

Clinical Cases

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Consultant Acute Physician

Case 1

- 28-year-old Afro-Caribbean male
- Paranoid Schizophrenia with forensic Hx
- Referred to AEC from Tamarind Centre
- 3/7 Hx of low grade fever, tachycardia, anorexia and malaise
- DHx amisulpiride 100mg BD, clozapine 75mg BD , procyclidine 5mg OD
- HR 130, T 37.8°C, other obs NAD
- Physical examination unremarkable
- WCC 13, CRP 152, CK 332 (U&E, LFT, eosinophils normal)
- ECG sinus tachycardia, CXR and urine dip NAD

Case 1

- Differential Diagnosis?
- Additional Investigations?
- D-dimer 443
- CTPA requested
- CTPA NAD
- Hs-TnI 1453
- Diagnosis?
- Management?

Clozapine

- Atypical antipsychotic
- Second-line Rx for refractory schizophrenia
- Low-grade fever, tachycardia, postural hypotension (during initiation)
- Weight gain, insulin resistance, excess salivation, urinary incontinence, seizures
- Gastrointestinal (pseudo)obstruction
- Agranulocytosis (0.8%, peak risk 6-18w from initiation)
- Increased risk of DVT/PE (high mortality)
- Myocarditis and cardiomyopathy

Clozapine-induced myocarditis

- Risk 1/500
- Usually occurs early (median 16d, 80% within 4w)
- Type 1 IgE-mediated hypersensitivity with eosinophilic infiltration of myocardium
- Initial non-specific flu-like symptoms (fever, tachycardia, chest pain, dyspnoea)
- Eosinophilia, raised CRP, CK, BNP and troponins
- May progress to fulminant cardiomyopathy
- Urgent TTE to assess LV function
- Stop clozapine (CI to future use)
- Supportive care (ACE-i, β -blockers, diuretics, inotropes)
- Corticosteroids remain controversial

Case 2

- 84-year-old female
- 2/52 Hx of vomiting, reduced oral intake and increasing confusion
- PMHx AF, HTN, MVD, bowel cancer, hypothyroidism
- DHx furosemide 80mg OD, lansoprazole 30mg OD, digoxin 250mcg OD, levothyroxine 50mcg OD
- Observations unremarkable
- Confused on examination, no other significant signs
- Initial ED impression ?bowel obstruction
- ECG – 'LVH, ST elevation in aVR, inferolateral ST depression' (no chest/abdominal pain or breathlessness)

Patient:

OLIVE SMITH

W. H. L. S. S.

Age: 71

2/8/1970

HR 78/min

Interval:

