CASE DESCRIPTION
A 19-year-old female university student presented with a 5-week history of generalised weakness, unsteady gait and breathlessness. There were no symptoms of recent infection. Her only medical history was long-standing symmetrical 40 dB sensorineural hearing loss. On neurological examination, she had hyperpnoea, mild non-fatigable global weakness, bilateral ptosis, soft speech and absent lower limb reflexes.

The MR scan of brain showed symmetric T2-hyperintensities surrounding the third ventricle, hypothalamus and brainstem on fluid-attenuated inversion recovery sequences, suggestive of Leigh syndrome (figure 1). Lumbar puncture showed an opening pressure of 8 cm water. Cerebrospinal fluid (CSF) was acellular, protein 0.38 g/L (normal <0.45) and glucose 3.5 mmol/L (normal 2.2–4.5). Serum lactate and pyruvate were both elevated: lactate 4.3 mmol/L (normal 1.2–2.8) and pyruvate 0.26 mmol/L (normal <0.1). Arterial blood gases confirmed a respiratory alkalosis with metabolic compensation (PO2 15.6 kPa; PCO2 3.1 kPa; pH 7.50; HCO3 18 mmol/L). Urine, blood and CSF cultures were negative.

Two days after the lumbar puncture, her conscious level rapidly declined. CT scan of head now showed marked vasogenic cerebellar oedema with posterior fossa compression causing effacement of the fourth ventricle and early tonsillar descent (figure 2). Despite immediate posterior fossa decompression, she did not recover consciousness and died 24 days later, 11 weeks after symptom onset. No post-mortem was performed.

A mitochondrial gene panel was sent within 1 week of presentation. This study took 6 weeks to process and posthumously confirmed a pathogenic Leigh syndrome mutation (NC_012920.1(MT-ATP6):m.9176 T>C) in blood and urine (heteroplasmy level 97%).

DISCUSSION
Leigh syndrome is a progressive and ultimately fatal inherited mitochondrial...
disorder typically of infants and children. While over 83% of Leigh syndrome presents by the age of 2 years, cases have been diagnosed up to 74 years old. Adult cases are rare and described mostly, as here, in single case reports. There is marked phenotypic and genotypic variability. About half of cases have a known mutation. A challenge of diagnosis remains the phenotypic heterogeneity including ataxia, psychomotor retardation and abnormal eye movements. Leigh syndrome has a recognised overlap with other mitochondrial disorders including mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes.

Advances in genetic testing and MRI have facilitated early accurate diagnosis. This has important implications for pre-implantation genetic diagnosis and counselling. Our patient developed fulminant, fatal cerebellar oedema within 11 weeks of first symptom onset and despite a recently normal lumbar CSF pressure. A stroke-like episode may offer a plausible explanation for the rapid posterior fossa compression.

Key messages

- Leigh syndrome encompasses a spectrum of clinical presentations.
- It can result in rapidly fatal posterior fossa oedema even without other major neurological manifestations.
- Genetic testing makes the diagnosis.

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FURTHER READING

1 Turnbull D. When to think about mitochondrial disease (editorial). Practical Neurology 2020 (this issue, linked paper).

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