Medical Report

Prepared by
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Consultant Neuroradiologist

Concerning the sudden illness and death of

Gaia Young

January 2025

I am a Consultant Neuroradiologist appointed in 1993 to perform diagnostic and interventional neuroradiology at the University Hospital of Wales in Cardiff. My qualifications are MBBS MRCP FRCR LLM. I did my sub-speciality training in neuroradiology at the National Hospital for Neurology and Neurosurgery in London as well as specialist paediatric neuroradiology training at the hospital for sick children at Great Ormond Street. I am currently Consultant Neuroradiologist and Chief Medical Officer at DMCi Ltd, a private teleradiology company. I retired from the NHS in2022.

I have been asked to review the brain imaging of Gaia Young.
I understand that there is an ongoing investigation into her death on 21st July 2021.
I will not repeat the full chronology, which is documented elsewhere, but briefly I note that Ms Young was admitted to ULCH on 17.7.21 with a history of headache and vomiting. Her conscious level deteriorated, and she had signs of an encephalopathy. A mildly low serum sodium was noted. An initial CT scan of her brain was reported as normal. She continued to deteriorate. She collapsed after a lumbar puncture. Further scans showed generalised brain swelling. Tragically she was pronounced dead on 21.7.21

I have been given the following terms of reference:

Terms of reference for an independent report by a Consultant Neuroradiologist

April 2024

1. To review and report Gaia's neuro imaging of 18-20th July 2021, in particular with reference to any indication for the aetiology and pathogenesis of Gaia's illness.
2. Please review specifically:
    - the first CT head scan of 18th July noting this was first reported by a general radiologist as showing no abnormality. Subsequent review by an on-call neuroradiologist detected abnormality on the images. Please comment on best practice for review and reporting of urgent CT imaging.
    - the first and second CT head scans for any evidence of Chiari type malformation.
3. Gaia's mother requests that you please consider the paper by Hershman and others on the radiological appearance in acute hyperammonaemic encephalopathy.

Documents attached.

1. Clinical records including imaging from UCLH.
2. Images from Specsavers One of my team will send you the link
3. Clinical records including imaging and optical coherence tomography from Moorfields Eye Hospital
4. Autopsy report for the coroner prepared by Professor S Al-Sarraj, neuropathologist, dated 07 October 2021 with addendum
5. Post-mortem report for the coroner prepared by Professor Michael Sheaff, histopathologist, dated 19 October 2021 with addendum
6. Toxicology Report from Imperial College London, dated 24 August 2021
7. a) The UCLH serious investigation report dated 07 February 2022 and 7b) action plan.
8. Review prepared by Dorit Young dated 1 January 2022 of UCLH investigation report
9. Revised memorandum prepared by Dorit Young dated 29 August 2022
10. Moorfields Eye Hospital investigation report dated 14 June 2022
11. Letter dated 7 March 2022 from Dr Ben Killingley of UCLH
12. Redacted results from Regional Genetic Laboratory, May 2023

Further results of genetic and biochemical testing as and when available

List of publications to be considered.

1. *Rose v R (Rev1)* [2017] EWCA Crim 1168 (for clinical history)
2. Mortality and Serum Sodium: Do Patients Die from or with Hyponatremia? Clin J Am Soc Nephrol. 2011 May; 6(5): 960–965. A Chawla and others
3. Fulminant idiopathic intracranial hypertension. M Thambisetty and others; Neurology 2007; 68 229 – 232
4. Ornithine Transcarbamylase Deficiency (OTC) in the Donor Liver, the Importance of Ascertaining the Cause of Death in the Brain Dead Donor. M George and others; Am J Transplant. 2017; 17 (suppl 3)
5. Urea cycle disorders: a life-threatening yet treatable cause of metabolic encephalopathy in adults. Blair NF, et al. Pract Neurol 2015;15:45–48
6. Acute Hyperammonemic Encephalopathy Resulting from Late-Onset Ornithine Transcarbamylase Deficiency M Hershman and others Radiology 2018; 287:353–

359

7. Suggested guidelines for the diagnosis and management of urea cycle disorders. Häberle et al. Orphanet Journal of Rare Diseases 2012, 7:32
8. Severe hyponatraemia due to water intoxication in a schizophrenic patient. T Day, P Nightingale. JICS Volume 9, Number 1, April 2008
9. Management of late onset urea cycle disorders – a remaining challenge for the intensivist? S Redant and others. Annals of Intensive Care 11, article number: 2 (2021)
10. What adult neurologists need to understand about ammonia. Meijer RI and others. Practical Neurology 2020 December 11
11. General Medical council “Practical skills and procedures”, (April 2019) at page 4 item 3

