

An Unusual Case of Postpartum Fever: Haemophagocytic Lymphohistiocytosis in Pregnancy

Sophia Violaris¹, Sujatha Thamban, Bethan Goulden, Kate Wiles
Whipps Cross University Hospital, Barts Health NHS Trust

Case Report

1. Delivery

43F P2 , nil PMHx

EMCS for pathological CTG

Treated for postnatal sepsis
Discharged day 13

3. ITU admission

Rapid deterioration with progressive multiorgan failure

- T1 RF, severe ARDS, intubated requiring 100% FiO2 with SpO2 80-90%
- Anuric, Stage 3 AKI
- Coagulopathy
- Referred for ECMO

2. Persistent fever with no source of infection

- 8x negative blood cultures, 4x negative urine cultures, 4x negative CT scans
- No clinical response to 9 antibiotics, 2 antivirals and anti-fungals

3. Pancytopenia

4. Lymphadenopathy

5. Empirical treatment

Risk to life > risk of treatment

Pulsed intravenous methylprednisolone started

Anakinra started (IL-1 antagonist)

Day 1-13

Day 20

Day 21

Day 22

Day 23

Day 24

Day 25-36

2. Re-admission

7-day history of daily fevers
No focal infective symptoms
No travel history or unwell contacts.

Treated for postpartum sepsis with broad-spectrum antibiotics

4. ?HLH

Hyper-inflammatory response in absence of infection

However, low H-score based on current investigations + inconclusive bone marrow biopsy

5. Recovery

- Rapid clinical response to steroids
- Afebrile within 8 hours
- FiO2 weaned to 40% within 24 hours

Extubated on day 28, discharged on day 36

Discussion

HLH is a rare but important differential to consider in the febrile pregnant or post-partum woman, conferring significant morbidity and mortality if not rapidly treated. Non-specific symptoms and clinical overlap with other syndromes, notably sepsis, make diagnosis challenging. The H-score is a useful tool for assessing probability of HLH based on biochemical, histological and clinical parameters, however, is not validated for use in pregnancy or puerperium.

Bone marrow biopsy is considered diagnostic “gold standard” but negative biopsy does not exclude HLH.

There are no guidelines for management of HLH in pregnancy. In practice, immunosuppression remains the cornerstone of treatment. This is best done within a multidisciplinary team, alongside advice from a specialist HLH MDT. Immunosuppression should be viewed as the starting point of treatment. Diagnosis should prompt further investigations to identify underlying triggers, including a full immunological, histological and genetic work-up.

Background

HLH in Pregnancy

- 2 deaths in latest MBRRACE report (2020) attributable to HLH
- 36 cases in literature with 7 deaths
- 12 cases attributed solely to pregnancy
- Other reported triggers include viruses (EBV, HSV CMV), infection (malaria, liver abscess), autoimmune disease (SLE, Sjogren's) and malignancy (lymphoma)

Whilst pregnancy is a recognized trigger for HLH, a thorough search for other causes is essential