RR 82 ms

P 1 ms

PR 1 ms

QRS 102 ms

QT 366 ms

QTc 398 ms

10 mm/mV

AV

QRS 12

12

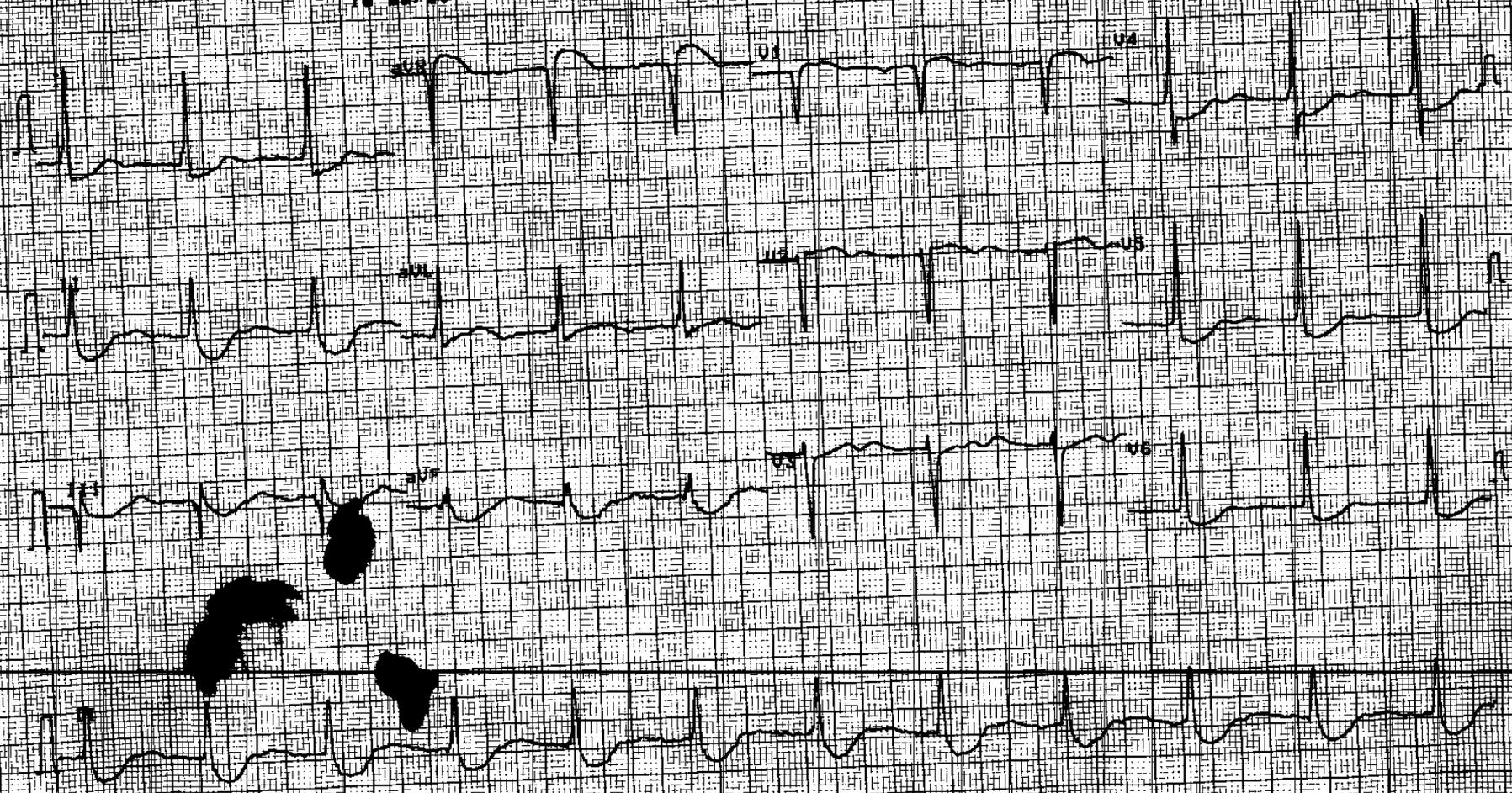
P (11)

P (10)

P (10)

Sokol 6.38 mV

5 mm/mV



Digoxin Toxicity

- Acute-on-chronic > acute > chronic
- Increased risk with AKI/CKD (reduce dose)
- Nausea, vomiting, diarrhoea, delirium, xanthopsia
- Hyperkalaemia due to blockade of Na-K-ATPase pump (prognostic marker in acute overdose)
- Bradycardia, hypotension, AV block, sinus arrest, atrial tachycardia, ectopics, bigeminy, TdP, VT/VF
- Risk of arrhythmias increased by hypokalaemia
- Stop digoxin (and nephrotoxics/diuretics)!
- IV fluids, correct electrolyte disturbances, IV bicarbonate (QRS prolongation), IV magnesium (QTc prolongation), IV atropine/pacing (bradycardia)

Digibind[®] & DigiFab[®]

○ Indications:

- Acute overdose of $\geq 10\text{mg}$
 - $\text{K}^+ > 5.5$ following acute overdose
 - Digoxin level $\geq 10\text{ng/mL}$ 6h post acute overdose or $\geq 15\text{ng/mL}$ at any time
 - Chronic toxicity associated with significant arrhythmias
 - Bradyarrhythmias unresponsive to atropine or life-threatening ventricular arrhythmias
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- Dosing information on Toxbase[®]
 - Risk of anaphylactic reactions
 - Less effective in renal impairment
 - Falsely elevated digoxin levels post-administration

