Diabetic Ketoacidosis in Type 2 Diabetics

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Case 1

- 82-year-old Caucasian female with T2DM (>30 years) and HTN
- BMI 19
- Metformin 500mg TDS , Gliclazide 40mg BD, Ramipril 5mg OD
- Admitted with 1/52 of increasing drowsiness, confusion and reduced oral intake
- Unwell, dehydrated, hypotensive
- CBG 46mmol/l, ketones 3.2mmol/l
- Na 158, urea 35, creatinine 323 (baseline 77), CRP 278
- Urine dip leucocytes 3+, nitrite +ve, blood and protein 2+
- VBG: pH 7.29, lactate 3.3, BE -8.9

Case 1

- Does she meet the criteria for HHS?
    - Glucose >33.3mmol/l
    - Osmolality = 2x [Na+] + glucose + urea = 2x 158 +46 + 35 = 397mOsm/kg (>320)
- Does she meet the criteria for DKA?
    - Glucose >11mmol/l
    - Ketones >3.0mmol/l or ≥3+ (urine)
    - Acidosis pH <7.30 and/or bicarbonate <15
- How should she be treated?
    - DKA protocol?
    - HHS protocol?

Differences with HHS

- presentation often subacute developing over days to weeks
- glucose often much higher than in DKA (usually >33mmol/l)
- more profound dehydration (sodium very high and fluid deficit >10l)
- acidosis is not required for diagnosis (patients often are acidotic due to sepsis or AKI)
- ketosis may occur due to starvation/acute illness and/or acute insulin deficiency
- fluid deficit should be corrected more slowly (e.g. over 72h rather than 24h) due to risk of fluid shifts and cerebral oedema
- FRIVII is not required (use rehydration alone initially then VRIVII reduced to 50% of usual rate if patient is insulin naïve)
- 10% dextrose is rarely required to maintain CBG
- invariably associated with severe precipitating illness e.g. MI, sepsis; TREAT
- prognosis much worse (mortality up to 50%)

Case 2

- 67-year-old Caucasian male with T2DM diagnosed 10 years ago
- BMI 32
- On metformin 1G BD and lantus 32 units ON
- Admitted with severe cellulitis of his right leg
- CBG 29mmol/l, blood ketones 6.5mmol/l
- Sodium 134, urea 12.1, creatinine 112
- VBG: pH 7.22, lactate 2.1, BE -12

WHAT IS THE DIAGNOSIS?

HOW SHOULD HE BE TREATED?

DKA in patients with T2DM

- Traditional teaching: lev[illegible] with T2DM are always sufficient to suppress li[illegible] OCCUR IN T2DM
- DKA in patients with T2DM is increasingly recognized
- 20-30% of patients admitted with DKA have T2DM in recent studies
- often in association with stress/intercurrent illness (commonly infection/sepsis) in contrast to T1DM where no trigger to DKA is common
- declining insulin levels in patients with longstanding T2DM
- Release of stress hormones (cortisol, glucagon, catecholamines, GH)
    - inhibit oxidation of fatty acids
    - promotes hepatic ketogenesis
    - further reduces insulin secretion and sensitivity

DKA in patients with T2DM

- Should be treated as for DKA in T1DM (FRIVII) and discharged on insulin
- Acute reduction in insulin secretion and action is reversible
- β-cell function recovers with time and insulin independence is achieved in 50% by 3-6m from index episode
- may remain insulin independent for many years
- 70% suffer a repeat episode of DKA within 2y and progressive requirement for insulin with time
- Chances of successfully coming off insulin or need for long-term insulin can be predicted by serial measurements of C-peptide levels in clinic ≥3w from episode of DKA

Case 3

- 21-year-old Afro-Caribbean male
- Recently diagnosed diabetic by GP 1/52 ago after presenting with increased thirst and polyuria (CBG 29mmol/l)
- BMI 28, some recent weight loss
- Family history of T2DM (maternal grandfather)
- Told by GP he needed to lose more weight, not started on any treatment, no plans for follow-up?!
- Admitted via ED with abdominal pain and vomiting
- CBG 27mmol/l, blood ketones 7.8mmol/l
- Sodium 136, urea 8.3, creatinine 102
- VBG: pH 7.15, lactate 2.2, BE -15

WHAT IS THE DIAGNOSIS?

DOES HE HAVE TYPE 1 or TYPE 2 DIABETES?

HOW SHOULD HE BE TREATED?

