

Think beyond sepsis:

Common themes from two maternal deaths
secondary to haemophagocytic
lymphohistiocytosis (HLH)

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Sepsis-like syndrome

Can be **genetic**, but in adults usually secondary to...



Infection



Cancer



Autoimmunity



Genetic mutations

Use **immunosuppression** to buy time, stabilise, find & treat the trigger – anakinra, corticosteroids & intravenous immunoglobulin

Look for the three Fs: **Fever**, **Falling** cell counts and hyper**Ferritinaemia**



Fever



High ferritin



Falling cell
counts

Pregnancy-associated HLH

- ↗ **High mortality** reported in HLH - 8 HLH deaths reported in 9 years via MBRRACE-UK
- 👤 **Pregnancy / labour** may also contribute to HLH risk
- 📖 United Kingdom Obstetric Surveillance System (**UKOSS**) 5-year prospective UK-wide study of HLH in pregnancy and up to 6-weeks postpartum – due to open late 2024

Maternity and Newborn Safety Investigations (MNSI)

The Maternity and Newborn Safety Investigations (MNSI) programme investigates patient safety events, working closely with staff, trusts and families, aiming to improve maternity safety in England.

They carry out an independent investigation and, where relevant, make safety recommendations to improve services at local level and across the whole maternity healthcare system in England.

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.

Common themes & questions



Two maternal deaths secondary to HLH investigated by MNSI

Both had underlying **autoimmune rheumatic disease** (AIRD)

Teams were concerned regarding **immunosuppression** in context of sepsis-like illness

Neither discussed at an **HLH MDT**



Are we missing cases of HLH not associated with AIRD?



When do teams consider alternative diagnoses in setting of a sepsis-like illness?



Treatment decisions often complex - do teams know how to access support of the national MDT in the UK?

Take home messages 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)

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

Take home messages for safety investigators



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



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



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



Do staff feel empowered to question the diagnosis?



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



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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