Periodic Paralysis

Description

A number of rare periodic paralytic conditions due to abnormal muscle Ca^{2+}, Na^{+}, or K^{+} ion channels causing episodes of generalised flaccid weakness or paralysis that may be associated with transient [K^{+}] changes.
Genetic mutations have been found at 17q23.1-q25.3, 1q32 or 11q13-q14
Variants:

- Hypokalaemic periodic paralysis – calcium channels most often affected.
  - Thyrotoxic periodic paralysis is most common subtype
- Hyperkalaemic periodic paralysis – sodium channels.
- Normokalaemic periodic paralysis – sodium channels
- Andersen's syndrome – Potassium channels, [K^{+}] may be abnormal. Arrhythmias can occur.

Epidemiology

Incidence: ~1:100,000
Autosomal dominant pattern with a penetrance that is ~100% in M but lower in F.
Around a third a cases give no family history and so may be spontaneous mutations.
Thyrotoxic periodic paralysis - Esp. Asian males.

Presentation

Most of the patients with PP have similar clinical features, which are as follows:

- Weakness may be slight & transient in an isolated muscle group or severe & generalized. The muscles that are constantly active (cardiac, respiratory, CN) are usually spared.
- Interictal lid lag and eyelid myotonia - May be the only clinical signs in hyperkalemic PP
- Normal sensation
- Fixed proximal weakness - May develop in either hyperkalemic or hypokalemic PP
- Diminished stretch reflexes during attacks
- Attacks intermittent and infrequent initially but may ↑frequency until attacks ~daily.
- The frequency declines by the age of 30 and it rarely occurs after the age of 50 years.

PP Syndrome	Age of Onset	Duration	Precipitating Factors	Severity	Associated Features
Hyperkalaemic	1st decade	<2hrs	↓CHO intake (fasting), Cold, Rest following exercise, Alcohol, Infection, Emotional stress, Trauma, Menstrual period	Rarely severe	Perioral and limb paresthesias, Myotonia frequent, Occasional pseudohypertrophy of muscles
Hypokalaemic	Childhood to 3rd decade. Most <16yrs	Usually <72hrs	Morning-after-exertion attacks, High-CHO meal, Cold	Severe, Complete paralysis	Occasional myotonic lid lag, Myotonia between attacks rare, Unilateral partial monomelic, Fixed muscle weakness late in disease
Thyrotoxic	3rd/4th decades	Usually <72hrs	Same as hypokalemic PP, Hyperinsulinemia	Same as hypokalaemic PP	Fixed muscle weakness may develop, Hypokalemia during attacks

Differential Diagnosis

- For hypokalaemic PP: Secondary hypokalaemia
  - Hyperaldosteronism
  - Conn's syndrome
  - Bartter's syndrome
  - Excessive consumption of liquorice
  - Renal loss, especially with renal tubular acidosis
  - Alimentary loss with chronic diarrhoea or purgative abuse
  - Excessive alcohol consumption
  - Drugs, especially amphotericin B. It also occurs with barium poisoning.
- For hyperkalaemic PP: Secondary hyperkalaemia
  - Addison disease
  - Chronic renal failure
  - Hyporeninaemic hypoaldosteronism
  - Ileostomy with tight stoma
  - Potassium load
  - Potassium-sparing diuretics
- Other causes of neuromuscular weakness

Investigations

Between attacks, parameters may be normal.
Urine: In HypoK$^+$ PP a high urinary K$^+$:Cr ratio (>2.5) makes 2° K$^+$ loss DDx likely.
Bloods: UEC (K$^+$ may still be in NR), CK (↑), CMP (may ↓Mg, ↓PO_4), TFTs
ECG: changes consistent with hypo- or hyperkalaemia.
Genetic analysis: preferred confirmatory test.
Nerve conduction studies, EMG.
Exercise tests.
Provocation Tests: Rarely used now as need intensive care setting and have assoc risks. In hypoK+ PP can give glucose, insulin or adrenaline. In hyperK$^+$ PP, a potassium challenge.
Biopsy: occasionally.

Management

HypoK$^+$ PP/Thyrotoxic PP
Acutely:

- **Potassium** 0.25mmol/kg q30min until improvement. IV only if necessary. ECG/serial UEC.
- **Propanolol** may be used for thyrotoxic periodic paralysis (also as prophylaxis)

Prophylaxis:

- Potassium supplements
- **Acetazolamide** 125-1500 mg/day in divided doses or potassium-sparing diuretics e.g. **triamterene** (25-100 mg/d) & **spironolactone** (25-100 mg/d)

HyperK+ PP – usually mild and often don't require much Rx.
Acutely:

- CHO- meal, or if severe potassium lowering Rx (dextrose/insulin, salbutamol)

Prophylaxis:

- Thiazide diuretics

Complications

Mortality low. In HypoK$^+$ PP, aspiration pneumonia or inability to clear secretions may occur.