CLINICAL IMAGES

# Cushing syndrome due to ritonavir–fluticasone interaction

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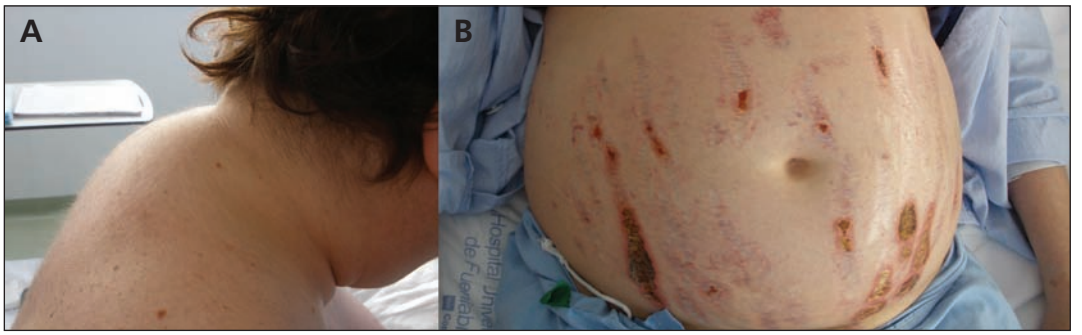


**Figure 1: Dorsocervical fat pad (A) and prominent abdominal striae with secondary impetiginization (B) in a 36-year-old woman with iatrogenic Cushing syndrome.**

A 36-year-old woman with HIV presented with recent weight gain, marked abdominal striae and proximal muscle weakness. She had a four-year history of type 2 diabetes mellitus that had been well controlled until recently by metformin and insulin glargine, and she had long-standing asthma that had been treated for the past two years with inhaled fluticasone–salmeterol. After one year of antiretroviral therapy with tenofovir, emtricitabine and efavirenz for treatment of HIV, her medication was switched to a ritonavir-containing regimen (atazanavir–ritonavir) because of virologic failure. Within three months, she developed proximal myopathy, increased abdominal girth, multiple abdominal striae and mild leg edema. She reported the onset of poor diabetes control, amenorrhea and weight gain of 8 kg.

On examination, she had cushingoid facies, dorsocervical fat pad, central obesity and prominent abdominal striae (Figure 1). Her morning serum cortisol level was low (25 [normal 118–618] nmol/L) as was her adrenocorticotropic hormone level (1.3 [normal 1.8–10.1] pmol/L), which was consistent with adrenal suppression.

The patient was given a diagnosis of Cushing syndrome with adrenal suppression by exogenous glucocorticoids caused by the interaction between fluticasone and ritonavir. Fluticasone was stopped. One week later, mild symptoms of hypocortisolism (fatigue, nausea, postural hypotension) developed, which resolved without the need for glucocorticoid replacement therapy. One month later, her early morning cortisol level normalized, and glycemic control was restored. The cushingoid features completely resolved within four months.

Ritonavir, a potent inhibitor of cytochrome P450–3A4 (CYP3A4), is commonly used in low doses to boost plasma levels of other protease inhibitors in patients with HIV. Fluticasone, a potent glucocorticoid, is rapidly metabolized by CYP3A4 and has minimal systemic effects at recommended dosages. However, coadministration of ritonavir with either inhaled or intranasal fluticasone results in increased serum concentrations of fluticasone and can lead to systemic complications.[1,2] Other inhaled glucocorticoids, such as beclomethasone and budesonide, appear to be safer options because of their lower binding affinity for glucocorticoid receptors and shorter elimination half-life.[1] However, they are also CYP3A4 substrates, and similar cases have been described.[3] Caution should be used when any inhaled glucocorticoid is combined with ritonavir.

## References

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