Review of images

CT Head 18.7.2021 at 13:14 hours

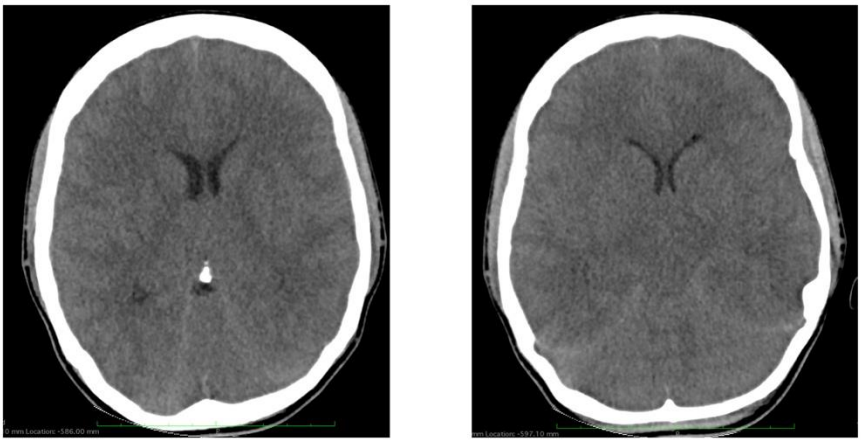
This is a routine volumetric acquisition. There is gross global cerebral and cerebellar swelling. There is effacement (literally meaning 'rubbed out': these fluid spaces should be visible but cannot be seen) of the cerebral sulci, the sylvian fissures, and the anterior interhemispheric fissure. There is loss of the normal fluid spaces around the brainstem including the peduncular cistern (the various pools of fluid around the brain are termed cisterns), the ambient cistern and the quadrigeminal cistern. There is crowding of the chiasmatic cistern. The third ventricle is not visible and is compressed. The fourth ventricle is small and is of abnormal shape; the aqueduct (a tunnel between the third and fourth ventricles) is compressed and is not visible. Cerebral grey matter generally is of low density, averaging around the high 20s in Hounsfield Units compared to an expected normal of 35. (Hounsfield units describe the opacity of a structure in an image. Structures that appear dark have a low HU; structures that appear light grey or white have a high HU).

The cerebellar tonsils are low and extend through the foramen magnum to the level of the arch of the C1 vertebra.

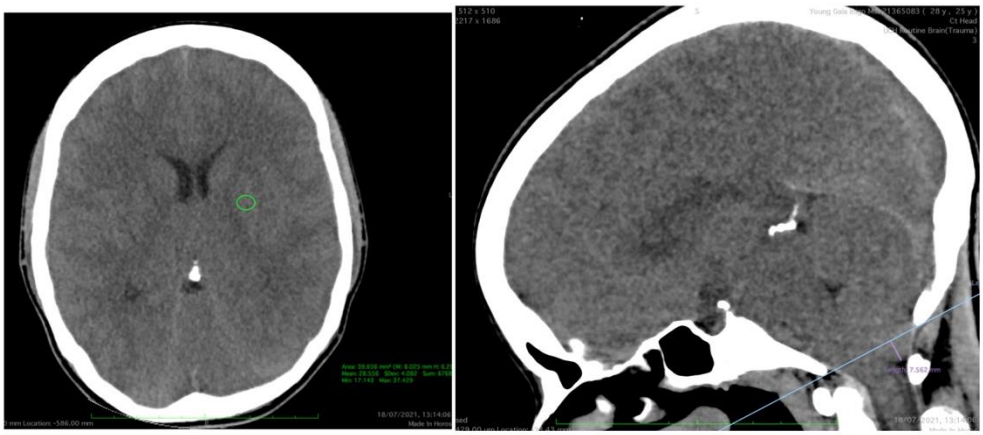
The cerebral veins appear slightly of high density but this is because of the low density of adjacent structures.

Choroid plexus is normal.

In summary, there severe cerebral and cerebellar swelling, with upward and downward herniation of the cerebellum.



Images from the 13.14 scan of 18.7.21, showing low density of cerebral and cerebellar tissue, and loss of the fluid spaces around the brainstem and cerebellum



Axial image, left, showing a mean density of the left lentiform nucleus of 28HU; and sagittal image, right, showing 7.6mm tonsilar herniation below the foramen magnum

The scan was reported as follows:

Study Date: 18/7/21 Accession No. RRV2101434 Exam Name: CT Head

Clinical Indications:
?encephalitis ? SOL ? bleed, young girl odd beahviour

Findings:
No previous neuroimaging available for comparison.

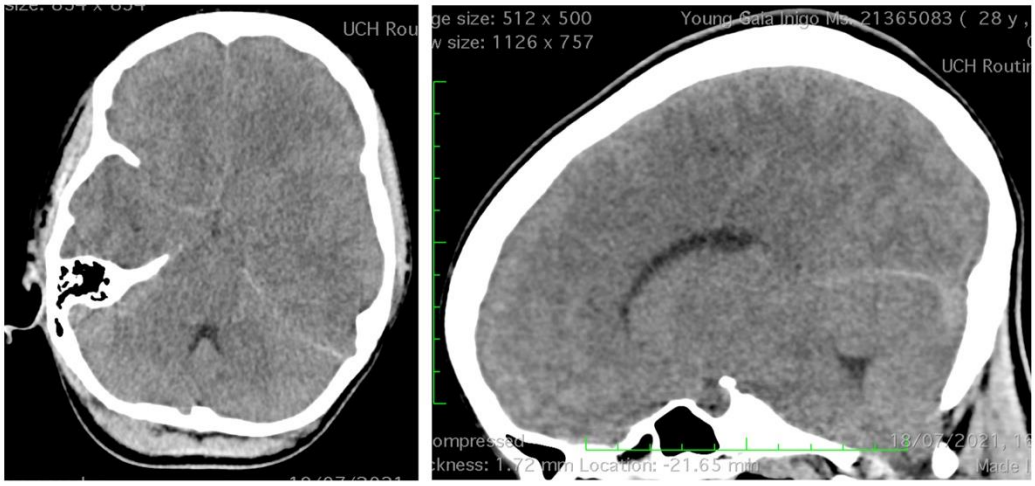
No intracranial haemorrhage. No acute infarct or mass. The ventricles and basal cisterns are patent.
No destructive bone lesion.