Case 3

- 74-year-old female
- Admitted with fatigue, generalized weakness and immobility
- Recent discharge from SH with similar symptoms (Rx for dehydration and UTI)
- PMHx of T2DM, CKD, hypothyroidism and severe RA
- DHx gliclazide, aspirin, ramipril, simvastatin, levothyroxine, ciclosporin, pregabalin
- Observations unremarkable
- Global reduction in proximal muscle strength, unable to transfer/stand independently

Case 3

- K⁺ 5.6, urea 14.6, creatinine 227 (190), TSH 4.8, CRP 23, ALT 178
- Urine dip – protein ++, blood +++
- CXR and ECG – NAD
- Diagnosis?
- Further Investigations?
- Additional history – started ciclosporin 2/12 ago for RA, pregabalin started 2/52 ago by GP for 'painful legs'
- CK 12,732
- Statin-induced rhabdomyolysis 2° to ciclosporin

Statin-induced rhabdomyolysis

Common CYP3A4 Inhibitors

- Macrolide antibiotics e.g. clarithromycin
 - Antifungals e.g. ketoconazole, posaconazole
 - Antiretroviral protease inhibitors e.g. indinavir
 - Ciclosporin
 - CCBs e.g. verapamil, diltiazem
 - Amiodarone
 - Grapefruit juice
- Reduce dose, change to pravastatin/riuvastatin, change to statin with long t_{1/2} (rosuvastatin, atorvastatin) 1-2x per week or switch to ezetemibe/colesevalam

Other drugs associated with rhabdomyolysis

- Fibrates
- Colchicine
- Alcohol
- Corticosteroids
- Amiodarone
- Lithium
- Phenytoin, lamotrigine
- Anti-retrovirals
- Methadone, heroin, cocaine, amphetamines
- SSRI and antipsychotic overdose

Rx of rhabdomyolysis

- Treat precipitating cause
- Stop offending drugs and nephrotoxics
- Aggressive IV crystalloid resuscitation
 - Up to 12L/24h aiming for urine output of $\geq 100\text{mL/h}$)
- Urinary catheter
- Monitor/treat electrolyte problems (hyperkalaemia, hyperphosphataemia, hypocalcaemia)
- In extreme cases consider:
 - Urinary alkalization (IV sodium bicarbonate 8.4% 225mL aiming for urinary pH ≥ 7.5)
 - Osmotic diuresis with IV mannitol
 - Haemodialysis/haemofiltration

Adverse Drug Events (ADEs)

- Account for 7% of UK hospital admissions
- Occur during 15% of UK hospital admissions
- >25% are considered preventable
- Risk increases with patient age
 - Multiple comorbidities
 - Polypharmacy
 - Reduced physiological reserve
- Most commonly implicated drugs are anticoagulants, NSAIDs, cardiovascular drugs, antibiotics, insulin and oral hypoglycaemics, benzodiazepines and opiates

Adverse Drug Reactions (ADRs)

○ Type A (Augmented)

- Predictable, exaggeration of drug's normal pharmacological actions
- Errors in dosing, overdoses
- Prescription of multiple drugs with similar effects
- Altered pharmacodynamics
- Altered pharmacokinetics e.g. reduced metabolism/excretion due to hepatic/renal impairment or drug-drug interactions

○ Type B (Bizarre)

- Unpredictable, idiosyncratic, immunogenetic basis
- Allergic, pseudoallergic and hypersensitivity reactions

Detection & Prevention of ADEs

- Know your poisons!
- Medication review for all acute admissions
 - Are all prescribed medications indicated? (stop unnecessary drugs)
 - Are dosages correct? (modify according to age and GFR)
 - Is the patient on any high-risk medications?
 - Are any drugs being prescribed solely to counteract SE of other drugs?
 - Are there any clinically significant drug-drug interactions?
 - Are there any clinically significant drug-disease interactions?
 - **Could this presentation be due to/exacerbated by medications?**
- Electronic prescribing and computerized CDSS
- Pharmacist medicines reconciliation and review

