WHAT?

Haemophagocytic Lymphohistiocytosis (HLH) is a hyperinflammatory condition, characterised by inappropriate survival of histiocytes and cytotoxic T-lymphocytes (CTL), which if undiagnosed and untreated, leads to cytokine storm and haemophagocytosis. It affects children, adolescents and adults, leading to multi-organ failure and high mortality. It can be familial (fHLH; Primary) or secondary/acquired (sHLH)

There is no definitive diagnostic criteria. Treatment is often extrapolated from the HLH-2004 immunosuppressive regimen

Evidence

- Lachmann et al (2018) in a retrospective study, suggested that as many as 7 out of 9 patients suffering with HLH remain undiagnosed

- Kapoor et al (2018) concluded that: “intensivists need to have a high degree of clinical suspicion for HLH in patients with septic shock/multi-organ failure and progressive bi/pancytopenia who are NOT responding to standard management in ICU

HLH: a rare association with pulmonary cryptococcosis

Singh, P. et al. (2019)

- 59-year-old diabetic patient, with no other risk factors
- Clinical course was complicated by 2° HLH
- Clinical condition continued to worsen despite t/m
- After excluding other causes of HLH and possible reasons of his decline, glucocorticoids added
- Patient experienced a remarkable improvement in his clinical and laboratory parameters.
- To our knowledge, this is the first case report of HLH being caused by pulmonary cryptococcosis and only second case report of cryptococcosis being complicated with HLH

High-dose anakinra as treatment for macrophage activation syndrome caused by refractory Kawasaki disease in an infant


- 12-week-old boy; incomplete refractory Kawasaki disease (KD) complicated with macrophage activation syndrome (MAS).
- SX: cerebral irritability, pain, tachypnoea, vomiting for 10d. Did not fulfil any of the classic diagnostic criteria for KD. Pericardial effusion on echocardiography in addition to severe dilatation of the coronary arteries in combination with leucocytosis and raised acute phase reactants led to the diagnosis of incomplete KD.
- No response to intravenous immunoglobulin and aspirin subsequently refractory to additional treatment with infliximab and high-dose methylprednisolone.
- His condition worsened, fulfilling the criteria for MAS. High-dose anakinra was initiated, and remission of the inflammation was achieved.

Disseminated CMV infection and HLH in a patient with well-controlled HIV and ulcerative colitis

Cockbain, B. et al. (2019)

- HLH in the context of disseminated cytomegalovirus (CMV) viraemia
- 50-year-old man with well-controlled HIV infection and ulcerative colitis (UC), for which he was receiving azathioprine.
- Peak CMV viral load was 371 000 copies/ml with evidence of end-organ CMV in the lungs and colon.
- Bone marrow biopsy showed evidence of haemophagocytosis of platelets, neutrophils and erythrocytes.
- Azathioprine was stopped, and he received intravenous ganciclovir and corticosteroids with suppression of the CMV viral load and resolution of the HLH
HLH as a consequence of untreated B-cell chronic lymphocytic leukaemia

Bailey, C. et al. (2017)

- 64-year-old woman; Rai stage 1 B-CLL, of 18 years, on watch and wait presented with fever, pancytopenia and splenomegaly to umbilicus.
- WBC count had gradually increased over many years
- Dx: HLH made 5/8 diagnostic criteria were fulfilled: fever, splenomegaly, cytopenias, hypertriglyceridaemia and hyperferritinemia.
- Investigations of an infective aetiology were negative.
- Tx: HLH-2004, = dexamethasone/etoposide, no ciclosporin
  - = marked improvement, ↓ ferritin level & splenomegaly.
  - 2 weeks later, pt developed fevers >39°C, night sweats and general fatigue. Ferritin level raised to 5222 µg/L and triglycerides 3.4 mmol/L/L. Bone marrow trephine showed extensive infiltration of CLL with no evidence of haemophagocytosis.
  - Etoposide/dexamethasone restarted, which resulted in initial symptomatic improvement.
  - 3 weeks into treatment, pt admitted to ICU with septic shock
  - She died 2 days into admission.

Marchiafava-Bignami disease with haemophagocytic lymphohistiocytosis as a postoperative complication of cardiac surgery

Takei K. et al. (2019)

- Marchiafava-Bignami disease (MBD) is a rare complication of chronic alcoholism;
- MBD in a non-alcoholic diabetic patient has rarely been reported, and aetiology or pathophysiology of MBD is still unknown.
- 50-year-old man with a history of untreated diabetes mellitus underwent on-pump beating CABG surgery for three-vessel and left main coronary disease.
  - 3 d post-surgery, developed a fever >40°C and entered a coma state.
  - MRI revealed multiple lesions which suggested MBD.
  - No response to thiamine therapy, partial to steroids
  - He ultimately died of respiratory failure.
  - The autopsy revealed MBD and HLH.
  - It is rare, but systemic inflammatory response syndrome induced by on-pump beating CABG could develop these complication

References


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Clinical learning