Impression:

No acute intracranial finding.

CT head 18.7.2021 at 16:53 hours

All the features seen on the earlier scan are again visible with generalised severe swelling, loss of sulci, loss of basal cisterns, loss of the sylvian fissures and compression of the third and fourth ventricles. The degree of descent of the cerebellar tonsils through the foramen magnum has worsened. There is also upward displacement of the cerebellum through the tentorial hiatus which is a little more marked than on the previous scan. There is slightly worse constriction of the chiasmatic cistern.



Axial, left, and sagittal images from the scan of 16.53 on 18.7.21 showing worsening swelling and tonsilar herniation

The scan was reported as follows:

Clinical Indications:
acute drop in GCS, now GCS 3, ?uintracranial bleed as per ITU consultant

Findings:

Comparison to the CT head performed 3 hours prior the same day.

There is slightly poor grey-white matter differentiation and loss of defined sulcal spaces. Findings are suspicious for generalised brain oedema. The cerebellar tonsils are at 1 cm below the foramen magnum. The ventricular system and basal cisterns are slightly effaced due to the generalised oedema.
No obstructive hydrocephalus.

No acute intra or extra-axial haemorrhage.
No major territory infarct.
No diffuse hypoattenuation within the temporal lobes on either side, however these areas are subject to beam hardening artefact from the skull base and better assessed on MRI.

Impression:

Slight degradation of grey-white matter differentiation as well as loss of sulcal spaces. Low-lying tonsils. In combination with the drop in GCS these findings are suspicious for generalised brain oedema.
No acute haemorrhage.

No infarction.
No obstructive hydrocephalus

Discussion with neurosurgery is advised.
Findings discussed with the referring team at the time of reporting.

CT head and CT venogram 18.7.2021 at 20:37 hours

Images were taken after the infusion of intravenous contrast medium. There is relatively poor opacification of the venous sinuses which reflects limited inflow due to the degree of cerebral swelling. I do not think there is evidence of significant venous thrombosis.

CT angiography has been acquired from the aortic arch up into the head. I note in the lower sections that there is opacification of the dependent parts of the lung. I am not a chest radiologist but I suspect this indicates consolidation, perhaps from aspiration .
The images show opacification of the common carotid arteries but there is no evidence of flow within the internal carotid arteries in the neck or at the skull base. There is no significant flow into the intracranial arteries.

The scan was reported as follows:

CT BRAIN , CT ANGIOGRAM NECK AND CIRCLE OF WILLIS

CLINICAL HISTORY
ICU patient post respiratory arrest - generalised cerebral oedema ? cause. severe acute intracranial hypertension. CTA and CTV advised by Neurology and Neurosurgery for ?venous sinus thrombus or ?intravascular occ FINDINGS:

Diffuse brain oedema is noted with effacement of the foramen Magnum CSF space, partial deformation of the fourth ventricle and also further defacement of the CSF spaces around the brain stem.

Loss of grey-white matter differentiation is noted.

The CT angiogram shows interruption of flow intracranially with complete loss of anterior/post previous circulation and nonvisualization of intracranial vasculature.

The neck vasculatures appear preserved

Post Aspiration changes seen in the posterior segment left upper lobe Visualised neck soft tissues are normal

CONCLUSION
Diffuse brain oedema post hypoxaemia.

There is no blood flow in the intracranial compartment as a consequence of diffuse brain oedema subsequent to hypoxia.

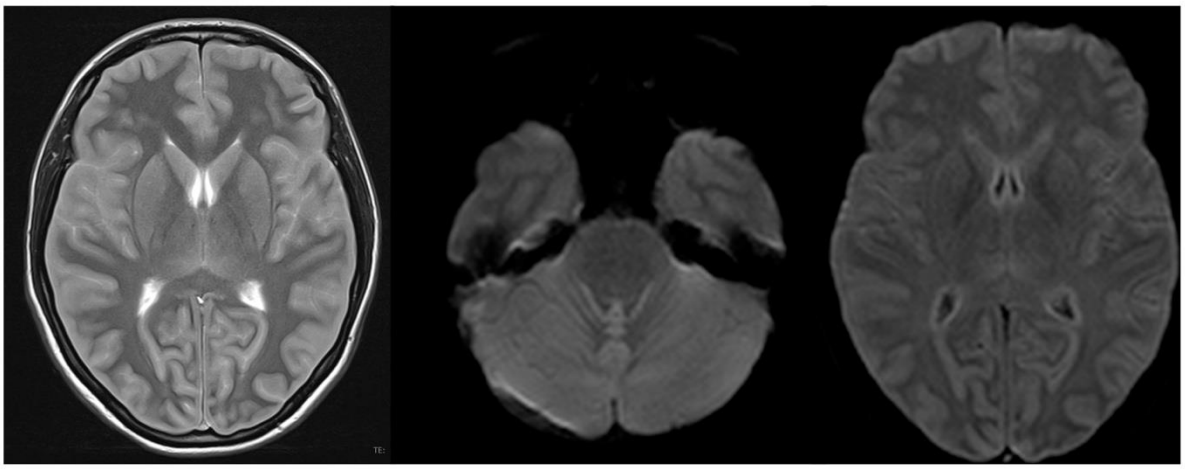
MRI brain and MRI venogram 20.7 2021 at 6:30 PM

There is marked upward and lower herniation of cerebellar tissue. There is gross abnormal signal throughout the cerebral grey matter and cerebellum. There is compression of the brainstem. There is some bright T2 signal in the thalami which likely represents ischaemic damage. There is bright signal within the internal carotid arteries and their branches, as well as the vertebral and basilar arteries indicating cessation, or at least marked reduction, of flow. Susceptibility weighted images (these images are designed to exaggerate magnetic effects within brain tissues and are primarily used to detect haemorrhage) show exaggeration of magnetic susceptibility within the cerebral veins indicating the presence of deoxyhemoglobin. This effect is not seen in the normal brain because of the presence of fully oxygenated haemoglobin, ie oxyhaemoglobin. The presence of deoxyhaemoglobin indicates very severe perfusion failure.

