中文題目：以噬血症候群表現之血管內大型 B 細胞淋巴瘤

英文題目：Intravascular large B-cell lymphoma with presentation of hemophagocytic lymphohistiocytosis

作　　者：蔡東霖[1]

服務單位：[1]臺北醫學大學附設醫院內科部

Introduction:

Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome which is also difficult to diagnose at the first presentation. This case-report would demonstrate an old male patient finally diagnosed with intravascular large B-cell lymphoma with presentation of HLH.

Case Presentation:

A 74-year-old man with a history of hypertension presented to the gastrointestinal outpatient department because of progressive malaise for one month. Before seeking help from medical service, he also suffered from poor appetite, body weight loss (63kg decreased to 56kg within 6 months). In recent one month, progressive malaise, dizziness, and chills developed. Because symptoms persisted weeks later, he visited the gastrointestinal outpatient department in a regional teaching hospital for further medical advice.

On examination, the temperature was 37.2°C, the blood pressure 124/80 mm-Hg, the pulse 98 beats per minute, the respiratory rate 18 breaths per minute, and the oxygen saturation 100% on ambient air. There was no palpable lymphadenopathy on the neck, arms, inguinal, femoral and legs regions. The remainder of the examination was normal. Laboratory tests at the hospital revealed Hb 6.1 g/dL, MCV 84.6. Hemogram also revealed platelet count and white blood cell count were within normal limits at initial presentation, 182 x 10^3 /uL and 5.98 x10^3 /uL respectively. Ferritin elevated significantly, 2894 ng/ml, in addition to serum iron 36 μg/dl, total iron binding capacity (TIBC) 195 μg/dl, transferrin saturation 18.5%. He was admitted to general ward for further evaluation and management.

Esophagogastroduodenoscopy (EGD) was performed, which showed no evidence of hemorrhage. On days 2 of hospitalization, he had fever and the body temperature was up to 40 celsius degree. Empirical antibiotics were administered with flomoxef at first, but fever still persisted even after antibiotics were substituted with piperacillin/tazobactam, then ceftriaxone, and then ciprofloxacin. The computed tomography (CT) of the whole body was performed for fever of unknown origin (FUO) survey and revealed there was neither definite infection source nor significantly enlarged lymph node but mild splenomegaly was found.

On days 12 of hospitalization, the patient was intubated due to acute hypoxemic respiratory failure, favor transfusion-related acute lung injury, TRALI related. Antibiotics were escalated to meropenem for suspected pneumonia, but fever still recurred, accompanied with chills. The serial cultures all showed no growth. Antigen tests or serum antibody tests of atypical pathogen, including Legionella, Pneumococcus, Mycoplasma pneumoniae, Cryptococcus, Aspergillus, syphilis, Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV), were all negative. Pathologic findings of bone marrow biopsy revealed mild hypercellular marrow with histiocytes infiltration. At the same time, the platelet count also decreased to 48 x 10^3 /uL. The serum ferritin level had increased from 2894 to 3756 (ng/ml). The fasting triclycerides level was 310 mg/dl. Conjugated hyperbilirubinemia, transaminitis, and hypoalbumienmia were also found (total bilirubin 2.5 mg/dl, direct bilirubin 1.6 mg/dl, AST 71 U/L, ALT 78, albumin 1.9). Six out of eight HLH diagnostic criteria, according to the HLH-2004 trial, were fulfilled.

He was then extubated after quick resolution of hypoxemia under supportive measures. Dexamethasone had been administered empirically for still suspecting lymphoma. B-symptoms subsided on 5 mg q6h Dexamethasone but recurred after Dexamethasone dose was tapered down. Finally, he was discharged against medical advice and was referred to another medical center. At the medical center, bone marrow biopsy was repeated and final pathologic findings showed intravascular large B-cell lymphoma (IVLBCL) or diffuse large B-cell lymphoma (DLBCL).

Discussion:

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome which may be related with over-expression of immune activation. It is most common in infants and young children, but can affect patients of any age, even if they don’t have any familial condition. Most patients are found in the acutely- and critically- ill status.

HLH has variable presentations and could involve multiorgan. Common presentations are fever, hepatosplenomegaly, rash, lymphadenopathy, and neurologic symptoms. Lab manifestations may be cytopenias, high serum ferritin, liver function abnormalities, typically. Non-genetic etiology mostly results from immunologic trigger, such as infection, malignancy, rheumatologic disorder, and other disorders associated with immune dysregulation.

We can establish the diagnosis of HLH by detecting mutation of an HLH-associated gene. Otherwise, HLH-2004 diagnostic criteria may be used for diagnosis: (1) Fever (2)

Splenomegaly (3) Cytopenias (affecting 2 lineages in the peripheral blood):Hemoglobin <9 mg/dL, Platelets <100000/μl, Neutrophils <1000/μl (4) Hypertriglyceridemia and/or hypofibrinogenemia, fasting triglycerides ≥ 265 mg/dL and/or Fibrinogen ≤ 1.5 g/L (5) Hemophagocytosis in bone marrow or spleen or lymph nodes (6) Low or absent natural killer cell (NK-cell) activity (7) Ferritin 500 ng/ml (8) Soluble CD25 2400 U/L. The criteria could be fulfilled if there are more than five out of the eight criteria above. Other supportive clinical criteria include neurologic symptoms and cerebrospinal fluid pleocytosis, conjugated hyperbilirubinemia, and transaminitis, hypoalbuminemia and hyponatremia.

Conclusion:

HLH is an immune-relating syndrome which may involve multiorgan. Because it is potentially life-threatening, early recognition and correct diagnosis is crucial. Identifying the possible contributory etiology of HLH is also important in management. We need to keep HLH in mind for differential diagnosis, especially encountering patients with fever, hepatosplenomegaly, multiorgan involvement, and cytopenias.

References

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