 24 hours with serum electrolyte, glucose and continuous cardiac monitoring.[1]

Parenteral glucocorticoid therapy in the form of Inj. Hydrocortisone as a 100 mg intravenous (IV) bolus followed by 50 mg IV every six hours (or 200 mg/24 hours as a continuous IV infusion) for the first 24 hours. If hydrocortisone is unavailable, alternatives include methylprednisolone 40 mg IV and dexamethsone 4 to 6 mg IV. However, since these agents have less mineralocorticoid activity than hydrocortisone, fludrocortisone (100-150 mcg) may also be needed in patients with known or suspected primary adrenal insufficiency.

In patients with loss of energy and libido despite mineralocorticoid and glucocorticoid replacement, 25-50 mg of DHEA once daily can be administered. Once the patient has stabilized, we taper hydrocortisone over one to three days to oral medications. Unless cortisol deficiency is excluded, we continue maintenance glucocorticoid replacement until the patient undergoes outpatient evaluation. For patients with known or suspected primary adrenal insufficiency, we begin fludrocortisone therapy when the hydrocortisone dose is tapered below 40 mg daily. Our case demonstrated significant in patient's symptoms following the administration of the treatment regimen. Previous studies on similar cases have shown varied outcomes. For instance, Kuster and Merlo et al documented a case involving a 44-year-old patient who presented with notable symptoms including significant weight loss (6 kg over 2 months), weakness, and diarrhea. Additionally, the patient exhibited photodermatosis, nephropathy, and pancytopenia. Patient showed a slower recovery in six months follow up period with similar treatment plan.[13]

Bhat and Khan et al reported a case involving a 20-year-old female who presented with acute adrenal insufficiency and was subsequently diagnosed with systemic lupus erythematosus (SLE) complicated by renal involvement. Treatment with steroids was initiated, resulting in significant clinical improvement.[12]

CONCLUSION

This case highlights a rare association of SLE and Addison's disease. Addison's disease should be considered in the differential diagnosis for patients with unexplained weight loss, with or without persistent vomiting. The diagnosis of Addison's involves simple blood tests; however, in acute settings, a random cortisol level can sometimes provide sufficient information. If there is a high index of suspicion, intravenous steroids can be administered without waiting for blood test results. If left untreated, Addison's disease can be potentially fatal, and prompt diagnosis can avoid unnecessary hospitalizations due to crisis. Given the association between autoimmune conditions, it is important to consider related conditions in patients diagnosed with Addison's disease, including autoimmune polyendocrine syndromes (APS). While the association between SLE and Addison's has been reported in many

cases, SLE presenting as acute adrenal insufficiency is rarely documented in the literature. This rarity may be due to the common autoimmune process found in both conditions or possibly due to vasculitis resulting from SLE.

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