

THINK BEYOND SEPSIS:

Common themes from two maternal deaths secondary to haemophagocytic lymphohistiocytosis

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PURPOSE

The Maternity & Newborn Safety Investigation (MNSI) programme perform independent investigations of maternal deaths in England. They then outline safety recommendations to improve services locally and nationally.

MNSI sought to ascertain shared themes following two maternal deaths secondary to HLH and consider learning points for future clinicians and investigators.

MNSI INVESTIGATION PROCESS

MNSI investigations

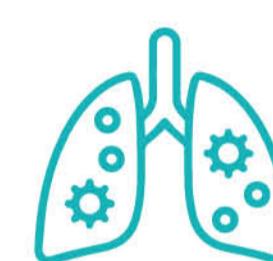
With a focus on system factors (not individuals), MNSI:

- ✓ Looks to understand what happened and why it happened (what made sense at the time).
- ✓ Involves families and staff, throughout the investigation.
- ✓ Draws on clinical advisors for clinical input.
- ✓ Undertakes analysis of what is found.
- ✓ Identifies areas for learning locally and nationally to improve maternity safety.
- ✓ Produces a learning report at the end of the investigation.

Haemophagocytic lymphohistiocytosis (HLH)

is a hyperinflammatory sepsis-like syndrome with high mortality characterised by persistent fever and multi-organ dysfunction. Immunosuppression (e.g., anakinra, steroids, IVIg) typically needed to buy time, stabilize, & find trigger.

WHAT CAN TRIGGER HLH?



Infection



Cancer



Autoimmunity



Genetic mutations

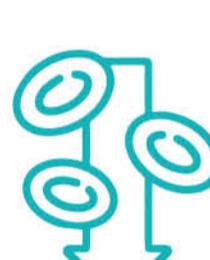
WHEN SHOULD I CONSIDER HLH?



Fever



High ferritin



Falling cell counts



Pregnancy & labour may also contribute to HLH risk

RESULTS

Autoimmune rheumatic disease (AIRD)

AIRD is a common trigger for HLH among young females & AIRD flare risk is increased postpartum – inadequate immunosuppression alongside changes in maternal immunity postpartum may allow transition to HLH.

Delays in immunosuppression due to concerns for sepsis

Both women had fever alongside multi-organ dysfunction. Despite HLH features & ongoing deterioration on broad spectrum antibiotics, ongoing concern for sepsis and diagnostic uncertainty for HLH led to hesitancy immunosuppressing – anakinra has safety data for use in the context of infection*.

HLH diagnosis made by rheumatologist due to known AIRD

In both individuals the possibility of HLH was first made by a rheumatologist consulted for the mothers known AIRD. Given limited awareness of HLH in many obstetric departments – it raises the possibility that mothers with HLH from alternative triggers (e.g., infection) are being missed.

*Opal S et al. Confirmatory interleukin-1 receptor antagonist trial in severe sepsis: a phase III, randomized, double-blind, placebo-controlled, multicenter trial. Crit Care Med. 1997.

TAKE HOME POINTS

FOR CLINICIANS



Think beyond sepsis in the critically unwell febrile mother



Screen for HLH using the 3 Fs of Fever, Falling cell counts and high Ferritin; consult guidelines for investigation*



Hesitancy in utilising immunosuppression delays care – seek support (e.g., national HLH MDT, or specialist center)

FOR SAFETY INVESTIGATORS



Explore whether non-bacterial causes were considered in women dying of “sepsis” e.g., HLH, disseminated herpes simplex virus, thrombotic microangiopathies



Evaluate for HLH retrospectively by examining obs charts, laboratory parameters (e.g., cell counts, ferritin), biopsies & imaging (e.g., hepatosplenomegaly)



A search satisfying bias may occur – a team continues to manage the case as bacterial sepsis despite ongoing deterioration whilst on antibiotics



Do staff feel empowered to question the diagnosis?



Are formal debiasing strategies in place (e.g., internal MDT, route for seeking external opinion)?

*Cox MF et al. Diagnosis and investigation of suspected haemophagocytic lymphohistiocytosis in adults: 2023 Hyperinflammation and HLH Across Specialty Collaboration (HiHAS) consensus guideline. Lancet Rheum. 2023.



To find out more about MNSI and our investigations or to attend a webinar discussing this topic further please scan the QR code.

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If you're interested in the association between HLH & pregnancy, I'd love to hear from you – please get in touch!

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