

Iatrogenic Cushing's secondary to inhibition of triamcinolone metabolism by cobicistat

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INTRODUCTION

- CYP3A4 is the most prevalent cytochrome P450 (CYP) enzyme in the liver
- It is used by the majority of medications for their metabolism and elimination from the body
- Inhibition of CYP3A4 can result in the accumulation of drug concentrations increasing the risk for side effects and possible toxicity

CASE

- 54 year old female presented with one week history of increasing neck and face swelling , fatigue and easy bruising
- PMH: HIV infection, previous TB, bronchiectasis, chronic hip pain
- DH : Rezolsta 800 mg/150 mg (Darunavir + Cobicistat) and Dolutegravir 50 mg once a day
- 2 weeks prior to admission she received an intracapsular injection of triamcinolone acetonide (equivalent to hydrocortisone 200mg) for hip pain
- 2 years ago she had received similar intracapsular injection but she was not on Rezolsta at the time
- On examination she appeared Cushingoid with a round face, facial plethora and dorsocervical fat pad

| Test | Result |
|--------------------------|----------------------------|
| Random cortisol | <40nmol/L |
| 30min cortisol post ACTH | 165nmol/L |
| 24hr urine cortisol | 85nmol/L (20-180nmol/L) |
| ACTH | 1.3pmol/L (2.2-17.6pmol/L) |

- The clinical picture was explained by exogenous steroid interference from triamcinolone
- Due to persistent symptoms her antiretroviral regimen was temporarily changed to facilitate metabolism of triamcinolone
- The patient required several doses of hydrocortisone to cover intercurrent illness
- Recovery of endogenous HPA axis was observed 10 weeks after the initial injection
- Her cushingoid features improved by 3months
- Subsequently she has been seen at the clinic twice with normal short synachten test

DISCUSSION

- Iatrogenic Cushing's syndrome secondary to the antiretroviral ritonavir is well recognised
- In this case Cushing's syndrome was related to an additional antiretroviral, cobicistat, which is known to be a strong inhibitor of the CYP3A4 metabolism
- At the same time patient manifested secondary adrenal insufficiency, requiring hydrocortisone for intercurrent illness
- Systemic complications from intracapsular corticosteroids are rare but when used simultaneously with cobicistat can lead to iatrogenic Cushing's syndrome and adrenal suppression
- This case highlights the importance of taking a robust drug history and considering potential drug interactions in patients on antiretroviral treatment
- It's important to consider that not all electronic systems will have access to specialist prescribing records, that sit outwith standard primary care prescribing systems