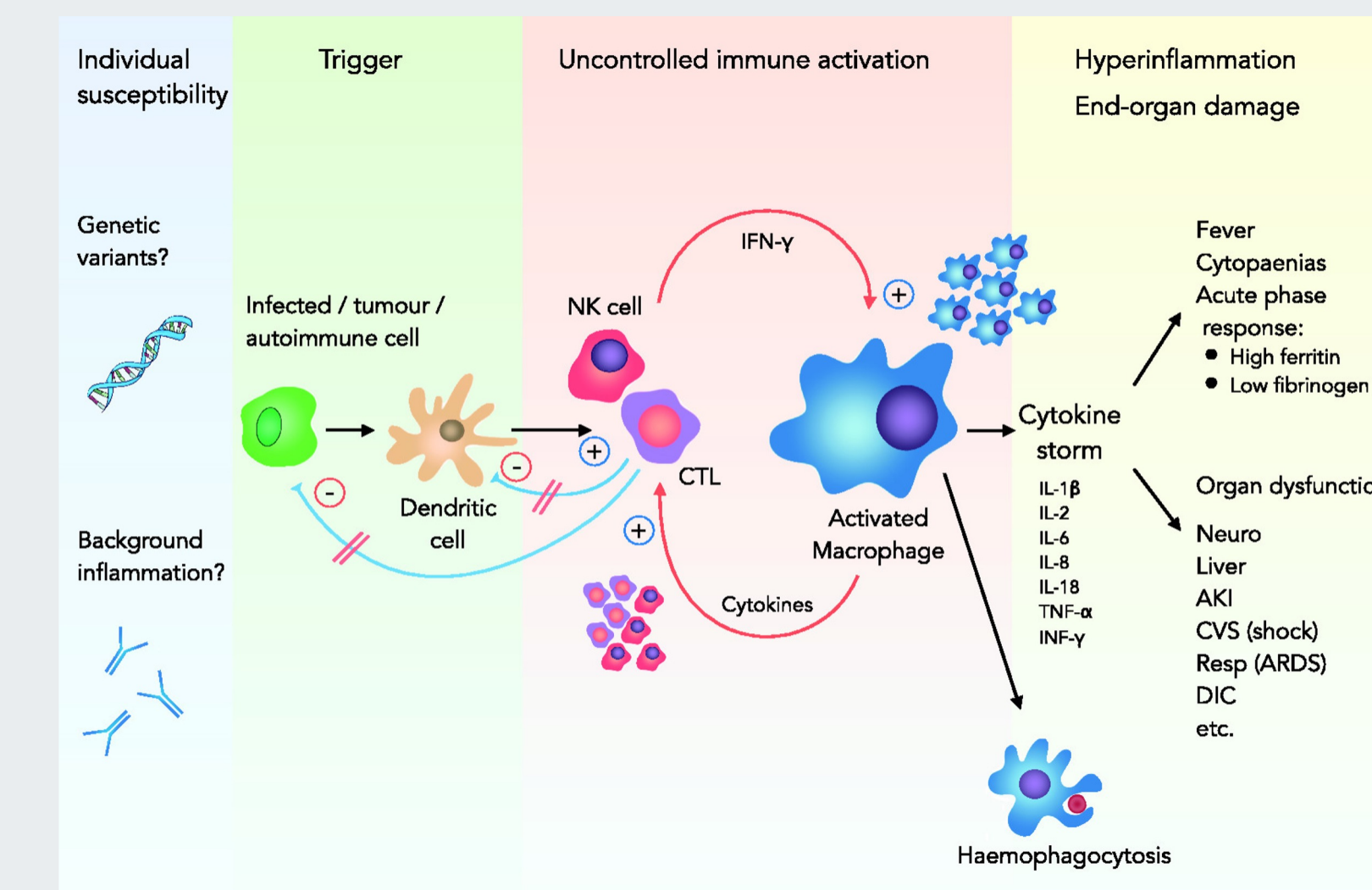
Pathophysiology of HLH

Haemophagocytic Lymphohistiocytosis is a rare but life-threatening systemic inflammatory disorder persistent fever, cytopenia and multi-organ dysfunction

1. Defects in natural killer cells and cytotoxic T cells. Immune deficiency may be genetic (primary HLH) or acquired by a recognized trigger (secondary HLH)

2. This leads to a failure to clear antigens from tumour cells, autoimmune cells or antigen presenting dendritic cells.

3. Persistent antigen stimulation leads to macrophage and cytotoxic T cell activation > a self-perpetuating cytokine storm and haemophagocytosis.