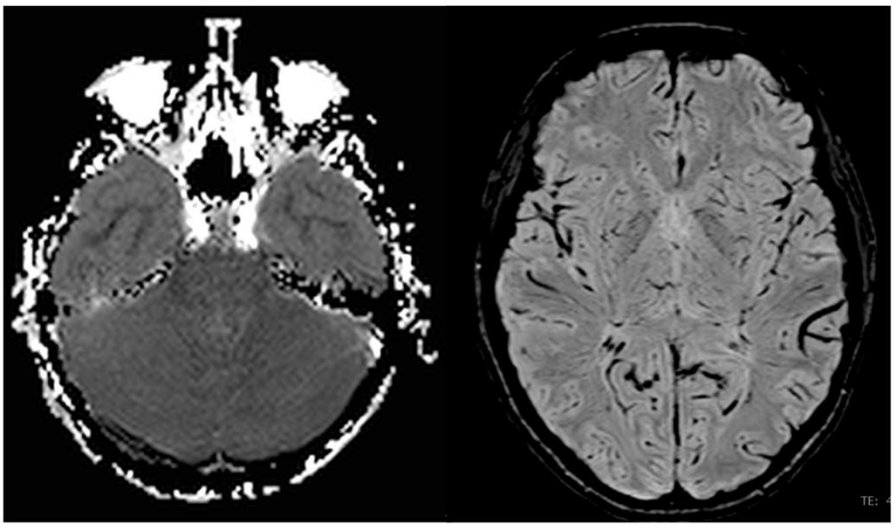
MR venography has been attempted (a technique to demonstrate flow within the cerebral veins). This is not successful due to the lack of inflowing blood into the cerebral circulation Diffusion-weighted images show extensively abnormal diffusion signal throughout the imaged cerebral and cerebellum (abnormal restriction of diffusion is seen when tissue is damaged. When severe, it usually indicates cell death). Diffusion is significantly more severely affected in the cerebellum than in the cerebral hemispheres.

The cerebral and cerebellar white matter return essentially normal signal throughout. Choroid plexus is normal.

There is focal abnormal signal in the uppermost cervical spinal cord, likely due to direct compression or possibly compression or occlusion of the anterior spinal arteries, which arise from the vertebral arteries.



Axial T2, left, and diffusion, middle and right, images showing diffuse cerebral and cerebellar cortical abnormality



Diffusion weighted image from the MRI scan of 20.7.21, left, showing more extreme abnormality in the cerebellum than in the cerebrum.
Susceptibility weighted image, right, showing deoxygenated blood in the cerebral veins

The scan was reported as follows:

Exam Name: MR Venogram MR Head with Contrast

Clinical Indications:
ICU patient, severe sudden onset cerebral oedema with unknown etiology, previously fit and well. catastrophic event with poor prognosis. MRI to investigate for possible Venous sinus thrombosis

Findings:
Comparison is made with the CT head studies dated 19 July 2021.

The MRI study confirms the presence of severe parenchymal swelling with consequent bilateral uncal, transtentorial and tonsillar herniation with compression of the cervico-medullary junction. The diffusion is diffusely abnormal throughout the cerebral hemispheres with convincing cerebellar infarction. There is trace filling of the intracranial arteries most

notably the left M1 and bilateral PCAs.

There is attenuation of the superior sagittal sinus and deep venous system with no flow signal on the MRV study. There is engorgement of the cortical veins. The transverse sinuses and sigmoid sinuses demonstrate loss of the normal flow void with trace enhancement of the left transverse sinus noted.

Ependymal signal abnormality is noted although there is no ependymal enhancement or any intracranial pathological enhancement.

Impression:

Severe parenchymal swelling with diffuse cerebral ischaemia and tonsillar herniation with cervico-medullary compression.
Poor intracranial arterial blood flow with attenuation of the superior sagittal sinus and slow flow within the transverse and sigmoid sinuses, most likely secondary to the severe cerebral swelling rather than the primary cause.

The ependymal signal abnormality raises ependymitis of possible viral aetiology although the FLAIR sequence is diffusely abnormal and the appearances may be artefactual. Happy to discuss.

Differential diagnosis of the radiology

In this section, I am considering the images almost in isolation from the clinical picture, although I make some reference to the presentation. Radiology should never be considered in isolation from the clinical picture, which is always of paramount importance. Therefore I defer to clinical colleagues regarding the final opinion regarding the cause of death.

The images show symmetrical cerebral and cerebellar cortical damage and swelling. Cerebral swelling will cause the intracranial pressure to rise, which, in turn, will result in a reduction in cerebral blood flow and eventually result in complete perfusion failure.

