Hemophagocytic lymphohistiocytosis

Hemophagocytic lymphohistiocytosis (HLH) is a hematological disorder that can be due to genetic (primary HLH) causes or excessive activation of the immune system in association with infection, malignancy, rheumatologic disorders, or immunosuppression (secondary HLH).

Hemophagocytic lymphohistiocytosis remains an under-recognized condition among neuropathologists, especially the secondary forms, where it may be diagnosed only at brain biopsy or autopsy due to confounding comorbidities. The CNS is frequently affected, but neuropathological features are underappreciated.

Klein et al., placed their own experience with HLH in context with review of neuropathological features from the literature. A 10-year database search for cases from the pediatric and adult hospitals from the University of Colorado School of Medicine Aurora, with re-review of neuropathological features revealed 1 biopsy and 5 autopsies. Literature that reported neuropathological features was tabulated and 8 adult and 12 pediatric cases were identified. Children had predominantly secondary HLH: 5/12 co-associated with Epstein Barr (or dual) viral infections, 3/12 with malignancy. One biopsy showed florid lymphohistiocytic infiltrates and hemophagocytosis and served as first diagnosis; 2/5 CNS autopsies had originally been reported as negative for HLH, but on re-review had subtle lymphohistiocytic infiltrates with hemophagocytosis confined to leptomeninges. In conclusion, the neuropathological features are highly variable in HLH; features such as focal erythrophagocytosis may be histologically subtle in early phases, but should be sought [1].

Case reports

Pyogenic brain abscesses treated with antibiotics in a patient with hemophagocytic lymphohistiocytosis on HLH-94 protocol [2].

A 56-year-old Japanese man presented with fever and diarrhea, followed by dysarthria. Diffusion-weighted magnetic resonance imaging demonstrated high signal intensity in the splenium of the corpus callosum. The severe fever with thrombocytopenia syndrome virus genome was detected in our patient's serum, and the clinical course was characterized by convulsion, stupor, and hemorrhagic manifestations, with disseminated intravascular coagulation and hemophagocytic lymphohistiocytosis. Supportive therapy not including administration of corticosteroids led to gradual improvement of the clinical and laboratory findings, and magnetic resonance imaging demonstrated resolution of the splenial lesion. The serum severe fever with thrombocytopenia syndrome viral copy number, which was determined with the quantitative reverse-transcription polymerase chain reaction, rapidly decreased despite the severe clinical course. Our patient's overall condition improved, allowing him to be eventually discharged.

Patients with encephalitis/encephalopathy due to severe fever with thrombocytopenia syndrome virus infection may have a favorable outcome, even if they exhibit splenial lesions and a severe clinical course; monitoring the serum viral load may be of value for prediction of outcome and potentially enables the avoidance of corticosteroids to intentionally cause opportunistic infection [3].

A patient diagnosed with HLH, in whom the brain pathology, but not the bone marrow pathology, showed hemophagocytosis. As the diagnosis of HLH is difficult in many cases, a high level of suspicion is required. Moreover, the pathologic diagnosis of organs other than the bone marrow, liver, and lymph nodes may be a useful alternative [4].

A 26-year-old patient who was victim of severe head trauma following a trafic road accident. Two days after trauma, she had fever, pancytopenia and multi-organ failure. The haemophagocytic lymphohistiocytosis syndrome was suspected. This diagnosis was confirmed by biologic findings (elevated serum levels of ferritin and triglycerid) and histological findings (examination of bone marrow smears showing histiocytes phagocytosing blood cells). The evolution was unfavorable despite of corticotherapy and symptomatic measures [5].

1)
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