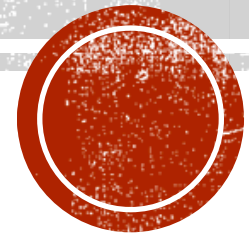


# ENDOCRINE EMERGENCIES

Pui-Ling Chan  
Endocrinologist  
GLMS/CIL Symposium  
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# ENDOCRINE EMERGENCIES

1. Diabetes – DKA, HHS, Severe hypoglycaemia
2. Addisonian crisis
3. Thyroid storm
4. Myxoedema coma
5. Pituitary apoplexy / haemorrhage
6. Severe hypercalcaemia
7. Severe hyponatraemia



# CASE STUDY

- Mr T
- 58 years old, Cook Island Maori
- PMH:
  1. Mixed ischaemia & hypertrophic cardiomyopathy (ICD, recurrent VT & VT storm)
  2. Deranged LFT from cardiac cirrhosis
  
- Medications:
  1. Amiodarone 200mg daily (since Oct 2016)
  2. Cilazapril
  3. Betaloc
  4. Bumetamide
  5. Dabigatran
  6. Omeprazole



# MR T - PRESENTATION

- 17 July 18: T4 **49** (10-20), TSH **<0.01** → Carbimazole 20mg OD started
- TFT prior was all normal
- 9 August 18: T4 **>100**
- 24 Aug 18: Carbimazole increased to 20mg TDS
  
- 11 Sep 18: admitted to hospital with febrile neutropenia (**WCC 0.4, Neut 0.05**); PBC grew *Moraxella nonliquifaciens*; rhino/enterovirus +; normal liver USS (GGT 291, ALT 69, AST 112)
  
- TSH receptor Ab **-NEG**; urine iodide **3699** (25-650)
- USS Thyroid: normal thyroid gland size, homogenous echotexture, decreased vascularity
  
- Diagnosis:  
**Amiodarone induced thyrotoxicosis (type II),**  
**Carbimazole induced agranulocytosis**



# MR T - MANAGEMENT

## PROGRESS

- Prolonged hospital stay : 11 Sep – 29 Oct 2018
- New confusion, hypoactive delirium
- Psychosis
- Exacerbation of heart failure
- Acute kidney injury

## PLANS

- Carbimazole & Prophylthiouracil absolutely contraindicated
- Amiodarone was stopped
- Prednisone 40mg daily
- Prednisone gradually weaned down, 20mg daily at discharge
- Risperidone, Co-trimoxazole 960mg twice per week as PJP prophylaxis



# MR T – CURRENT PROGRESS

- TFT normalised since 27/11/18
- Endocrine OPC 4 Jan 19: Prednisone down to 10mg daily, slow tapering
- TFT (4/1/19) – T4 16 (10-20); TSH 5.1 (0.3-4.0)
- GGT 615; WCC 13.2, Neut 11.0
- Heart Failure Nurse clinic

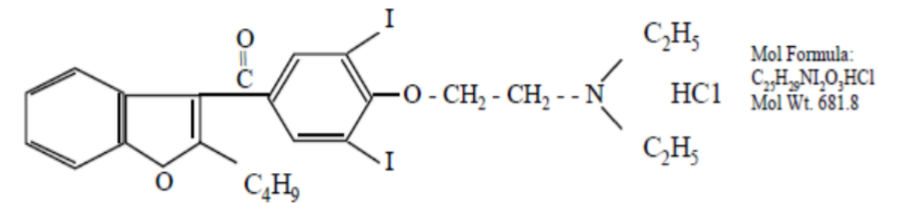


# AMIODARONE

- Class III anti-arrhythmic
- 200mg Amiodarone contains 75mg iodine
- Provides >100x the daily iodine requirement
- Half life 14-110 days
- Very lipophilic
- Accumulates in thyroid, adipose tissue, cardiac & skeletal muscles, liver, lungs