Cerebral blood flow relies on a gradient between blood pressure and intracranial pressure so that raised ICP reduces cerebral blood flow. As well as causing an increase in intracranial pressure, cerebral swelling will tend to compress the intracranial arteries and veins. This happens particularly in three circumstances:

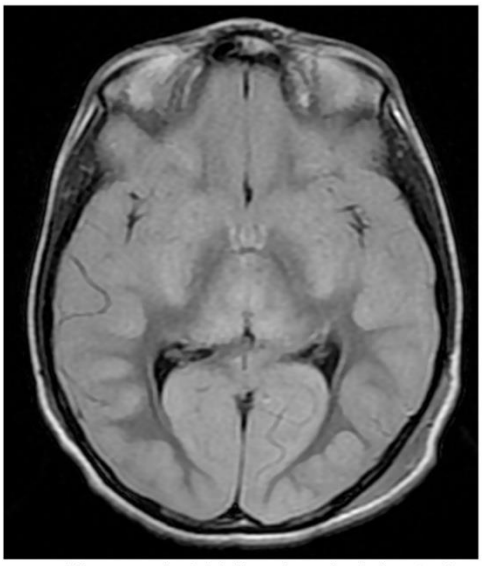
- When cerebellar tissue herniates upwards through the tentorial hiatus (the brain and cerebellum are separated by a rigid membrane called the tentorium cerebelli [literally the tent of the cerebellum]). This directly obstructs and compresses the basilar artery and the posterior cerebral arteries. These supply blood to the brainstem, cerebellum, and the posterior brain and thalami.

- When cerebellar tissue herniates downwards into the foramen magnum. This compresses the vertebral arteries, which form the basilar artery, which supplies blood to the cerebellum, and forms the posterior cerebral arteries.
- When the temporal lobes of the brain are forced underneath the tentorium ("uncal herniation"). This compresses the carotid arteries.

All three mechanisms are present, even on the first CT scan. It is therefore extremely likely that whatever caused the initial insult, the ultimate cause of death will have been global cerebral, cerebellar, and brainstem hypoxia.

The differential diagnosis of the initial insult would fall into three main groups: ischaemia/hypoxia; toxic/metabolic; and infection/inflammation.

By far the commonest cause of global cerebral swelling is following an episode of **profound global hypoxia**. This is most commonly seen after an out-of-hospital cardiac arrest, when there has been a significant interval between onset of the cardiac arrest, and restoration of circulation. Hypoxia tends to affect the most metabolically active tissue before that with lower oxygen demand, and therefore in milder cases affects only the central grey matter (basal ganglia). In more severe or prolonged hypoxia, cerebral cortex is affected, but since the cerebellum has a lower metabolic demand, it is often spared, or only involved in the most severe cases.



Library example of global hypoxia. ore the similar extensive abnormality with cortical swelling and loss of fluid spaces

Case courtesy of Bouhouche Abdeldjalil, Radiopaedia.org, rID: 173038

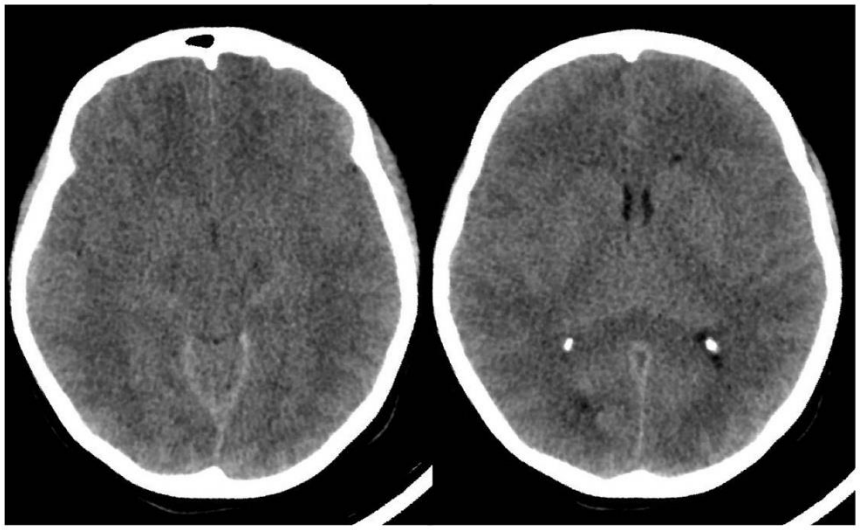
A notable feature of the scans here is that the cerebellum is more severely affected than the cerebral hemispheres, with grossly abnormal diffusion restriction on MRI.

Cerebellar hypoxia could result from severely raised ICP or severe brain herniation, but I would still expect cerebral hypoxia to be more advanced than cerebellar hypoxia, because of the lower metabolic demands of the cerebellum.

For hypoxia to cause such widespread and severe damage, there would have to be a major index event involving collapse and loss of consciousness. I defer to clinical colleagues, but I understand there was no such event.

Toxic/metabolic causes would include inborn errors of metabolism which can sometimes present for the first time in early adult life. They also include abnormalities of electrolytes and metabolites, and extrinsic poisons.

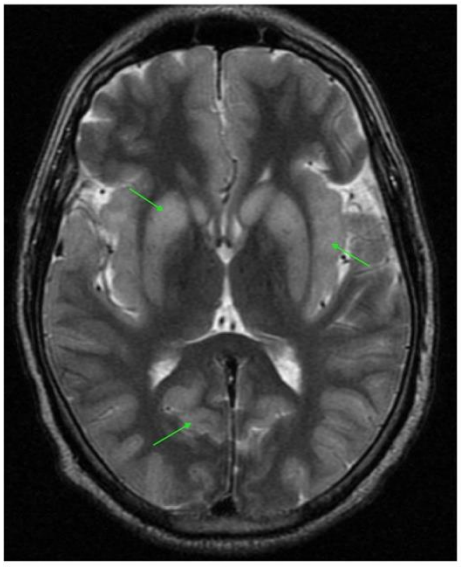
Severe hyponatraemia can lead to cerebral swelling and even death. Swelling can affect the cerebral hemispheres and the cerebellum, and its initial pattern on CT scans could exactly mimic those in this case. However, I understand that Ms Young's sodium level did not fall below 120millimole/litre, which is the level below which sequelae are said to occur, and I would not expect hyponatraemia of this level to be associated with brain swelling.



