GRAVES DISEASE AND HIV INFECTION: BAD RESPONSE TO ANTITHYROID DRUGS DUE TO INTERACTION WITH HIV THERAPY

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INTRODUCTION

Immune restoration disease can develop in HIV-infected patients after highly active antiretroviral therapy (HAART) initiation as unmasking or paradoxical worsening of opportunistic infections and, rarely, as autoimmune phenomena.[1] Graves disease is one of the multiple autoimmune diseases that have been reported in HIV-infected patients. It usually occurs after a rise in the CD4 T-cell count and it's unique nature is typified by it's late presentation, usually 8-33 months after starting HAART.[2]

CASE REPORT

51 years old
Male

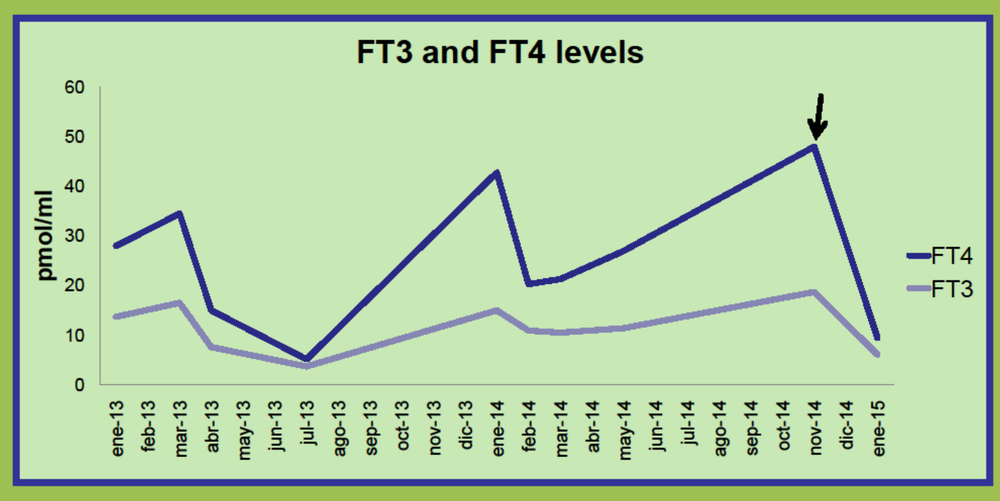
Personal History
- Mitral Insufficiency
- HIV-1 infection

Medication
- HAART since 2007: emtricitabin, tenofovir, atazanavir and ritonavir;
- Propranolol 80mg/day.

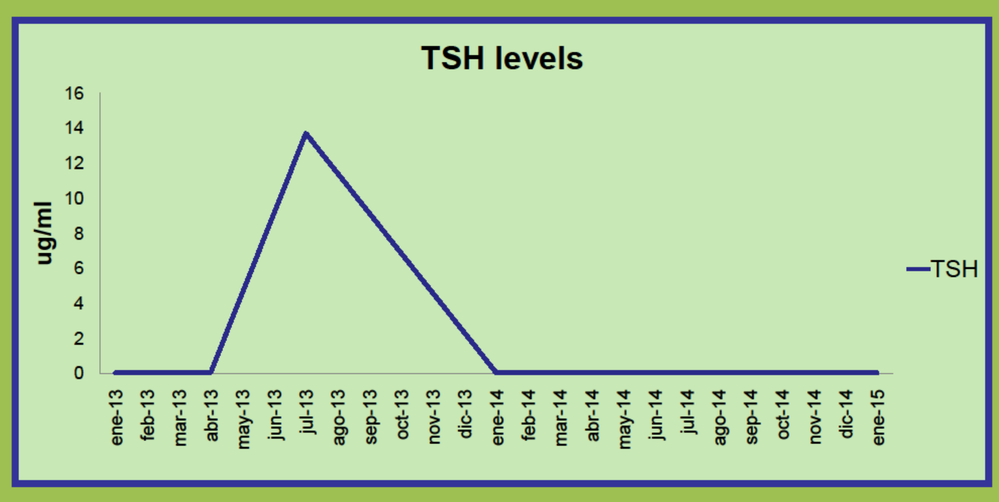
Anxiety
Sudoresis
Palpitations

TSH <0.02 µU/ml (0.46-4.68)
FT4 28pmol/L (10.0-28.2)
FT3 13.7pmol/L (4.26-8.10)

Graves Disease
TRAbs: 45.3 U/L (<1)



During follow-up, most of the time, it wasn't possible to achieve euthyroidism (Fig 1). We offered other therapeutic options (Iodine-131 or surgery) but the patient rejected them.



23rd month of thiamazole
- The patient complains of ictericia:
  - Hyperbilirubinemia (total bilirubin 8.1 mg/dl);
  - AST 31 U/L (17-59); ALT 51 U/L (21-72);
  - FT4 48.1pmol/L and FT3 18,7pmol/L.

HYPERBILIRUBINEMIA
↓
Atazanavir adverse effect

- Boosted atazanavir (with ritonavir) was replaced by rilpivirine;
- We maintained the same dosis of thiamazole (15mg/day).

Six weeks later
- Total bilirubin (0.64 mg/dl)
- FT4 9.45pmol/L and FT3 6.05pmol/L.

CONCLUSIONS

Pharmacokinetic drug interaction have the potential to reduce significantly the antiretroviral or drug treatment benefit. Ritonavir is used as a booster protease inhibitor to enhance therapeutic properties of co-administered protease inhibitors, in this case Atazanavir, due to is capacity to inibit CYP3A4.[3] Methimazole is also a potent inhibitor of CYP3A4 contributing to higher atazanavir levels and it's side effects. Hyperbilirubinemia results from atazanavir inibition of UGT (Uridinophosphoglucoronosyltransferase) which is responsible for the glucuronidation of bilirubin.[4] Methimazole is also metabolized by glucuronidation in liver by UGT, producing Methimazole-S-glucuronide (pharmacologicaly inactive) and Methimazole-N-glucuronide (pharmacologicaly active). The interaction between atazanavir and methimazole is not clear as methimazole metabolism is not clarify as well. One explanation could be that UGT inibition by Atazanavir could reduce Methimazole-N-glucuronide, the pharmacologicaly active form of methimazole. To the best of our knowledge this is the first time the interaction between atazanavir and methimazole is reported.

17 ECE
1068--EP
Thyroid non-cancer
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DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY