

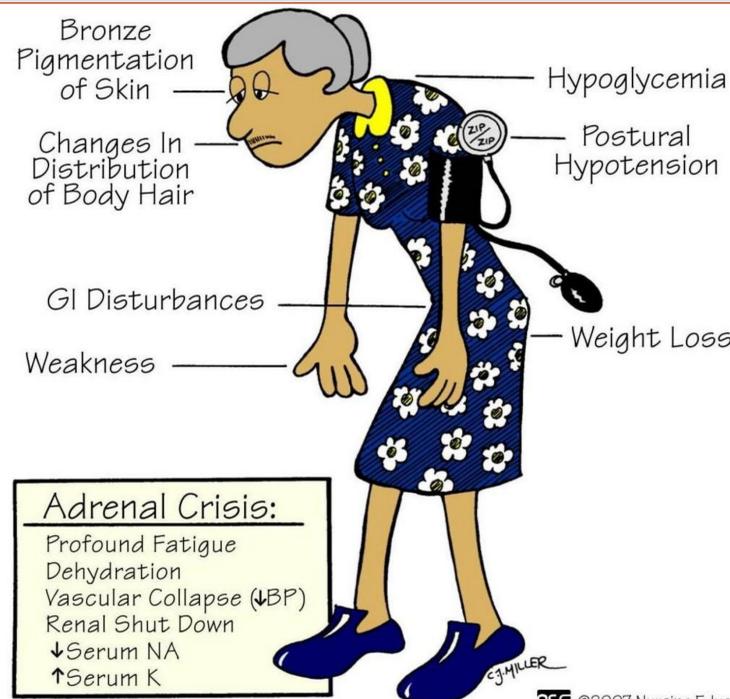
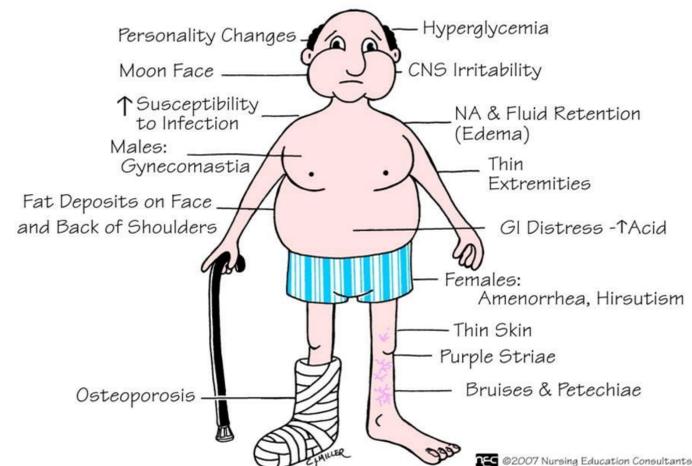
Secondary Adrenal Insufficiency from Intra-articular Triamcilonone Injections while on Ritonavir- boosted Anti-Retroviral Therapy (ART)

Pooja Srikanth MD, Sahitya Bhandari MD, Leonard Sowah MBChB, MPH, Marjorie Pennant MD



Reporting a case of Secondary Adrenal Insufficiency resulting from Intra-articular Triamcinolone acetate (TCA) injection while on Ritonavir- based ART therapy