Library example: Generalised swelling due to hyponatremia Case courtesy of Yaïr Glick, Radiopaedia.org, rID: 89826

Hypernatraemia, or over-correction of hyponatraemia, can also cause brain swelling by osmotic effects; but there is no laboratory evidence to support hypernatremia.

Hypoglycaemia can cause widespread cortical swelling, but tends to spare the cerebellum, basal ganglia and thalami. I understand there was no laboratory evidence of hypoglycaemia.



Library example of hypoglycaemia causing swelling and abnormal signal in the basal ganglia, insulae and occipital lobes

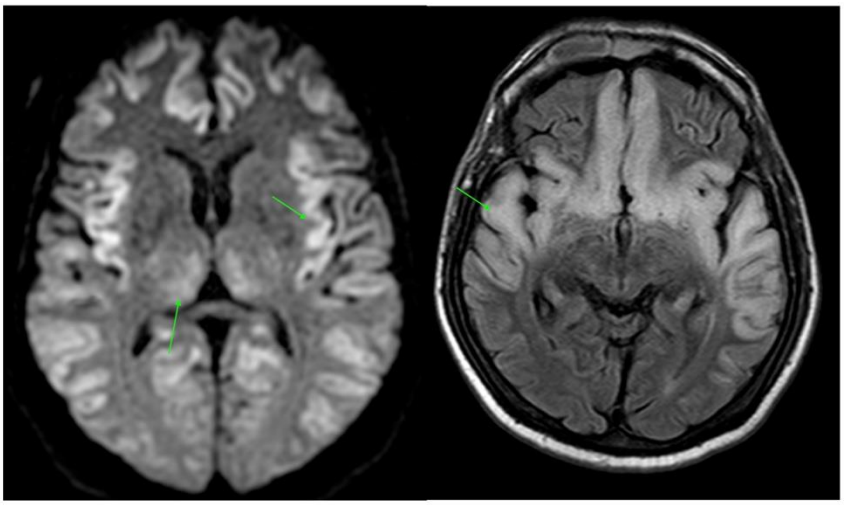
Case courtesy of Nikos Karapasias, Radiopaedia.org, rID: 25687

Similarly **hyperglycaemia** can cause cerebral swelling, usually in the context of a diabetic ketoacidosis. There was no evidence of this clinically, I understand.

High levels of urea seen in acute renal failure similarly affect the central grey matter, but I believe there was no evidence of renal failure

Hyperammonaemia is a recognised cause of brain swelling. It is most commonly seen in the context of liver failure, and I understand there was no clinical evidence of hepatic disease.

Moderate hyperammonaemia causes high signal on MRI scans within the insulae, thalami, internal capsules and cingulate gyri. At higher levels, there can be diffuse cortical oedema, although the occipital lobes and brain around the motor and sensory gyri are often spared: they were involved in Ms Young’s scans.

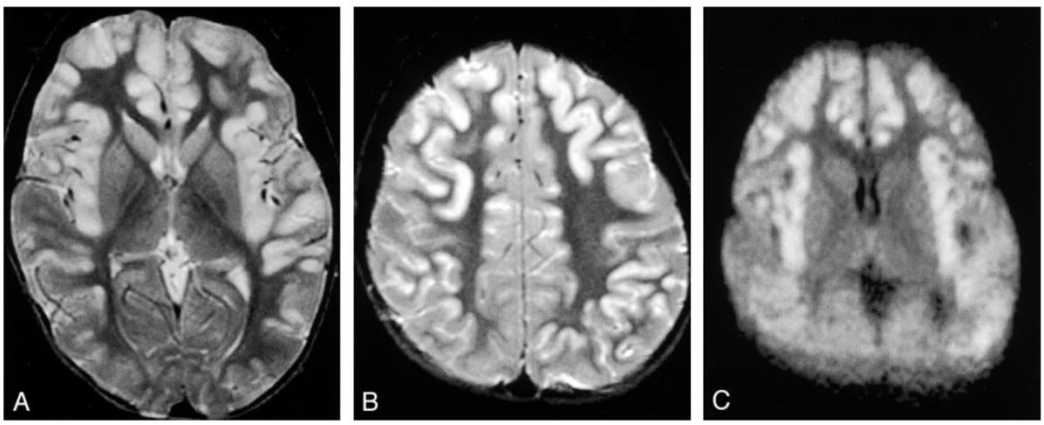


Library examples of hyperammonaemia with typical distribution in basal ganglia, insulae, thalami, and temporal cortex, sparing the occipital lobes

Case courtesy of Andrew Dixon, Radiopaedia.org, rID: 39037

Case courtesy of Sanhita Shyam Pokle, Radiopaedia.org, rID: 189197

Ornithine transcarbamylase deficiency is an inborn error of metabolism that may present in adult life. It is one of the enzymes involved in the metabolism of urea, and affects the brain in a similar way to other abnormalities of the urea cycle or other causes of hyperammonaemia. The CT and MRI scan appearances usually reflect hyperammonaemia, and are not specific to the condition. Fatalities are reported, and the published examples in the literature that I have been able to review reveal less extensive abnormality that in Ms Young's case.



