

# World Journal of *Clinical Cases*

*World J Clin Cases* 2023 September 16; 11(26): 6031-6317



**MINIREVIEWS**

- 6031 Diabetes among Muslims during Ramadan: A narrative review  
*Ochani RK, Shaikh A, Batra S, Pikale G, Surani S*

**ORIGINAL ARTICLE****Retrospective Cohort Study**

- 6040 Clinical evaluation of ventilation mode on acute exacerbation of chronic obstructive pulmonary disease with respiratory failure  
*Wang JJ, Zhou Z, Zhang LY*

**Retrospective Study**

- 6051 Predictive value of preoperative albumin-bilirubin score and other risk factors for short-term outcomes after open pancreatoduodenectomy  
*Zavrtanik H, Cosola D, Badovinac D, Hadžialjević B, Horvat G, Plevel D, Bogoni S, Tarchi P, de Manzini N, Tomažič A*

- 6066 Lyophilized recombinant human brain natriuretic peptide for chronic heart failure: Effects on cardiac function and inflammation  
*Li F, Li H, Luo R, Pei JB, Yu XY*

- 6073 Continuous renal replacement therapy with oXiris® in patients with hematologically malignant septic shock: A retrospective study  
*Wang J, Wei SR, Ding T, Zhang LP, Weng ZH, Cheng M, Zhou Y, Zhang M, Liu FJ, Yan BB, Wang DF, Sun MW, Cheng WX*

- 6083 Serum basic fibroblast growth factor and interleukin-1 $\beta$  predict the effect of first-line chemotherapy in patients with advanced gastric cancer  
*Zheng L, Gan LH, Yao L, Li B, Huang YQ, Zhang FB, Kuang MQ, Fang N*

- 6091 Multinucleated giant cells of bladder mucosa are modified telocytes: Diagnostic and immunohistochemistry algorithm and relation to PD-L1 expression score  
*Gulinac M, Velikova T, Dikov D*

**Clinical Trials Study**

- 6105 Comparing the efficacy of regen-cov, remdesivir, and favipiravir in reducing invasive mechanical ventilation need in hospitalized COVID-19 patients  
*Hegazy SK, Tharwat S, Hassan AH*

**META-ANALYSIS**

- 6122 Risk factors for stroke recurrence in young patients with first-ever ischemic stroke: A meta-analysis  
*Xia Y, Liu H, Zhu R*

**SCIENTOMETRICS**

- 6132** Unveiling the hidden world of gut health: Exploring cutting-edge research through visualizing randomized controlled trials on the gut microbiota  
*Zyoud SH, Shakhshir M, Abushanab AS, Koni A, Shahwan M, Jairoun AA, Abu Taha A, Al-Jabi SW*

**CASE REPORT**

- 6147** Rivaroxaban for the treatment of heparin-induced thrombocytopenia with thrombosis in a patient undergoing artificial hip arthroplasty: A case report  
*Ly FF, Li MY, Qu W, Jiang ZS*
- 6154** Mepolizumab induced palmoplantar psoriasis: A case report  
*Artosi F, Diluvio L, Vultaggio M, Campione E, Bianchi L*
- 6159** Early diagnosis of renal pelvis villous adenoma: A case report  
*Li LL, Song PX, Xing DF, Liu K*
- 6165** Identification of the dominant loop of a dual-loop macro-reentry left atrial flutter without prior intervention using high-density mapping technology: A case report  
*Yu SD, Chu YP*
- 6170** Surgery for fibrous dysplasia associated with aneurysmal-bone-cyst-like changes in right proximal femur: A case report  
*Xie LL, Yuan X, Zhu HX, Pu D*
- 6176** Efficacy of abatacept treatment in a patient with enteropathy carrying a variant of unsignificance in *CTLA4* gene: A case report  
*Musabak U, Erdoğan T, Ceylaner S, Özbek E, Suna N, Özdemir BH*
- 6183** Postpartum hemophagocytic lymphohistiocytosis: A case report  
*An JH, Ahn JH*
- 6189** Non-arteritic anterior ischemic optic neuropathy combined with branch retinal vein obstruction: A case report  
*Gong HX, Xie SY*
- 6194** Large colonic lipoma with a laterally spreading tumor treated by endoscopic submucosal dissection: A case report  
*Bae JY, Kim HK, Kim YJ, Kim SW, Lee Y, Ryu CB, Lee MS*
- 6200** T/myeloid mixed-phenotype acute leukemia treated with venetoclax and decitabine: A case report  
*Park S, Jeong EJ, Kang JH, Lee GW, Go SI, Lee DH, Koh EH*
- 6206** Severe inflammatory disorder in trisomy 8 without myelodysplastic syndrome and response to methylprednisolone: A case report  
*Pan FY, Fan HZ, Zhuang SH, Pan LF, Ye XH, Tong HJ*