CUSHING'S SYNDROME



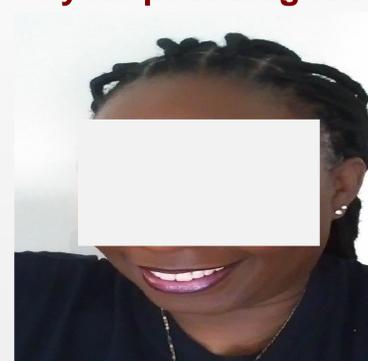
Before Cushings



Cushings syndrome



1 year post diagnosis



Case discussion

- 47 yr old female with PMH of hypertension, knee osteoarthritis, left rotator cuff tear, depression and HIV diagnosed in 1997 treated with emtricitabine/tenofovir and darunavir boosted with ritonavir from 2010 to 2014.
- She received a single shot of triamcinolone acetate injections 40 mg dose each once to both her shoulders and knees each injection a week apart.
- Approximately 4 weeks after her first injection, she experienced fatigue, lightheadedness, irritability, abdominal pain, polydipsia, polyuria, worsening depression, and palpitations.
- On examination, she had moon facies, increase in the dorsal cervical fat pad, and bilateral proximal muscle weakness.
- Initial laboratory tests showed potassium-3.3 and random blood sugar 200 mg/dL.
- She was started on metformin and mirtazapine. Her Antiretroviral regimen was changed to dolutegravir and emtricitabine/tenofovir.
- Two weeks later, the patient was admitted for hypotension, diaphoresis, and hypoglycemia.
- Co-syntropin stimulation test was positive for adrenal insufficiency, with baseline cortisol 5, 30 minute level 9.4, and 60 minute level 12. The ACTH level was 16 (Normal-6-50). The patient was started on prednisone 40 mg daily with taper.
- However, she again experienced similar symptoms following discharge suggesting inadequate symptom control with her prednisone dose.
- She was started on hydrocortisone 100mg iv q8h while inpatient. Discharged on 30mg po AM and 20 mg po PM. The dose was eventually tapered down to 25mg at day time and 15 mg at night over two months, and then over the following 3 months, the dose was further tapered to 10 mg every other day.
- After a year, she still had impaired glucose tolerance, and remains on 5mg hydrocortisone every other day for adrenal insufficiency.

Conclusions:

- Though rare, iatrogenic Cushing Syndrome with secondary adrenal insufficiency has been reported with ritonavir based- HAART therapy following intra-articular steroid injections.
- The mechanism is most likely related to systemic absorption of intra-articular corticosteroids with accompanying decreased clearance.
- Cases have been reported with use of triamcinolone injections while on ritonavir based therapy due to inhibition of their shared cytochrome P450 3A4 degradation pathway, which leads to increased bioavailability of triamcinolone.
- Clinicians should be aware of this potential interaction when subjecting patients on ritonavir boosted ART therapy to intra-articular corticosteroid injections.

Learning objectives

- Steroid injections are retained in the joints for 2–3 weeks after a single administration
- Significant portion of the injected corticosteroid is absorbed into the systemic circulation^{1,2,3} and can cause iatrogenic Cushing's syndrome (ICS) leading to suppression of endogenous cortisol secretion
- The risk of this adverse event is increased in patients on ritonavir boosted ART based therapy for HIV.

