

# What is your diagnosis? History as it presents in the consulting room

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# Catherine

- 44 years old.
- Autism, ID.
- Epilepsy, mild left hemiparesis (weakness).
- Medication sensitivities and side effects much of her life.



Running, roller skating & pirouetting independently

# Catherine

- 13 years ago that all gradually changed, but it wasn't due to illness or accident.
- I am going to present her as she would (repeatedly) present in your consulting room, for you to work out the 2 additional diagnoses, and treatment.
- Its difficult to know when each of the conditions began to cause symptoms, as one thing seemed to insidiously lead to another, so I will start from when she seemed to be relatively well.
- In the past couple of months Catherine has finally started to improve, and smile again.

# Impact of medication change 2001

- Multiple anticonvulsant sensitivities.
- Admitted to Austin Hospital for epilepsy workup.
- Low dose Lamotrigine stopped suddenly.
- 8/1/02: Epilim levels rose to 1368, close to toxic levels, as more than small reduction resulted in status epilepticus.
- Wetting profusely at night (high Epilim interfered with ADH).
- Unexplained fever & lymphocytosis with pain.
- Urine into vagina resulted in endometritis & cervicitis, not responding to antibiotics. Hysterectomy.
- Reasonably well for about 12 months

# Recurrent seizures

- Prescribed Rivotril, but when developed severe swallowing difficulties changed to drops sublingually.
- Increased Rivotril to control 'seizures', swallowing got worse, unable to get even anti-convulsants in.
- Admitted Flinders Medical Centre
- Nasogastric tube for 18 days
- Epilim being reduced
- Severe diarrhoea from formula, dietician refused to alter formulation
- Lost 6 kg in weight

# Keppra

- 11/7/08: Discharged on Keppra
- Extra-pyramidal signs
- Walking stiff-legged
- Couldn't relax down onto toilet, difficulty voiding
- Jerky movements, banging into things
- Unable to hold cup without spilling
- Lying on floor, hands over her eyes (couldn't close them)
- Difficulty swallowing
- Crying, squealing, groaning, restless, coughing repetitively
- 17/10/08 Keppra ceased

# Clinical Features

- Marked hypertonia/muscle weakness, unable to get off the floor, or relax into chair
- Walking very slowly, always needing her hand held to prevent her falling
- Tactile defensive, if even brushed past object, threw herself backwards and fell
- Caught foot on bath getting out, marked clonus
- Unable to cross lines, thresholds, walk on slopes
- Tried to 'climb up' a striped pedestrian crossing
- Difficult to feed – tongue constantly against hard palate
- Speech very difficult to understand.
- Physio dismissed it as typical deterioration of CP in thirties.

# Neurologist

Dr Michael Harbord

- Had been seeing Catherine for many years, concerned about her deterioration.
- Recently got a manual wheelchair for mobility, as tired easily
- ‘Unusual gait pattern, some clomping of her foot when walking. Barefoot appears to have a spastic diplegic gait, no obvious focal abnormality R leg compared with L leg’.
- ‘This change is not explained by her known disabilities, and needs investigation’.

# Tests ordered in 3 batches, all negative

- Subtelomeric FISH, Angelman, Fra X, Rett syndrome, Dravets, Spino-cerebellar Ataxia, MR1 MLPA, CGH Array, karyotype
- Mucopolysaccharides, Oligosaccharides, urine purine & pyrimidines, guanidinoacetate, serine, glycine
- Plasma creatine/creatinine ratio, alpha amino adipic semialdehyde GAA, Bratton-Marshall
- Later tests Amino acids, organic acids, VLCFA, lactate, white cell enzymes, transferrin isoforms

WHAT IS YOUR NEXT STEP IN BLOOD TESTS?

OR DO YOU KNOW THE DIAGNOSIS?

# GUTHRIE!

2011

Acyl-carnitine profile showed increases in C8 (the one for MCAD) plus C10, C12, C14:1.

- Hexanoglycine negative
- Orotate slightly increased
- Catherine had a low level of carnitine for which she was prescribed carnitine replacement 500 mg caps tds with definite improvement in mobility and eating.

Jane will be talking about the genetics of Catherine's deficiency.