Bauchmuller K et al. Journal of the Intensive Care Society. 2020

Principles of Management

Acute treatment

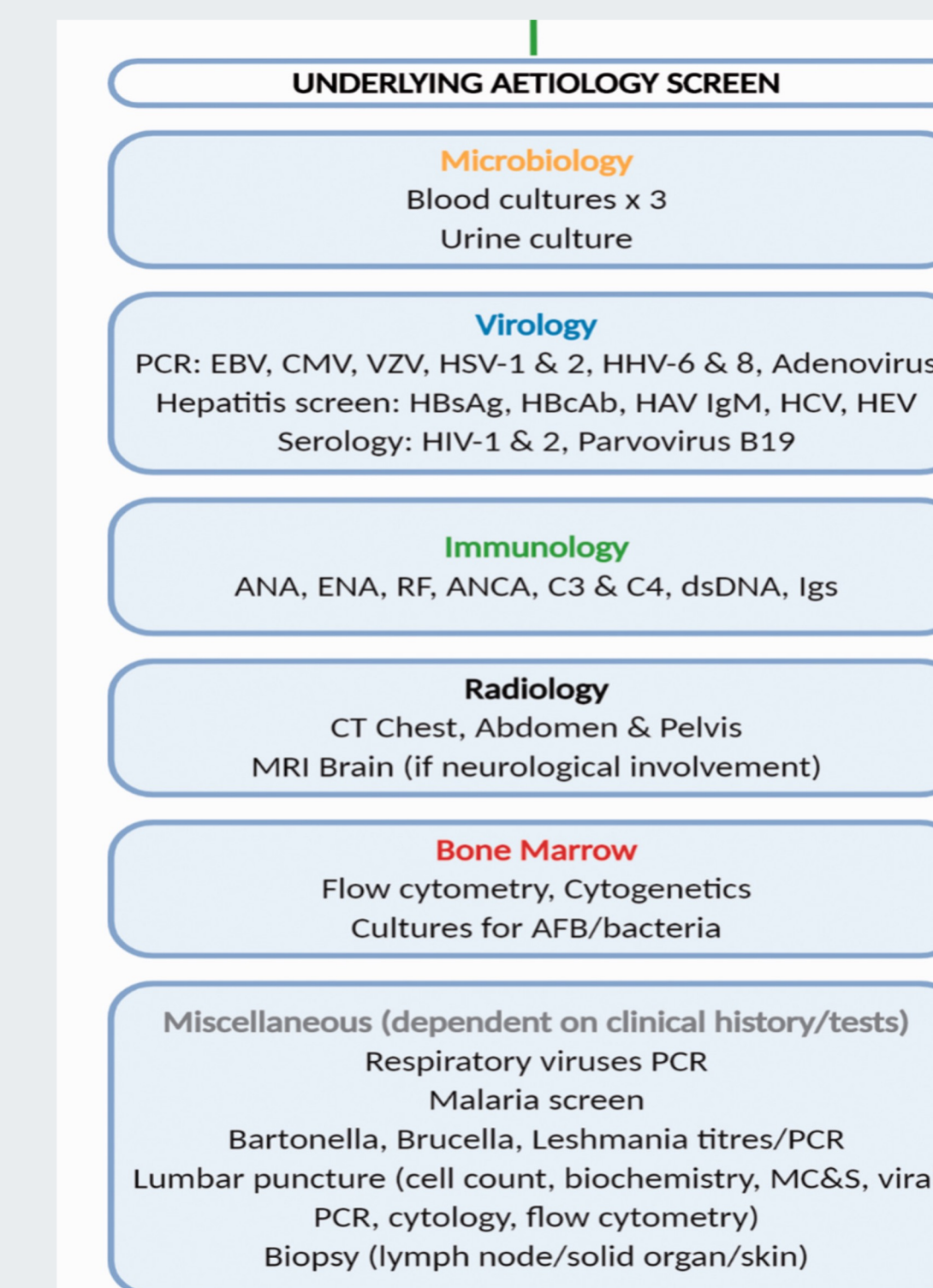
- Immunosuppression to treat extreme, unregulated inflammation.
- Cornerstone medications: steroids, anakinra (IL-1 antagonist), IVIg, cyclosporin