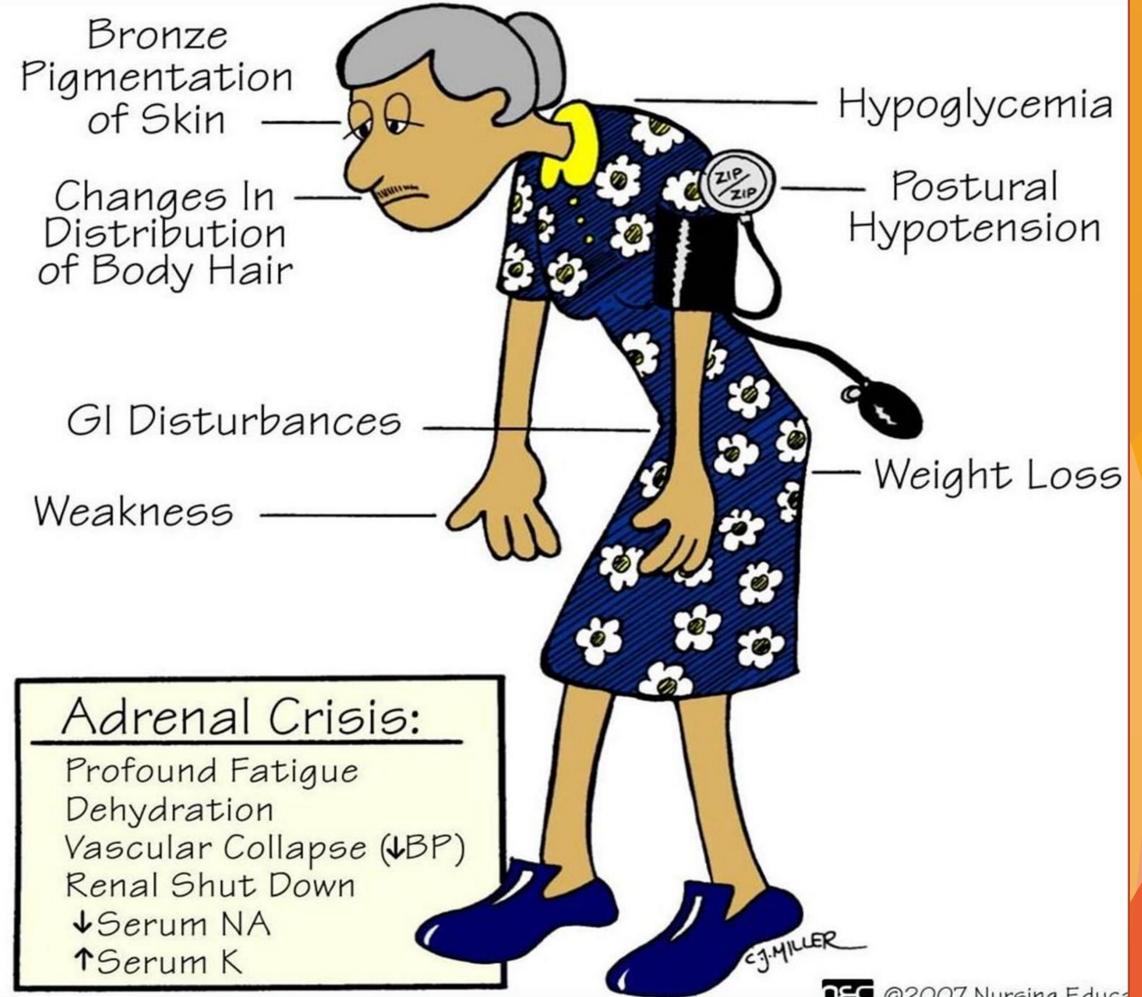
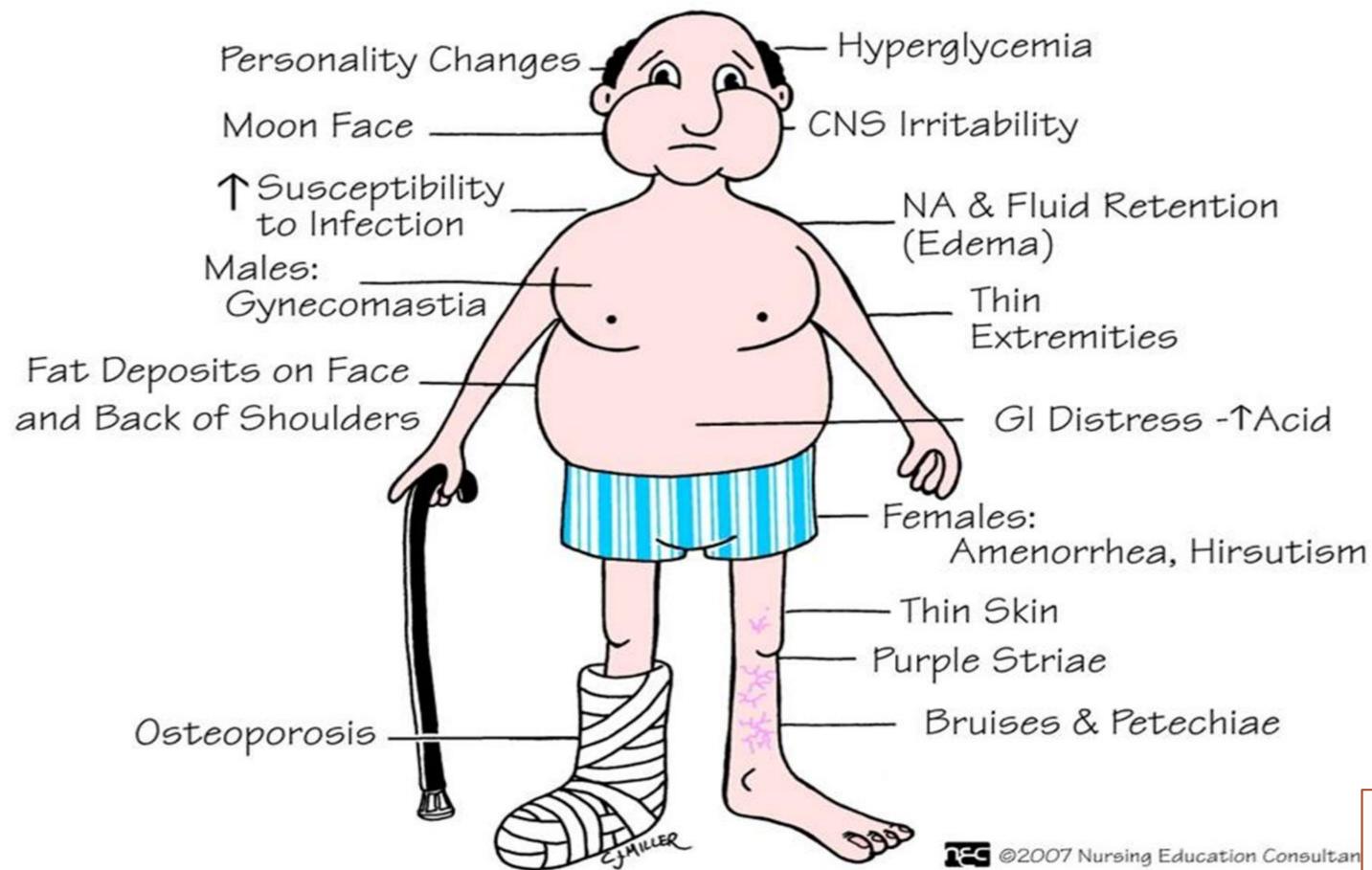
References:

- Jansen TL, Van Roon EN (2002) Four cases of a secondary cushingoid state following local triamcinolone acetate (Kenacort®) injection. Neth J Med 60:151–153.
- Köhler BE, Urowitz B, Killinger DW (1974) The systemic effects of intra-articular corticosteroids. J Rheumatol 1:117–1243.
- Möllmann HW, Barth J, Haack D et al (1986) Comparative studies on the pharmacokinetics and duration of effect of intraarticular application of glucocorticoid crystal suspensions. Aktuelle Rheumatol 11:55–60.

CONCLUSIONS

- ▶ Though rare, iatrogenic Cushing Syndrome with secondary adrenal insufficiency has been reported with ritonavir based- HAART therapy following intra-articular steroid injections.
- ▶ The mechanism is most likely related to systemic absorption of intra-articular corticosteroids with accompanying decreased clearance.
- ▶ Cases have been reported with use of triamcinolone injections while on ritonavir based therapy due to inhibition of their shared cytochrome P450 3A4 degradation pathway, which leads to increased bioavailability of triamcinolone.
- ▶ Clinicians should be aware of this potential interaction when subjecting patients on ritonavir boosted ART therapy to intra-articular corticosteroid injections.

CUSHING'S SYNDROME



▶ Case presentation

47 yr old female with PMH of hypertension, knee osteoarthritis, left rotator cuff tear, depression and HIV diagnosed in 1997 treated with emtricitabine/tenofovir and darunavir boosted with ritonavir from 2010 to 2014.

She received a single shot of triamcinolone acetate injections 40 mg dose each once to both her shoulders and knees each injection a week apart.

Approximately 4 weeks after her first injection, she experienced fatigue, lightheadedness, irritability, abdominal pain, polydipsia, polyuria, worsening depression, and palpitations.

moon facies, increase in the dorsal cervical fat pad, and bilateral proximal muscle weakness.

Initial laboratory tests showed potassium-3.3 and random blood sugar 200 mg/dL.

After a year, she still had impaired glucose tolerance, and remains on 5mg hydrocortisone every other day for adrenal insufficiency.

She was started on metformin and mirtazapine. Her Antiretroviral regimen was changed to dolutegravir and emtricitabine/tenofovir.

Two weeks later, the patient was admitted for hypotension, diaphoresis, and hypoglycemia.

Co-syntropin stimulation test was positive for adrenal insufficiency, with baseline cortisol 5, 30 minute level 9.4, and 60 minute level 12. The ACTH level was 16 (Normal-6-50). The patient was started on prednisone 40 mg daily with taper.

However, she again experienced similar symptoms following discharge suggesting inadequate symptom control with her prednisone dose.

She was started on hydrocortisone 100mg iv q8h while inpatient. Discharged on 30mg po AM and 20 mg po PM. The dose was eventually tapered down to 25mg at day time and 15 mg at night over two months, and then over the following 3 months, the dose was further tapered to 10 mg every other day.

Learning Objectives

- ▶ Steroid injections are retained in the joints for 2-3 weeks after a single administration
- ▶ Significant portion of the injected corticosteroid is absorbed into the systemic circulation^{1,2,3} and can cause iatrogenic Cushing's syndrome (ICS) leading to suppression of endogenous cortisol secretion
- ▶ The risk of this adverse event is increased in patients on ritonavir boosted ART based therapy for HIV.