- 6213** Aggressive variant prostate cancer: A case report and literature review  
*Weng XT, Lin WL, Pan QM, Chen TF, Li SY, Gu CM*
- 6223** Typical Zollinger-Ellison syndrome-atypical location of gastrinoma and absence of hypergastrinemia: A case report and review of literature  
*Zhang JM, Zheng CW, Li XW, Fang ZY, Yu MX, Shen HY, Ji X*
- 6231** Left epigastric isolated tumor fed by the inferior phrenic artery diagnosed as ectopic hepatocellular carcinoma: A case report  
*Liu HB, Zhao LH, Zhang YJ, Li ZF, Li L, Huang QP*
- 6240** Squamous cell carcinoma associated with endometriosis in the uterus and ovaries: A case report  
*Cai Z, Yang GL, Li Q, Zeng L, Li LX, Song YP, Liu FR*
- 6246** Intestinal obstruction due to giant liver cyst: A case report  
*Küçük A, Mohamed SS, Abdi AM, Ali AY*
- 6252** Difficulties in diagnosing angiomatoid fibrous histiocytoma of the head and neck region: A case report  
*Michcik A, Bieñ M, Wojciechowska B, Polcyn A, Garbacewicz Ł, Kowalski J, Drogoszewska B*
- 6262** Efficacy of tolvaptan in an infant with syndrome of inappropriate antidiuretic hormone secretion associated with holoprosencephaly: A case report  
*Mori M, Takeshita S, Nakamura N, Mizuno Y, Tomita A, Aoyama M, Kakita H, Yamada Y*
- 6268** Recurrent hemoptysis in pediatric bronchial Dieulafoy's disease with inferior phrenic artery supply: A case report  
*Wang F, Tang J, Peng M, Huang PJ, Zhao LJ, Zhang YY, Wang T*
- 6274** Variant of Guillain-Barré syndrome with anti-sulfatide antibody positivity and spinal cord involvement: A case report  
*Liu H, Lv HG, Zhang R*
- 6280** Secondary pulmonary infection by *Fusarium solani* and *Aspergillus niger* during systemic steroid treatment for COVID-19: A case report  
*Usuda D, Kato M, Sugawara Y, Shimizu R, Inami T, Tsuge S, Sakurai R, Kawai K, Matsubara S, Tanaka R, Suzuki M, Shimozawa S, Hoichi Y, Osugi I, Katou R, Ito S, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Oba J, Nomura T, Sugita M*
- 6289** Collision tumor of primary malignant lymphoma and adenocarcinoma in the colon diagnosed by molecular pathology: A case report and literature review  
*Jiang M, Yuan XP*
- 6298** Successful resolution of gastric perforation caused by a severe complication of pancreatic walled-off necrosis: A case report  
*Noh BG, Yoon M, Park YM, Seo HI, Kim S, Hong SB, Park JK, Lee MW*
- 6304** Bilateral dislocation of the long head of biceps tendon with intact rotator cuff tendon: A case report  
*Sohn HJ, Cho CH, Kim DH*