# Further deterioration

- Episodes of low grade fever lasting 1-3 days, never any signs of illness.
- Facial pallor, and looked unwell.
- Virtually stopped talking
- Unable to close eyes to go to sleep at night.
- During day lying with hands covering eyes
- Used to like lying on the lounge – lay down but soon sat up again as not comfortable
- At night after about an hour, she either lay on her back with her arms along her body, with her elbows up in the air, or both arms straight up above her chest, head above pillow.
- Sometimes legs up in the air as well.

# Further deterioration

- Liked resting her head on my shoulder, but could only hold that positions for a minute or so, had to sit up again, as too stiff.
- Unable to curl up in her favourite armchair.
- Walking very slowly, difficulty with changing colours on floor, lines, thresholds.
- Banged into things.
- Tripped over a lot, couldn't get herself up
- Unable to step onto scales, as too unsteady
- If dropped something couldn't bend to pick it up.
- Wetting herself a lot only recently

# Further deterioration

- Problems swallowing, very slow to eat – often needed to be fed with 50 ml syringe sublingually, as tongue always against hard palate. Other times tongue thrust.
- Drooling and spitting markedly.
- Used to spoon feed and finger feed quite well, no longer able to get her arm to her mouth.
- Visual-perceptual difficulties. When reached for glass of water, knocked it over by accident.
- Once her glass was guided to her mouth, she might drink a few sips, but then as she tried to take the glass away from her mouth, she jerked and spilt it.
- Overall has lost 10 kgs since episode with N-G tube, now 44 kg

# Rivotril effect

- On Rivotril 0.25 mg daily regularly
- Ordered an extra 0.5 mg when had a cluster of seizures
- On 3 occasions given the extra 0.5 mg
- In each case, 2 days later she had extremely severe swallowing problems
- The only way to get nourishment in was to syringe in meal replacements sublingually

# Further deterioration

- Catherine was in RAH for 3 weeks before Christmas 2015 because of facial pallor, fever, swallowing difficulties, spitting excessively, unable to lie down, groaning, not eating, shrieking.
- She hadn't managed to sleep day or night for the previous week, and didn't sleep in hospital. Neither diazepam nor midazolam helped her sleep.
- Eating and drinking was difficult.
- We thought it was her carnitine deficiency causing the problems, so she was on a 10% dextrose drip.

# Worsening of symptoms

- All her symptoms became progressively worse, particularly her insomnia, and she was becoming distressed at not being able to sleep (usually a very good sleeper, didn't need medication).
- We continued trying a combination of diazepam and midazolam, but she only got a couple of hours of sleep at a time.
- The night before we commenced her current medication, she was extremely distressed, sitting up in bed, eyes open, groaning, spitting, rocking, arms going like pistons the whole night, wet bed.
  - WHAT IS YOUR DIAGNOSIS?
  - WHAT TREATMENT ARE YOU GOING TO GIVE?

# Treatment

- Given 1 mg of Lorazepam at 10.50 am, by 2 pm she was getting her head down onto the cushion for a few minutes before having to sit up.
- With a gradual increase in Lorazepam based on clinical picture, currently 7.5 mg per day, she has improved markedly (reports state dose usually about 14 mg per day).
- Walking very fast
- Able to bend over to pick up something off the floor without losing her balance.
- Better able to pick up her glass and drink, not yet back to what she was but much better.

# Trying to feed herself

- Sitting at the table after Catherine finished her therapy at My Therapy House, Catherine asked for tomato.
- I had cherry tomatoes, so I gave her one.
- She took it from my hand, and put it to her mouth, but was unable to get it in, even though she was trying to push it into her mouth.
- We realised that she was trying to push the tomato in against closed teeth.
- Realising the problem, the OT who was in Catherine's line of vision opened her mouth wide.
- Catherine opened her mouth, and in the tomato went!

# Treatment

- Mostly able to walk across thresholds.
- Starting to talk, sing and laugh more again.
- Speech still indistinct, but improving.
- Still twirling a lot.
- A week ago it took 10 minutes to get her from her bedroom to the bathroom next to her bedroom, as she was constantly twirling or 'freezing' (standing motionless on the spot). Lesser episodes I wondered if she was having an absence, but now I realise she was probably 'freezing'.

Dr Jenny Curran is now going to talk more about Catatonia.