An example of Ornithine Transcarbamylase deficiency taken from the literature. Note the similar distribution to the case of hyperammonaemia

Images from Brain MR Imaging in Acute Hyperammonemic Encephalopathy Arising from Late-Onset Ornithine Transcarbamylase Deficiency
Jun-ichi Takanashi. AJNR Am J Neuroradiol 24:390–393, March 2003

Mitochondrial enzyme defects can cause encephalopathy. Of these, **Leigh disease** and **MELAS** (mitochondrial encephalomyelopathy lactic acidosis and stroke like episodes) can present in early adult life. Leigh disease typically affects the central grey matter, and brainstem, but spares the cortex and the cerebellum. MELAS involves cortex, mimicking stroke, but this is usually limited in extent, and I am not aware of a case involving the entire cerebrum.

Poisons such as methanol and ethylene glycol cause encephalopathy and can be fatal in relatively low dose.

Methanol primarily affects the lateral parts of the basal ganglia (putamena), optic nerves, cerebral white matter, and the cerebellum. I have not seen diffuse cortical involvement, but I have not seen any cases severe enough to result in death. Limited views of the optic nerves on the MRI scan of 20.7.21 do not show any optic nerve abnormality, although the scans are not targeted at the orbits.

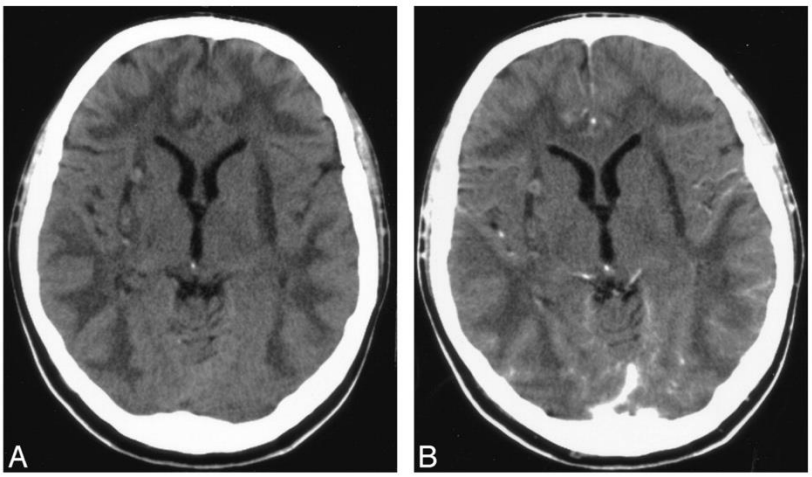


illustration of methanol poisoning taken from the literature

CT and MR Imaging Findings in Methanol Intoxication
M. Blanco, R. Casado, F. Vázquez and J.M. Pumar
AJNR 2006 27 452-454

Ethylene glycol poisoning can be fatal, and causes brain oedema, although scan changes are usually most obvious in the thalami, basal ganglia and brainstem. I have seen a case of ethylene glycol poisoning diffusely involving cerebral cortex.

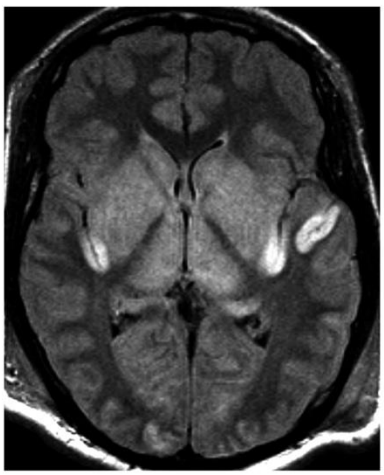


Illustration of ethylene glycol poisoning. Note the basal ganglia, thalamic and insular involvement

Toxic and Acquired Metabolic Encephalopathies: MRI Appearance
Pranshu Sharma, Muneer Eesa, and James N. Scott AJNR 2009, Volume 193, Issue 3

Illicit drugs, or the substances used to dilute them, can be associated with a severe encephalopathy. These would include **opioids, cocaine, and MDMA** (Ectasy) . I understand a drug screen was negative in Ms Young's case, and there were no lifestyle indications of drug use.

Infectious/inflammatory causes of encephalopathy would include viral infections. **Herpes, cytomegalovirus (CMV) and chicken pox** can all be associated with an encephalopathy, but it is usually confined to the temporal lobes, and spares the cerebellum.

In children, **fulminant cerebellitis** can present with atypical clinical signs not suggestive of cerebellar dysfunction, and deaths are reported. Cerebellitis is seen in adults but is usually relatively mild. It may be associated with viral infection or autoimmune states. I have no personal experience of fulminant disease, but one would expect hydrocephalus as a result of compression of the 4th ventricle, and Ms Young's ventricles were small due to cerebral swelling. Cerebellitis does not primarily affect the cerebral hemispheres, but one could invoke secondary hypoxia due to vascular compression as a possible cause of coincident cerebral damage.

Opinion.

The first CT scan taken at 1pm on July 18th is very abnormal. I am sorry to say that the report of the scan fails to record severe cerebral swelling, abnormal brain density; compression of the third ventricle; loss of the basal fluid spaces; and hindbrain herniation.

I have no doubt that if it had been correctly reported, a lumbar puncture would not have been attempted. Such severe herniation represents an absolute contra-indication to lumbar puncture.