**6311** Delayed diagnosis of abdominal Henoch-Schonlein purpura in children: A case report

*Guo H, Wang ZL, Tao Z*

**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Vikram K Mahajan, MD, Professor, Dermatology, Venereology and Leprosy, Dr. Radhakrishnan Government Medical College, Kangra 177001, Himachal Pradesh, India. vkm1@rediffmail.com

**AIMS AND SCOPE**

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

*WJCC* mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

**INDEXING/ABSTRACTING**

The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJCC* as 1.1; IF without journal self cites: 1.1; 5-year IF: 1.3; Journal Citation Indicator: 0.26; Ranking: 133 among 167 journals in medicine, general and internal; and Quartile category: Q4.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Hua-Ge Yu*; Production Department Director: *Xu Guo*; Editorial Office Director: *Jin-Lei Wang*.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

September 16, 2023

**COPYRIGHT**

© 2023 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Postpartum hemophagocytic lymphohistiocytosis: A case report

Ju Ho An, Jung Hwan Ahn

**Specialty type:** Medicine, research and experimental

**Provenance and peer review:** Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B  
Grade C (Good): 0  
Grade D (Fair): D  
Grade E (Poor): 0

**P-Reviewer:** He YF, China;  
Roganovic J, Croatia

**Received:** April 26, 2023

**Peer-review started:** April 26, 2023

**First decision:** July 3, 2023

**Revised:** July 12, 2023

**Accepted:** August 15, 2023

**Article in press:** August 15, 2023

**Published online:** September 16, 2023



**Ju Ho An, Jung Hwan Ahn**, Department of Emergency Medicine, Ajou University School of Medicine, Suwon 16499, Gyeonggi-do, South Korea

**Corresponding author:** Jung Hwan Ahn, MD, Chief Doctor, Department of Emergency Medicine, Ajou University School of Medicine, No. 164, World Cup-ro, Yeongtong-gu, Suwon 16499, Gyeonggi-do, South Korea. [erdrjah@naver.com](mailto:erdrjah@naver.com)

### Abstract

#### BACKGROUND

Postpartum hemophagocytic lymphohistiocytosis (HLH) is a rare disease with unclear pathophysiology. It is a secondary HLH diagnosed using the pediatric diagnostic criteria; however, the clinical diagnosis of postpartum HLH remains challenging. Hence, HLH may remain undiagnosed, leading to poor patient prognosis. Therefore, improvements in the accuracy of postpartum HLH diagnoses and treatments are necessary.

#### CASE SUMMARY

We report the case of a 40-year-old female with postpartum HLH. The patient attended the postpartum care center for 3 wk after giving birth and underwent needle aspiration due to thyroid gland enlargement 11 d before an emergency department visit precipitated by fever and abdominal pain. Since no abnormal emergency room findings were noted, the patient was discharged with a prescription for broad-spectrum antibiotics. Three days later, she returned to the emergency room in a hemodynamically unstable state and was admitted to the intensive care unit with suspected sepsis or hematologic disease. The patient was treated, without effect, for sepsis using broad-spectrum antibiotics, and for suspected hematologic disease with steroid therapy. However, she died due to rapidly worsening symptoms.

#### CONCLUSION

Rapid recognition and appropriate treatment of postpartum HLH are needed to improve the prognosis.

**Key Words:** Bone marrow; Pregnancy; Lymphohistiocytosis; Infection; Steroids; Case report

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Postpartum hemophagocytic lymphohistiocytosis (HLH) is a rare disease that is not often considered clinically and is difficult to diagnose because of its rarity and varied clinical presentations. Its clinical features are similar to those of sepsis or some pregnancy-related diseases, but the treatment is different. Therefore, an accurate diagnosis is necessary, and early recognition and treatment are needed, to improve patient prognoses. Although clinicians are unfamiliar with postpartum HLH, awareness of the disease is necessary to improve the prognoses of patients with postpartum HLH.