Amiodarone hydrochloride

Chemical structure



# AMIODARONE THYROID DISORDER

- Thyroid disorder is common - observed in 14-18% of patients on long term amiodarone
- Mechanism: inhibits peripheral conversion of T4 to T3; inhibits T4 and T3 uptake into peripheral tissue; direct toxicity on thyroid cell (destructive thyroiditis)
- T4 rises by 20-40% within the first few months of taking amiodarone
- Underlying autoimmune thyroid disease carries highest risk of hypothyroidism
- Nodular goitre: increased risk of Amiodarone Induced Thyrotoxicosis (AIT) type 1
- No underlying thyroid disorder : AIT 2 (destructive thyroiditis)
- Dietary iodine also affects risk of thyroid disorder (iodine sufficient – hypo; iodine deficient – AIT 1)





# AMIODARONE THYROID DISORDER - MX

- Hypothyroid – continue on amiodarone, LT4 replacement
- Hyperthyroidism – consult Cardiologist re: amiodarone
  
- AIT 1 – carbimazole 30-40mg od or PTU 450-600mg od; perchlorate; lithium; thyroidectomy
- AIT 2 – steroid (start 40-60mg od for 1-2 months then taper)
- Unknown mechanism – prednisone + carbimazole



# CARBIMAZOLE

- Anti thyroid, inhibits thyroid hormone synthesis by inhibiting thyroid peroxidase
- Doses:
  - Maintenance dose 10-15mg daily
- Iodine deficiency will increase response to carbimazole;
- Iodine excess will attenuate it

<b>Mild</b>	<b>20mg daily</b>
<b>Moderate</b>	<b>40mg daily</b>
<b>Severe</b>	<b>40-60mg daily</b>

## Contraindications

- Previous Adverse reaction
- Granulocytopenia
- Simple goitre
- Severe hepatic insufficiency



# CARBIMAZOLE AGRANULOCYTOSIS

- Rare but serious
- Prevalence 0.1-0.5%
- If develop agranulocytosis with either carbimazole or PTU, other is contraindicated due to risk of cross-reactivity
  
- Usually occurs within first 2-3 months of treatment, average 69 days
- Risk is dose dependent
- Higher risk if >40mg/day
- Check WCC immediately if develop fever, sore throat or other infection
  
- American Thyroid Assoc. does not recommend monitoring CBC
- Japanese suggest checking CBC every 2 weeks for first 2 months of treatment



# CARBIMAZOLE AGRANULOCYTOSIS

- Recovery takes a few days but could be prolonged and cause death
- G-CSF has been used in severe cases
- Steroid ineffective

## Hepatotoxicity

- Rare
- Jaundice, dark urine, light stool, abdominal pain, anorexia, nausea
- Cholestatic & hepatitis pictures
- Should be stop if liver enzymes X3 ULN
- **PTU** – fulminant hepatic necrosis



