Gaia Young (deceased) born 4 March 1996, died 21 July 2021: summary

History

Previously well aged 25 admitted to hospital, symptoms included headache, vomiting, and acting strangely. No fundoscopy or blood ammonia. 3L Hartmann over 9 hours, sodium fell from 129 to 122. CT scan at 16 hours reported as "no acute finding". Coned at 18 hours.

Post-mortem report

Cause of death:

1a. Tonsillar herniation
1b. Raised intracranial pressure
1c. Cerebral oedema

A mechanism of death, not aetiology: causal sequence uncertain; the brain had no circulation – non-specific, hypoxic ischaemic changes – exam describes tissues at death, not the process.

Report: "Although the ultimate cause of death was apparent (raised intracranial pressure) the underlying cause of the brain injury was not clear…the autopsy cannot establish the underlying cause of the brain oedema and raised intracranial pressure in this case…"

Death must be explained by pathophysiology, not pathology – fulminant, malignant:
(a) atypical presentation of recognised condition; (b) rare condition; (c) unknown condition.

Differential diagnosis

A primary process at its most general:

Originated in the brain
Confined to the brain
Fatal catastrophic raised intracranial pressure
No pathological "smoking gun" – a silent assassin

Excluded conditions includes (non-exhaustive):

Intracranial vascular event: haemorrhage, occlusion, vasculitis
Infection: meningitis or encephalitis
Auto-immune encephalitis: inflammation and demyelination
Trauma; non-traumatic injury; acceleration/deceleration; shaken head
Space-occupying lesion giving rise to mass effect
Obstructive lesion giving rise to hydrocephalus, and
Chiari
Posterior reversible encephalopathy syndrome (PRES)
Osmotic demyelination syndrome (ODS), central pontine myelinolysis (CPM)

Medical information silent: no noise, no signal; but medical information *not* exhaustive, answer outside clinical and pathological materials. Ante-mortem, not post-mortem condition.

Exclusive, specific: suggest receptor, enzyme; catastrophic - positive feedback or cascade.

Remaining possibilities include (eliminate the impossible, what remains must be true):

Metabolic encephalopathy
Neurotoxin
Idiopathic intracranial hypertension

Consideration of possible aetiologies

Metabolic encephalopathy

Initial thoughts: Reyes syndrome (absent liver disorder), or mitochondrial disease? Then urea cycle disorders tip off after the inquest – but why not at the inquest? Best fit: ornithine transcarbamylase deficiency (OTC) hyperammonaemic crisis (see below): provides complete, simple, coherent, robust explanation (Occam's razor):

Conforms with published cases
All evidence supportive
No evidence contradicts
No plausible alternative

So far a clinical diagnosis pending genetic tests and biochemistry.

Neurotoxin

Neurotoxin target organ is neural tissue but act by bodily system: but ionic gates? But note endogenous ammonia; highly selective for brain: specific and exclusive. Accumulation of glutamine in astrocytes, powerful osmolyte. Ammonia uninterpretable post-mortem – the perfect "silent assassin" – see above.

Idiopathic intracranial hypertension (Dandy/Friedmann: normal scan, papilloedema)

Gaia referred to neuro-ophthalmology in 2019 because of headache and blurred discs. Optical coherence tomography negative. Literature has described "fulminant" IIH but not fatal malignant IIH. Good fit but not as good as OTC.

Bias in diagnosis

Cognitive bias: mistaken belief the answer must be (1) in one's knowledge and (2) in materials examined; leads to overinterpreting abnormal findings to seek answer: consider elephant and the 6 blind men. Explains the hyponatraemic fallacy – we say hyponatraemia was incidental rather than causal; SIADH due to encephalopathy.

Intellectual laziness bias: lack of curiosity
This is a good enough answer – look no further; just accept an unexplained tragedy.

Semmelweiss reflex bias:
I did not think of it – so it must be wrong.