**Citation:** An JH, Ahn JH. Postpartum hemophagocytic lymphohistiocytosis: A case report. *World J Clin Cases* 2023; 11(26): 6183-6188

**URL:** <https://www.wjgnet.com/2307-8960/full/v11/i26/6183.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v11.i26.6183>

## INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare and potentially life-threatening condition that develops concurrently with various conditions, including infection, immunodeficiency syndrome, hematologic malignancy, autoimmune disease, and pregnancy[1-3]. Postpartum HLH is often overlooked due to its low incidence rate[4]; currently, only 11 cases have been reported in English literature[3,5-8]. Therefore, patient symptoms may not prompt this disease to be considered in a differential diagnosis, which may delay accurate diagnosis and lead to adverse outcomes. To prevent this, awareness of this disease should be increased.

This case report aims to augment the existing body of medical evidence regarding postpartum HLH and enhance its awareness among healthcare professionals. Additionally, the 11 reported cases of postpartum HLH, including 8 patients in a case series[3] and 3 case reports[6-8], have been reviewed in this report. We compared the diagnostic criteria used in these cases, focusing on initial treatment and mortality, to help increase the awareness of this disease.

## CASE PRESENTATION

### Chief complaints

A 40-year-old female patient visited the emergency department (ED) with a 3 d history of fever, minor headache, and abdominal pain.

### History of present illness

The patient had been living in a postpartum care center after giving birth by cesarean section 3 wk prior to her ED visit. Eleven days prior, the front of her neck was swollen, and a needle aspiration was performed at a private surgical hospital; however, her thyroid gland showed no specific findings.

### History of past illness

The patient had no relevant medical history, apart from a cesarean section performed 3 wk before presentation.

### Personal and family history

The patient denied any family history of malignant tumors.

### Physical examination

During physical examination in the ED, the patient's vital signs were measured: Body temperature (40.6 °C), blood pressure (100/48 mmHg), heart rate (100 bpm), and respiratory rate (18 breaths/min). No specific findings were observed in the thyroid gland. Moreover, no notable clinical findings such as neck stiffness, tonsil hypertrophy, abdominal tenderness, abnormal breath sounds, or costal spine angle tenderness were observed. Additionally, the patient exhibited no signs of infection at the site of abdominal surgery (cesarean section) or thyroid fine-needle aspiration. Colposcopy was performed to preclude endometritis; however, no specific findings were observed.

### Laboratory examinations

The patient's laboratory test results revealed bicytopenia (hemoglobin: 14.0 g/dL; platelets: 133000/ $\mu$ L; absolute neutrophil count: 2512/ $\mu$ L). However, other laboratory tests including total bilirubin level measurement (0.3 mg/dL), liver enzyme level measurement [aspartate transaminase (AST): 65 U/L; alanine transaminase (ALT): 35 U/L], thyroid function test (T3: 65.1 ng/dL; free T4: 0.88 ng/dL), and urinalysis (one white blood cell/high-powered field), showed no significant abnormalities. The C-reactive protein (CRP) level was elevated at 4.46 mg/dL.

### Imaging examinations

The patient's chest radiograph was normal. Abdominal computed tomography (CT) was performed due to elevated CRP

levels and intermittent post-delivery abdominal pain. However, a prominent infectious focus was not observed.

### Further diagnostic work-up

After administration of an antipyretic drug, the patient's fever subsided, and vital signs remained stable during long-term follow-up in the ED. Four days later, the patient was discharged with a prescription for broad-spectrum antibiotics and a referral to the infectious disease outpatient department to evaluate her fever of unknown etiology. However, 4 d after discharge, the patient returned to the ED with a fever of 38 °C and decreased blood pressure of 60/30 mmHg. Laboratory test results revealed thrombocytopenia (platelets: 94000/ $\mu$ L), and other test results [total bilirubin level: 3.1 mg/dL; liver enzyme levels (AST: 202 U/L; ALT: 444 U/L)] and renal function indicators (blood urea nitrogen: 42.1 mg/dL; creatinine: 3.35 mg/dL) indicated multiorgan failure. The patient's ferritin and triglyceride levels were 3429.0  $\mu$ g/L (normal range: 13.0-150.0  $\mu$ g/L) and 957 mg/dL (normal range: 10.0-150.0 mg/dL), respectively.

