Royal Liverpool & Broadgreen University Hospitals NHS Trust

It's a MADD, MADD world?

A returning traveller with meningism after a flight: an unusual presentation of multiple acyl-CoA dehydrogenase deficiency

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Presenting Complaint:

- A 28-year-old male presented to a UK hospital emergency department with a two-day history of headache, vomiting, and photophobia.

Travel History:

- Travel from Goa, India, three days previously.
- Two month stay in a rural village with family.
- No contact with bats or unwell people.

Past Medical History:

- One previous hospital admission:
  - Generalised discomfort and vomiting; also occurring shortly after a long-haul flight.
  - Extensively investigated, final diagnosis of dehydration.

Initial assessment:

- Drowsy, stiff neck, without focal neurology
- HR 123, BP 133/82, temperature 37.1
- Raised anion gap metabolic acidosis on ABG
- ***Treated as meningitis***
- Subsequent LP showed normal cell counts

Progress:

- On day 2, developed a worsening metabolic acidosis, hypoglycaemia, and hyperammonaemia

Results:

- Urinary organic acid analysis: ↑ dicarboxylic acids
- Acylcarnitine test: ↑ medium and long chain acylcarnitines (C5 – C18) with normal C8:C10 ratio, and low free carnitine
- Investigations for malaria, HIV, viral hepatitis, and leptospirosis were negative.

Final Diagnosis:

Multiple acyl-CoA dehydrogenation deficiency (MADD)

- The patient responded well to treatment with continuous IV dextrose infusions, and subsequently oral dextrose supplementation and specialist dietician advice.

Conclusions / Lessons

Clinicians must consider the potential for the mode of transport to precipitate decompensation of non-infective illnesses in the returning traveller.

Air flight may unmask inborn errors of metabolism

Surveillance systems of illness in returning travellers should report non-infectious aetiologies to help alert clinicians to non-infectious differentials.

All about Multiple acyl-CoA dehydrogenation deficiency (MADD):

- MADD is an autosomal recessive inherited disorder.
- It is a fatty acid β-oxidation disorder.
- Fatty acids are an important source of energy in periods of catabolic stress
- In healthy individuals:

- In MADD, enzymes ETF* and ETFQo* are defective
- Fatty acids are metabolised by different routes to generate dicarboxylic acids and precursors accumulate (leading to lab abnomalities)
- Gluconeogensis is unable to maintain plasma glucose

- Potential mechanisms which may explain our patient's decompensation after air travel may include:
  - reduced barometric pressure
  - reduced air humidity and dehydration secondary to this
  - disruption of circadian rhythms ('jet lag')
  - Avoidance of aeroplane food resulting in prolonged fasting

*electron transfer flavoprotein (ETF)
*electron transfer flavoprotein–ubiquinone (co-enzyme Q) oxidoreductase (ETF-QO)

Further reading:
Grünert SC. Clinical and genetical heterogeneity of late-onset multiple acyl-coenzyme A dehydrogenase deficiency. Orphanet Journal of Rare Diseases. 2014;9:117
Wajner M, Amaral A. Mitochondrial dysfunction in fatty acid oxidation disorders: insights from human and animal studies, Journal of Bioscience Reports. 2016 Feb; 36(1)

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