Hypocortisolaemia masquerading as anaphylaxis

Sarah Kennie[1], Linda Nel[1], Jana Bujanova[2], Adam Ditchfield[3] and Efrem Eren[4]

1Shackleton Department of Anaesthesia, University Hospital Southampton NHS Foundation Trust, Southampton, UK 2Department of Endocrinology, University Hospital Southampton NHS Foundation Trust, Southampton, UK 3Department of Radiology, University Hospital Southampton NHS Foundation Trust, Southampton, UK 4Department of Allergy and Immunology, University Hospital Southampton NHS Foundation Trust, Southampton, UK

Correspondence to **kenniesarah@gmail.com**

University Hospital Southampton NHS Foundation Trust

INTRODUCTION - Profound hypotension is a recognised clinical feature of both anaphylaxis and an acute hypoadrenal state. Central hypoadrenalism is seen in intra-cranial disease processes affecting the hypothalamic–pituitary–adrenal axis. We present an unusual case of apparently typical peri-operative anaphylaxis in a man with intra-cranial lymphoma, the anaphylaxis was treated as such but the negative allergy testing led to a subsequent diagnosis of hypocortisolaemia being made. The patient and his relatives gave permission for his case to be discussed in medical literature.

Case description

- A 69 year old man presented to a neurosurgical centre for urgent biopsy of a posterior fossa lesion ?intra-cranial lymphoma (see Image 1). He had been transferred from a DGH where he had received initial treatment for a presumed ischaemic cerebellar stroke after presenting with vertigo and vomiting. 4 months prior to this, he was diagnosed with diabetes insipidus and hypogonadotrophic hypogonadism. Initial assessment of his adrenocortical function appeared normal. An MRI of the pituitary was also normal.
- The biopsy procedure was deferred for 1 week due to previous antiplatelet therapy. Dexamethasone was withheld to avoid tumour shrinkage prior to the biopsy. [1]
- The patient underwent general anaesthesia for biopsy of his posterior fossa. Anaesthesia was induced with TIVA (propofol, remifentanil) , 90mg of rocuronium was also given to aid intubation. Immediately following induction, he became profoundly hypotensive, this was unresponsive to first measures (ephedrine) but ultimately responded to intravenous fluid and adrenaline (boluses followed by an infusion). Intravenous hydrocortisone and chlorphenamine were given, as per AAGBI guidelines. [2] He was admitted to the Neurosciences Intensive Care Unit (NICU) with a working diagnosis of anaphylaxis. The suspected trigger agents were remifentantil, propofol and rocuronium; with the latter deemed the most likely.
- Dexamethasone was commenced on NICU. Unfortunately, the patient developed a Takotsubo cardiomyopathy secondary to resuscitative adrenaline. In terms of allergy testing, blood which had been taken prior to the reaction was tested for specific IgE antibodies for pholcodine and suxamethonium (which could have been suggestive of possible rocuronium allergy), and for chlorhexidine. These were all negative. Serum tryptase levels were taken at 1, 3 and 24 hours after the event. No deflection from a normal baseline was demonstrated. None of these results were considered to have made the diagnosis of anaphylaxis less likely.
- The neurosurgical plan was to wean dexamethasone and plan for a repeat procedure at a later date, pending a full assessment in the anaesthetic allergy clinic. Dexamethasone was weaned on NICU. Prior to stopping it completely, the NICU medical team ensured that this patient did not previously take any steroids regularly. Following an endocrine review, he was discharged home on his previously prescribed desmopressin, levothyroxine and testosterone.
- 19 days after being discharged, he required a short course of dexamethasone for neurosurgical symptom control. A concurrent repeat CT brain revealed stable intracranial appearances with no change in ventricular volume. 22 days later, he presented to anaesthetic allergy clinic for formal allergy testing at which time he was no longer taking dexamethasone. Unfortunately, he was unwell with sepsis due to a likely aspiration pneumonia. This resulted in a second NICU admission. Dexamethasone was re-started.
- The scheduled allergy testing was carried out during this inpatient admission, approximately 8 weeks following the index event. A Basophil activation assay (Histamine release assay, Reflab Copenhagen) did not show positive results for any neuromuscular blocking drugs or chlorhexidine. Skin prick and intradermal tests were negative for all drugs tested (propofol, remifentanil, chlorhexidine, rocuronium, fentanyl and cisatracurium). This panel of negative allergy tests, in combination with the observed clinical deteriorations when off steroids alongside other endocrine abnormalities, led to a suspicion of hypocortisolaemia being the underlying reason for the index episode of cardiovascular collapse. Regular oral hydrocortisone supplementation was started. A general anaesthetic with additional steroid cover was deemed safe.
- On day 12 of this admission, he underwent the planned neurosurgical procedure (posterior fossa biopsy) via a burrhole incision. The anaesthetic was uneventful, and the drugs used were propofol, remifentanil and rocuronium. Additional perioperative steroids were given as planned. After initially waking uneventfully postoperatively, he rapidly developed complications related to a posterior fossa bleed. This necessitated emergency posterior fossa craniectomy and haematoma evacuation (see Image 2). Sadly, he failed to recover neurologically from this complication and died from a hospital acquired pneumonia 2 months later. Histology did indeed confirm a non GC type diffuse large B cell lymphoma.