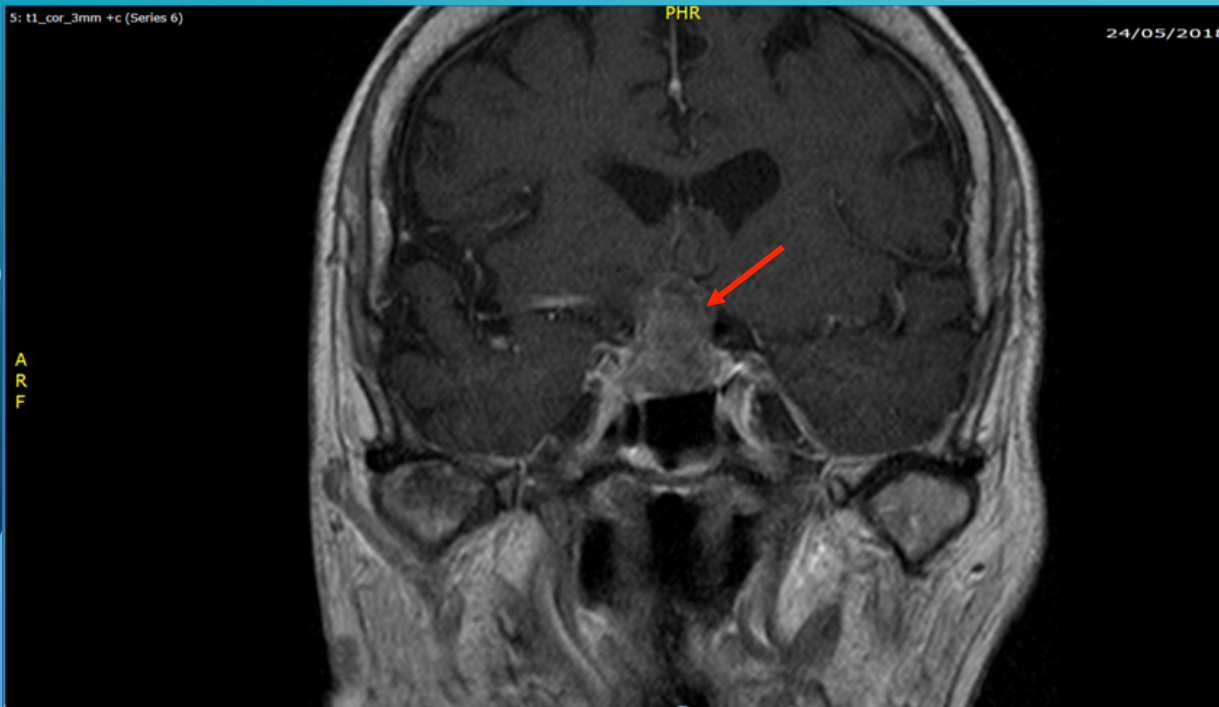
# SUMMARY

- Amiodarone has very high iodine content
- Amiodarone increases risk of thyroid disorder
- Monitoring of thyroid function is important
  
- Carbimazole can cause rare but serious side effects
- Dose dependent, esp. if  $>40\text{mg/day}$
- Monitor CBC, LFT, TFT
- Stop carbimazole immediately if develop high fever, sore throat, infection
- If carbimazole causes agranulocytosis, PTU also contraindicated
- Teratogenicity
- Female of reproductive age – advise to stop carbimazole as soon as conceive



# QUIZ – AN ENDOCRINE EMERGENCY

- 81 year old man
- Acute bitemporal hemianopia
- Third nerve palsy



Na 131  
T4 10.2 (10-20), TSH 0.13 (0.3-4.0)  
7am cortisol 104 (200-700)  
FSH 3, LH <1, Testosterone <0.4  
IGF-1 26 ng/ml (39-206)  
Prolactin 172 (<240)

# ACUTE HYPOPITUITARISM - AETIOLOGY

- Adenomas (macroadenoma  $>10\text{mm}$ )
- Sellar masses – craniopharyngioma, Rathke's cleft cyst
- Apoplexy / SAH / Obstetric haemorrhage
- Pituitary surgery
- Radiation therapy to sella
- Vascular – aneurysm, malformation
- Hypophysitis, sarcoidosis
- Pituitary abscess
- Traumatic Brain Injury (TBI)
- Genetic

# ACUTE HYPOPITUITARISM -CLINICAL FEATURES

- Prostration, Nausea, vomiting
- Orthostatic hypotension, dizziness
- Fatigue, unexplained weight loss
- Headache, visual loss, cranial neuropathies, ophthalmoplegia
- **ABSENT hyperpigmentation or hyperkalemia**
- Possible myxoedema coma
- Central diabetes insipidus
  - Onset within 24-48 hours of TBI/pit surgery
  - UO >200ml/hour for >2h
  - Urine OSM <300; urine SG <1.005
  - Raised serum Na



# ACUTE HYPOPITUITARISM

## Investigations

- T4, TSH
- Cortisol, ACTH
- GH, IGF-1, Prolactin, FSH, LH, T/E2
- Electrolytes, BUN
- Urine & plasma Osmolality

## Management

- Glucocorticoid – IV Hydrocortisone 50-100mg q8h
- Defer thyroxine until after GC replacement (may precipitate acute adrenal crisis): IV LT4 300-500mcg then 50-100mcg daily ( $\sim 1.6$  mcg/kg/day), lower dose in elderly
- Desmopressin in CDI

# ACUTE HYPOPITUITARISM - SUMMARY

- Wide variety of pathologies/causes
- Prompt glucocorticoid (GC) administration
- Defer thyroxine until after GC
- Careful monitor of fluid & electrolytes can be life-saving
- Remains a serious condition with excess mortality
- Early recognition is important