## FINAL DIAGNOSIS

Postpartum HLH.

## TREATMENT

Given the possibility of septic shock and hematologic disease, the patient was admitted to the Department of Infectious Disease Intensive Care Unit (ICU) and treated with broad-spectrum antibiotics and steroids; however, a high-dose steroid regimen (HLH-2004, recommended for HLH) was not administered. This was because the results of the patient's bone marrow biopsy had not been confirmed. Furthermore, the immune system might be weakened after childbirth, leaving her vulnerable to infection.

## OUTCOME AND FOLLOW-UP

During the ICU admission, the patient's thrombocytopenia had worsened, and serum ferritin levels had increased. The patient's condition rapidly deteriorated, and she died with a large amount of hematochezia due to disseminated intravascular coagulation. HLH diagnosis was confirmed following a bone marrow examination; however, its etiology was unclear.

## DISCUSSION

HLH, a rare disease associated with uncontrolled inflammatory response[9], is characterized by dysregulated hyperinflammatory immune response resulting in histiocytic proliferation, significant bone marrow hemophagocytic activity, and massive release of inflammatory cytokines[1,2]. The disease may be classified as primary or secondary[2,10], with underlying causes of secondary HLH including infections, malignancies, and autoimmune diseases. Pregnancy-related HLH is a type of secondary HLH, with postpartum HLH being the less well-known subtype. To date, only a few cases of the latter have been reported[3,5]. Yildiz *et al*[5] described 21 cases of pregnancy-related HLH, only three of which were postpartum. Additionally, Song *et al*[3] described a case series of eight patients with postpartum HLH. Despite the paucity of published information, understanding this disease is important to minimize diagnostic delays leading to poor patient prognoses.

HLH is characterized by tissue cell proliferation, hyperinflammation, bone marrow hemophagocytic activity, and release of large amounts of inflammatory cytokines produced by lymphocytes. These characteristics are similar to those observed during pregnancy[4,11-15]. However, unlike pregnancy-related HLH, postpartum HLH is characterized by disease onset after childbirth. Here, HLH may have been induced by an infection and the resultant inappropriate immune response where the pathophysiology of pregnancy/childbirth was similar to that of HLH. Since the pathogenic factors associated with pregnancy and childbirth have been eliminated, they cannot be part of the etiology of postpartum HLH. However, even after childbirth, the altered immune system may have been confounded by infection, leading to postpartum HLH[16].

Since no diagnostic criteria exist for postpartum HLH, pediatric HLH diagnostic criteria have been used (Table 1)[4, 17]. In this case, when the patient returned to the ED, the diagnostic criteria for HLH were not met, except fever and elevated ferritin levels. Cytopenia, hypertriglyceridemia, and bone marrow hemophagocytosis were not confirmed until after ICU admission. In clinical practice, all tests necessary to meet the HLH diagnostic criteria cannot be conducted in the ED. Blood test results may not meet diagnostic criteria during the early stages of the disease, which are characterized by rapid disease progression. As in our case, if a postpartum patient visits the ED with fever, but the symptoms are nonspecific and ferritin levels are high, the patient should be advised to undergo a bone marrow biopsy under the outpatient setting.