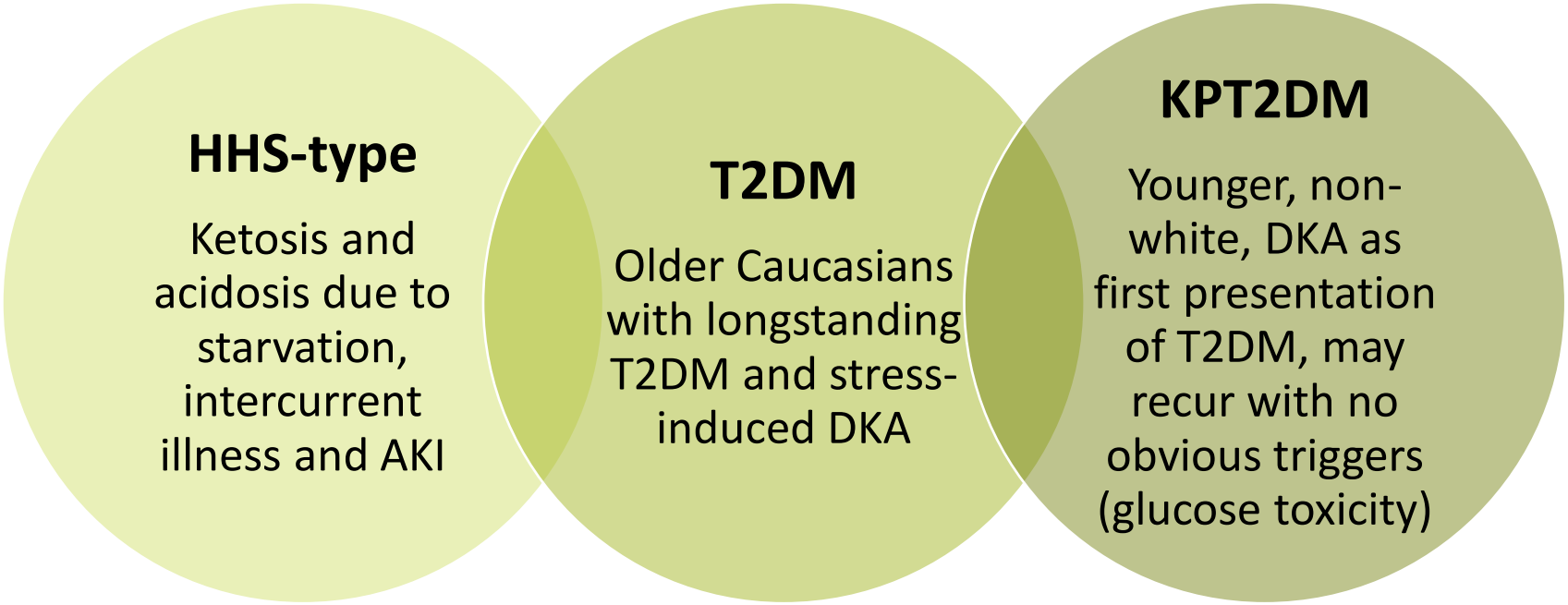
Ketosis-Prone T2DM
(Type 1b or 'flatbush' diabetes)

- More common in non-white patients with T2DM (especially Afro-Caribbean and Hispanic ethnicities)
- DKA common at time of presenting with diabetes
- Recurrent episodes of DKA may occur with no obvious trigger other than prolonged hyperglycaemia
- Reversible hyperglycaemia-induced suppression of β-cell function – 'glucose toxicity'
- Genetic polymorphisms in islet cell transcription factors e.g. PAX4 and glucose-6-phosphate dehydrogenase deficiency more common in patients with KPT2DM
- Islet cells more susceptible to hyperglycaemia-induced oxidative stress
- Recovery of β-cell function and insulin independence is common following resolution of DKA

Determining whether patients have T1DM or T2DM at presentation (with DKA)

- Age is a poor discriminator; 20-30% of T1DM presents >20 (including LADA) and (KP)T2DM may present in childhood
- Short history of polyuria, polydipsia and weight loss may occur in KPT2DM
- Non-white ethnicity and family history of diabetes more common in (KP)T2DM
- Patients with T2DM are more likely to be obese and have higher levels of HbA1c (e.g. >10%) at presentation
- Pancreatic autoantibodies (anti-GAD, anti-ICA and anti-IA2) are more common in T1DM
- Persistence of insulin independence >6-12m and normal/high fasting C-peptide levels following resolution of DKA are best discriminators

Spectrum of DKA in T2DM



Key Learning Points

- DKA is relatively common in patients with T2DM
- Distinguish different subtypes/phenotypes
- Treat HHS with ketosis/acidosis as HHS
- Treat true DKA in T2DM as for T1DM and discharge on insulin
- Important to consider KPT2DM in non-white obese patients who present for first time in DKA
- Check autoantibodies and fasting C-peptide levels in clinic
- Majority can achieve prolonged periods of stability on oral hypoglycaemics after recovery of β-cell function