## CASE REPORT

# Steven Johnson Syndrome in a Patient with Cushing's Disease

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**SUMMARY**

**Cushing's syndrome is a pathological condition associated with excessive cortisol production, the commonest etiology being Cushing's disease. Corticosteroids in high doses have been used in the management of Steven Johnson Syndrome (SJS) with favourable outcome. We describe a patient with Cushing's disease who developed SJS, one week after taking sperulina a product from sea-weed while waiting for transphenoidal surgery.**

**KEY WORDS:**
*Cushing's disease, Steven Johnson syndrome, Corticosteroids, Sperulina*

### INTRODUCTION

Steven Johnson syndrome (SJS) is a disorder of the skin and mucous membrane, induced by exposure to drugs or infections. The incidence is about two cases per million people per year. Drug induced SJS usually begin one to three weeks after the initiation of therapy. The pathogenic mechanisms for SJS have been proposed due to immune-complex mediated hypersensitivity reaction in response to the offending drug and its metabolites[1]. Corticosteroid used in the treatment of SJS is controversial, with studies showed conflicting results. Tegelberg and colleagues reported an improvement in SJS in their patients after administration of high dose steroids[2]. SJS also is reported to be more frequent in the setting of compromised immune system. Cushing's disease (CD) is a condition where the circulating serum cortisol is elevated throughout the day. Patients who are on high dose corticosteroids or have excess of plasma cortisol are immunocompromised and thus increased the risk of having SJS.

### CASE REPORT

A 40-year-old Chinese lady was referred to our institution for Cushing's syndrome. She was diagnosed to have diabetes for four months duration, associated with increased in weight. Investigations confirmed Cushing's disease (CD) and while waiting for surgery, she developed extensive maculo popular rashes including the mucous membrane. Skin biopsy confirmed Steven Johnson Syndrome (SJS). She gave history of taking sperulina one week prior to the symptoms and also history of taking lactulose about two days prior to the development of Steven Johnson syndrome (SJS). There was no history of drug allergies before, and no symptoms to suggest any viral infections. Examination revealed an obese lady with moon face, buffalo hump and fullness of supraclavicular fossa. There were no bruises or pigmentation. She had proximal myopathy. Blood pressure was 140/90 mmHg and pulse rate was 76/min regular. Systemic reviews were normal.

Laboratory studies revealed the following: haemoglobin 15.9 g/dl, total white count $7.1x10^9/l$, platelet $169x10^9/l$, serum sodium 135 mmol/l, potassium 3.8 mmol/l, urea 5.8 mmol/l, creatinine 52 mmol/l, normal liver profile, and glycosylated haemoglobin at presentation was 8.1%. The electrocardiography and chest X-ray were normal. Diagnostic investigations were done and the results were: random cortisol 981 nmol/l (normal 68-469 nmol/l), low dose dexamethasone test showed serum cortisol was not suppressible, cortisol post high dose dexamethasone was suppressible, serum corticotrophin (ACTH) was 39 pg/ml (normal < 46). Magnetic resonance imaging (MRI) of pituitary gland showed no evidence of microadenoma. Adrenal glands were normal on computed tomography (CT). Inferior petrosal sinus sampling (IPSS) was performed confirmed CD. Her blood pressure and diabetes were controlled with nifedipine, spironolactone and glucophage.

Intravenous immunoglobulin (IVIG) was administered over three days (total of 3gm/kg) to treat her SJS, along with supportive therapy and close monitoring. She was discharged well six weeks later. Following that, left pituitary adenomectomy was performed, and random cortisol post operatively was 120 nmol/l. Her blood glucose normalized and she no longer required anti hypertensive medications.

### DISCUSSION

Cushing's disease (CD) usually manifests by its' metabolic complications namely diabetes and hypertension. It is caused by pituitary microadenoma which secretes adrenocorticotrophic hormone (ACTH) which in turn stimulates the adrenals to produce cortisol in excessive amount. The proportion of patients with CD in which no pituitary tumor is identified on MRI varies between 20% and 50%. Inferior petrosal sinus sampling allows the determination of the site of a ACTH-secreting lesion. Our patient had a normal ACTH, but suppressible cortisol on high dose dexamethasone suppression test suggesting CD. We were able to localize the adenoma, and appropriate management was then carried out.

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The most preferred hypothesis of SJS is cell mediated hypersensitivity reaction, and this is based on the responsiveness of SJS to steroids. Studies have shown that if corticosteroids are tapered down rapidly, there is exacerbation of SJS which is reversible by increasing the corticosteroids dose[3]. On the other hand, a case control study reported that the risk of developing SJS is increased with corticosteroid therapy. It is interesting to note that our patient developed SJS whilst in hypercortisolism state. This denotes that although much has been postulated regarding immune-complex hypersensitivity reaction as the cause of SJS, the pathogenic mechanisms of this disease remain unknown.

High dose IVIG is now used to treat many autoimmune and inflammatory diseases, and SJS is one of them. The IgG levels in the serum and intralesional skin are raised after infusion of IVIG, and this provide protection to the keratinocytes of the patient[4].

Our patient was taking sperulina, a sea-weed based supplement about one week prior to development of SJS. Drug-induced SJS usually begin one to three weeks after the initiation of the offending drug. This is very consistent with the temporal response of known cell-mediated hypersensitivity reactions. In the presence of hypercortisolism, one would have assumed that the patient would be less likely to mount a reaction due to the immunocompromised state. However, in severely altered immune systems as in this patient, the offending agent like sperulina may induce SJS. There have been few reported cases of patients developing SJS while receiving glucocorticoid treatment for oral lichen planus. SJS has also been reported in a girl with systemic lupus erythematosus whilst on high doses corticosteroid therapy[5] and SJS occurring in a patient receiving treatment with cyclophosphamide and prednisolone.

Corticosteroids have been proven as a treatment for SJS in some cases[2] although IVIG has also been proposed as a treatment in patient with this problem. Pretreatment with corticosteroids has also been shown to alleviate reactions to the offending agent. SJS is a disease that has been long associated with multiple drugs, including supplements. Supportive treatment remains the mainstay of the treatment of SJS, together with early identification of the culprit drug and immediate withdrawal.

## CONCLUSION

This case demonstrates that we do not fully understand the pathogenic mechanisms of SJS. Despite the recommendation of using high dose steroids for its treatment, excess cortisol in the body alters immune systems and thus may induce SJS.

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