Suspected Haemophagocytic Lymphohistiocytosis (HLH)

HLH is a life-threatening disorder of immune regulation. The diagnosis is often challenging; symptoms are non-specific, often mimicking sepsis. While HLH is considered a rare disease, the incidence is increasing, and it is likely under-diagnosed. HLH has a high mortality rate, therefore the key to management is early recognition, referral to an HLH specialist for prompt treatment and identification of underlying drivers.

SUSPECT IF: unexplained, persistently unwell patient with sepsis-like syndrome and high fever >38.5, despite appropriate antimicrobials and interventions

CHECK for 3Fs = persistent FEVER + FALLING counts (pancytopenia) + raised FERRITIN

HSCORE

If suspected, calculate HScore and escalate to a senior medical doctor.

Search ***'HLH-HScore/daily monitoring'*** on EPR orders and send bloods urgently.

HScore bloods: FBC, LFTs, AST, U+Es, Coag, fibrinogen, ferritin, triglycerides

Click here to calculate score or search on MDCalc:
https://www.mdcalc.com/calc/10089/hscore-reactive-hemophagocytic-syndrome

If confirmed, please request bloods daily and calculate HScore daily. Bloods need to be taken early as they are sent to CGH for processing.

HScore >169 and/or HIGH clinical suspicion → manage as HLH
Ensure referrals, investigations and treatments are commenced

REFERRALS

If suspected, please refer urgently to Haematology (EPR refer and bleep) and /or Rheumatology (EPR refer and bleep).

Please refer ALL patients with HScore >169 to DCC for admission. These patients can often deteriorate quickly and should be managed in a critical care environment.

Patients not deemed to require DCC admission should be reviewed by the Haem Consultant to determine suitability for management under Haem in CGH. Depending on clinical risk, some patients may be suitable for management on a medical ward with Rheum/Haem input.

OTHER INVESTIGATIONS

If raised HScore and/or high clinical suspicion, please request the following:

Search ***'HLH-initial investigations'*** on EPR.

This panel includes blood cultures, blood film, immunology screen (ANA, ENA, dsDNA, RF, anti-CCP, complements, electrophoresis) and extended microbiology panel (HIV, Hep B/C, EBV/CMV, COVID).

Please consider requesting imaging with USS or CT to assess for organomegaly/ lymphadenopathy.

TREATMENT

Urgent treatment is required if HLH is diagnosed or if there is a high clinical suspicion (in discussion with Rheumatology or Haematology).

1st line treatment - methylprednisolone 1g IV OD for 3 days followed by oral prednisolone.

Cover with appropriate antimicrobials if concerns about concomitant infection. Start bone and gastrointestinal prophylaxis.

Steroids may mask lymphoma diagnosis. If clinical suspicion, discuss urgently with Haematology, but do not allow concern to delay corticosteroid therapy.

2nd line treatment - Anakinra. Use of Anakinra is off-label and requires specialist/MDT decision.

Please click below to access the British Society of Rheumatology 'GIRFT' HLH guidance:

HLH-Guide-final-version-v1.1-July-2024.pdf

A.Dyson, S.Jamal, R.Mcculloch, July 2025. Haematology and Rheumatology Departments, Gloucestershire Hospitals NHS Foundation Trust. Review date July 2027