**Table 1 Diagnostic criteria of hemophagocytic lymphohistiocytosis: Hemophagocytic lymphohistiocytosis-2004**

Criteria	Diagnosis will be established if one of either 1 or 2 below is fulfilled
A	A molecular diagnosis consistent with HLH: Pathogenic mutations of PRF-1, UNC13D, STXBP2, Rab27a, STX11, SH2D1A, or XIAP
B	Diagnostic criteria for HLH fulfilled (5 of 8 criteria below)
1	Fever $\geq 38.5$ C for $\geq 7$ d
2	Splenomegaly $\geq 3$ finger breadth below left subcostal margin
3	Cytopenia affecting $\geq 2$ of 3 lineages in peripheral blood: Hemoglobin $< 9$ g/L; platelets $< 100 \times 10^9$ /L; absolute neutrophil count $< 1.0 \times 10^9$ /L
4	Hypertriglyceridemia ( $> 265$ mg/dL) and/or hypofibrinogenemia ( $< 150$ mg/dL)
5	Hemophagocytosis in bone marrow or spleen or lymph nodes or liver
6	Low or absent natural killer cell activity
7	Ferritin $> 500$ ng/mL
8	Elevated soluble CD25 (sIL-2 receptor) $\geq 2400$ U/mL

CD25: Cluster of differentiation 25; HLH: Hemophagocytic lymphohistiocytosis; PRF-1: Perforin 1; SH2D1A: SH2 domain-containing 1A; sIL-2: Soluble interleukin 2; STXBP2: Syntaxin binding protein 2; STX11: Syntaxin 11; UNC13D: Unc-13 homolog D; XIAP: X-linked inhibitor of apoptosis protein.

The first case series of patients with postpartum HLH was described by Song *et al*[3]. In addition, three more cases reported in English were identified[6-8]. Eleven patients were compared in Table 2, which shows the number of diagnostic criteria met by each patient, as well as initial treatments and patient outcomes. Nine patients survived; however, the two patients who died met five or seven of the diagnostic criteria described in Table 1. The time from disease onset to diagnosis is not described for each patient. However, considering the rarity of the disease in the postpartum setting, the relationship between treatment regimen and survival described for the eight patients is important. In our case, although five of the diagnostic criteria were met, the prognosis was poor due to diagnostic treatment delays. Based on the criteria reported by Song *et al*[3], fever was reported in 11 patients, splenomegaly in 9, cytopenia in 7, hypertriglyceridemia and/or hypofibrinogenemia in 11, hemophagocytosis in 9, low natural killer cell activity in 6, ferritin level elevation in 11, and soluble cluster of differentiation 25 level elevation in 7. Where a differential diagnosis is required based on clinical symptoms and results, conducting a ferritin test is important after confirming cytopenia, hypertriglyceridemia, and/or hypofibrinogenemia. In addition, a bone marrow biopsy should be performed to confirm hemophagocytosis, as this provides clinicians with more information than other nonspecific symptoms and test results.

Because HLH diagnosis is made according to diagnostic criteria, accurate diagnosis of the disease remains difficult. In our study, we faced similar challenges. Although the diagnostic criteria for HLH were met, they were not differentiated from those for other diseases. However, no particular reaction was observed upon administration of antibiotics; therefore, the possibility of infection-related diagnosis seemed low. A final consensus on HLH diagnosis was reached when experts discussed the diagnosis after the patient's death.

Currently, no standard therapeutic regimen exists for postpartum HLH treatment[4,18]. Based on previous studies, the standard post-abortion HLH-94/04 treatment seems to be the most efficient and safe option[19]. In this regimen, etoposide and dexamethasone, with or without cyclosporine A, are used to treat active HLH. A recent review estimates the mortality rate for secondary HLH as approximately 41%[14]. Additionally, doxorubicin, etoposide, and high-dose methylprednisolone[20], as well as fludarabine with prednisolone, can be used to treat refractory HLH in adults[21].

During the postpartum period, the effects of cytotoxic drugs on the fetus are negligible. However, the patient's general condition deteriorates markedly after childbirth, and use of high-dose steroids may increase risk of infection. In addition, most postpartum HLH cases are confused with sepsis, metabolic disorders, or hemolysis, elevated liver enzymes, and low platelets syndrome (characterized by hemolytic anemia, elevated liver enzyme levels, and thrombocytopenia)[22,23]. These factors delay postpartum HLH diagnosis, and may contribute to the high mortality rate.