References

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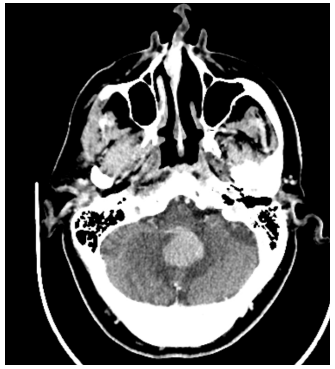

Image 1 – suspected cerebral lymphoma on CT head with contrast.

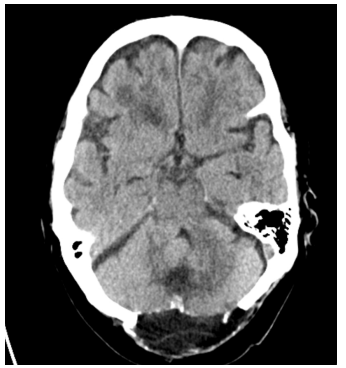

Image 2 – following emergency posterior fossa craniectomy.

Discussion and key learning points

- We believe that the unifying diagnosis for this patient's apparent anaphylaxis was hypocortisolaemia secondary to intra-cranial pituitary and/or hypothalamic lymphoma infiltration. Anaphylaxis had been ruled out and the drugs used at the index general anaesthetic were used again without incident, once the patient was receiving a maintenance dose of hydrocortisone. Serial imaging was reviewed retrospectively by a neuroradiologist, images were inclusive of the first MRI brain that was performed to investigate diabetes insipidus. Microscopic infiltration that was not visible radiologically is a possible explanation, this has been described in a case series comparing primary CNS lymphoma appearances on MRI and autopsy. [3]
- We felt that this was of relevance to anaesthetic practice due to the unrecognised hypocortisolaemia that presented as anaphylaxis. In NAP6, anaphylaxis presented within 5 minutes in 66% of cases, furthermore hypotension was the presenting feature in 46% of cases. [4] The unexplained anterior and posterior hypopituitarism in this patient, despite normal radiological pituitary appearances, may have been secondary to microscopic infiltration from the suspected intra-cranial lymphoma. Diffuse infiltration has previously failed to correlate with the burden of disease on MRI. [3]
- In summary, patients with evidence of abnormal pituitary function should be specifically considered for peri-operative steroid cover. In this case, there was significant associated immediate morbidity (Takotsubo cardiomyopathy) resulting from the adrenaline required to maintain cardiovascular function. Full guidelines for peri-operative steroid administration are available and include treatment in the post-operative period. [5]