Identify trigger

- Screen for underlying aetiology

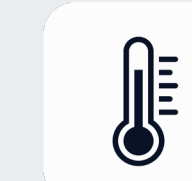
Counselling

- Recurrence risk in future pregnancies discussed on a case-by-case basis



Wilson-Morkeh H et al. Obstetric Medicine. 2021

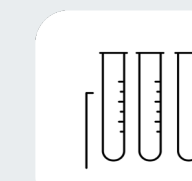
Features of HLH



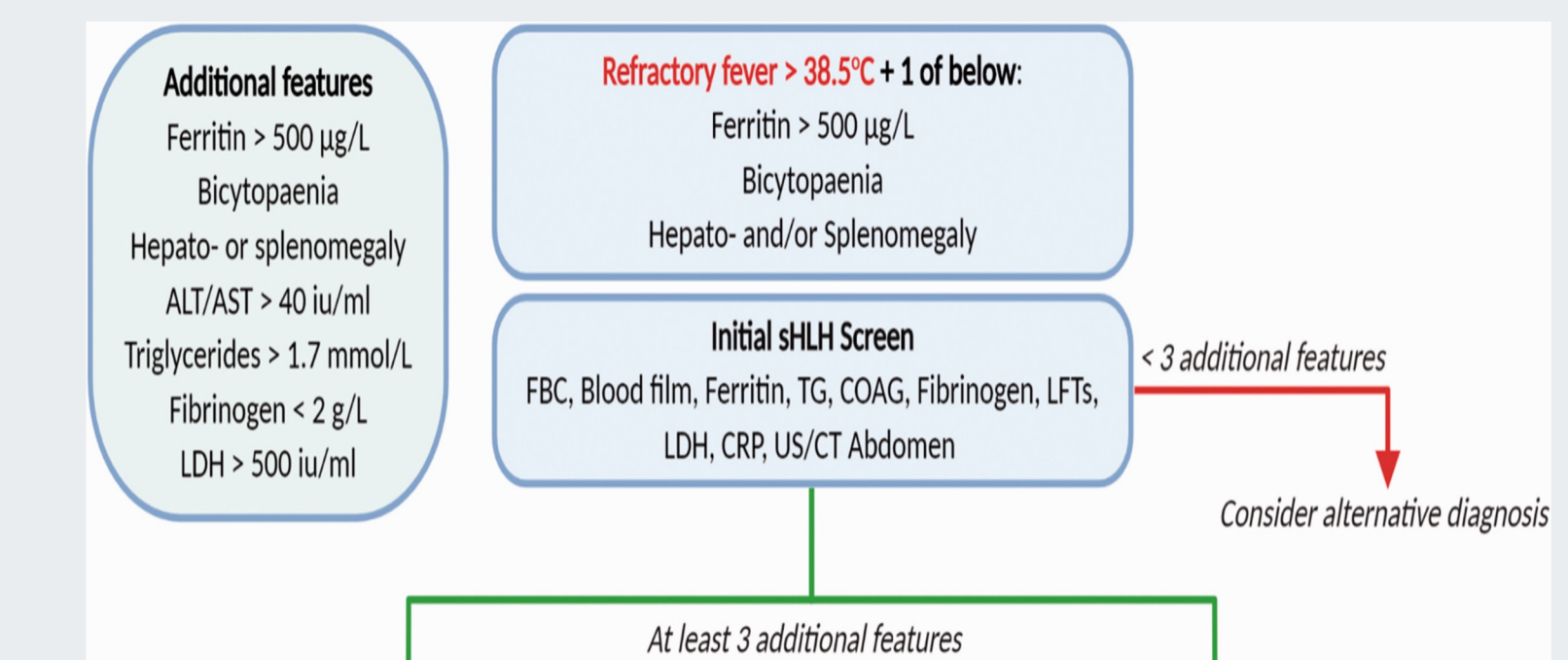
Fever



Falling counts



hyperFerritinaemia



Wilson-Morkeh H et al. Obstetric Medicine. 2021