In my opinion, it is likely, although I would defer to senior clinical colleagues, that the catastrophic collapse in Ms Young's condition following the lumbar puncture was due to 'coning', where the increased pressure gradient induced between the cranial and spinal compartments causes a further descent of the hindbrain into the foramen magnum, resulting in brainstem and vascular compression.

The second and third scans showed progression of all abnormalities present in the first scan, and, in my opinion, were correctly reported, although I quibble with a few minor details. I also think that the significance of some of the findings was under-emphasised.

For example, the CT angiographic images showed a lack of flow in the internal carotid arteries, and the intracranial arteries. This is incompatible with life. In some countries, this finding has been used to confirm brain death, and very sadly, I think Ms Young's condition was almost certainly unsurvivable from the evening of the 18th July, if not earlier.

Subsequent MRI images unfortunately shed no further light. The brain is irretrievably globally damaged, but to my knowledge, the pattern is not specific to any given condition.

Conclusion

It is clear that Ms Young died from a massive cerebral insult resulting in global cerebral and cerebellar perfusion failure. I do not know what caused the insult. I defer to clinical colleagues, but I see no evidence to suggest a global hypoxic event, which would have had to have been at the severity of a cardiac or respiratory arrest. My feeling on the scans is that a toxic or metabolic cause is the most likely, but even then the degree of damage and rapidity of onset is extreme, and the global extent of the damage lacks any specific feature that allows confident identification of the cause. The most likely intrinsic metabolic origin would be within the urea cycle/ammonia pathway, although I note the absence of abnormality in the

biopsy taken from Ms Young's liver, and the negative genetic screen. I wonder if it possible that Ms Young unknowingly ingested a neurotoxic substance.

My personal experience in treating patients with aneurysmal subarachnoid haemorrhage has included a small number of tragic events whereby I witnessed the occurrence of subarachnoid haemorrhage in young patients which led to an immediate global shutdown of cerebral blood flow, and to the death of the patient. These lead me to consider the role of cortical spreading depolarisation in acute brain injury, and I speculate that spreading depolarisation may play in role, particularly in young people, by magnifying and extending the breadth and depth of cerebral perfusion failure following an acute event.

I offer my sympathy to Lady Young and her family following this tragic event.

Appendix

I have been asked for my comments on some scientific and legal papers.

1. *Rose v R (Rev1)* [2017] EWCA Crim 1168 (for clinical history)
    - *This concerns the sudden, initially unexplained death of a young person who presented with headache and confusion, and who was eventually found to have died from acute hydrocephalus caused by obstruction of the 4th ventricle. The question has arisen, could there have been an undetected structural abnormality in Ms Young's brain that led to a subsequent deterioration?*
    - *I do not think there is any real similarity between the cases. Unfortunately, undiagnosed hydrocephalus is a recognised cause of death and disability. There was no underlying structural abnormality in Ms Young's brain.*
2. Mortality and Serum Sodium: Do Patients Die from or with Hyponatremia? Clin J Am Soc Nephrol. 2011 May; 6(5): 960–965. A Chawla and others
3. Severe hyponatraemia due to water intoxication in a schizophrenic patient. T Day, P Nightingale. JICS Volume 9, Number 1, April 2008
    - *These two papers discuss the cause and effect of severe hyponatremia. Both hypo-and hypernatraemia can result in cerebral cortical damage. I would agree that it seems likely that deaths associated with hyponatremia are related to the underlying condition causing hyponatremia rather than the low sodium per se. Raised intracranial pressure can cause variation in sodium levels, and is likely the cause of the low to moderate hyponatremia in Ms Young's case.*
4. Fulminant idiopathic intracranial hypertension. M Thambisetty and others; Neurology 2007; 68 229 – 232
    - *This paper describes acute onset severely raised intracranial pressure. Although described a fulminant IIH, the onset was acute, with the patients presenting with visual loss rather than collapse. I do not think IIH is a viable diagnosis here.*
5. Ornithine Transcarbamylase Deficiency (OTC) in the Donor Liver, the Importance of Ascertaining the Cause of Death in the Brain Dead Donor. M George and others; Am J Transplant. 2017; 17 (suppl 3)
6. Urea cycle disorders: a life-threatening yet treatable cause of metabolic

encephalopathy in adults. Blair NF, et al. Pract Neurol 2015;15:45–48

7. Acute Hyperammonemic Encephalopathy Resulting from Late-Onset Ornithine Transcarbamylase Deficiency. M Hershman and others. Radiology 2018; 287:353–359
8. Suggested guidelines for the diagnosis and management of urea cycle disorders. Häberle et al. Orphanet Journal of Rare Diseases 2012, 7:32
9. Management of late onset urea cycle disorders – a remaining challenge for the intensivist? S Redant and others. Annals of Intensive Care 11, article number: 2 (2021)
10. What adult neurologists need to understand about ammonia. Meijer RI and others. Practical Neurology 2020 December 11.

- *These papers describe the consequences of severe hyperammonaemia, and the rare diagnosis of OTC deficiency presenting in adults. The routine measurement of ammonia levels is recommended in patients presenting with an acute undiagnosed encephalopathy. I agree that hyperammonaemia is a possible cause for the scan findings in Ms Young's case, although sparing of the occipital lobes would be expected, and was not seen. However, it must be possible that in extreme cases, the whole cerebrum may be affected.*

- General Medical council "Practical skills and procedures", (April 2019) at page 4 item 3

    - *I defer to clinical colleagues regarding the use of ophthalmoscopy before lumbar puncture in this case*.

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January 2025