Early diagnosis and prompt immunosuppressant administration are required to improve the prognoses of patients with postpartum HLH[24,25]. However, complications may occur if a severe infection is mistaken for HLH and immunosuppressants are administered[26]. Nevertheless, it is necessary to consider treatment methods, including high-dose steroids, that improve prognosis. Unfortunately, the paucity of reported studies dealing with postpartum HLH prognosis makes determining the optimal treatment regimen challenging; therefore, more research is needed on methods to improve prognosis.

## CONCLUSION

Postpartum HLH is a type of secondary HLH that is difficult to diagnose and that can be fatal if treatment is delayed. As

**Table 2** Number of diagnostic criteria met, treatments, and outcomes

Case No	Diagnostic criteria met	Primary therapy	Outcome
1	1,2,3,4,5,7,8	HLH-04	Died
2	1,2,3,4,5,6,7	HLH-04	Survived
3	1,3,4,5,7,8	HLH-04	Survived
4	1,2,4,5,6,7,8	HLH-94	Survived
5	1,2,4,5,6,7,8	HLH-94	Survived
6	1,3,4,5,7	HLH-94	Died
7	1,2,4,6,7,8	FD	Survived
8	1,2,4,5,6,7,8	DEP	Survived
9	1,2,3,4,5,6,7,8	HLH-94 with anakinra	Survived
10	1,2,3,4,5,7	HLH-04	Survived
11	1,2,3,4,7	Methylprednisolone	Survived

Diagnostic criteria met, 1: Fever; 2: Splenomegaly; 3: Cytopenia affecting  $\geq 2$  of 3; 4: Hypertriglyceridemia and/or hypofibrinogenemia; 5: Hemophagocytosis in bone marrow or spleen or lymph nodes or liver; 6: Low or absent natural killer cell activity; 7: Ferritin elevation; 8: Elevated soluble cluster of differentiation 25. DEP: Doxorubicin + etoposide + methylprednisolone; FD: Fludarabine + prednisolone; HLH: Hemophagocytic lymphohistiocytosis.

patients usually visit the ED with postpartum fever, emergency medicine physicians should consider other postpartum diseases in differential diagnoses. Absent established diagnostic criteria, conscious efforts are needed to identify postpartum HLH through blood tests included in the HLH diagnostic criteria and clinical symptoms in the ED. Furthermore, if necessary, invasive tests such as bone marrow biopsy should be conducted.

## FOOTNOTES

**Author contributions:** An JH contributed to manuscript writing, editing, and data collection; Ahn JH contributed to conceptualization and supervision; All authors have read and approved the final manuscript.

**Informed consent statement:** Informed written consent was obtained from the patient for publication of this report and any images.

**Conflict-of-interest statement:** The authors have no conflicts of interest to declare.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** South Korea

**ORCID number:** Ju Ho An 0000-0002-7407-426X; Jung Hwan Ahn 0000-0002-4676-1716.

**S-Editor:** Fan JR

**L-Editor:** Filipodia

**P-Editor:** Fan JR

## REFERENCES

- 1 **Buyse S,** Teixeira L, Galicier L, Mariotte E, Lemiale V, Seguin A, Bertheau P, Canet E, de Labarthe A, Darmon M, Rybojad M, Schlemmer B, Azoulay E. Critical care management of patients with hemophagocytic lymphohistiocytosis. *Intensive Care Med* 2010; **36**: 1695-1702 [PMID: 20532477 DOI: 10.1007/s00134-010-1936-z]
- 2 **Hayden A,** Park S, Giustini D, Lee AY, Chen LY. Hemophagocytic syndromes (HPSs) including hemophagocytic lymphohistiocytosis (HLH) in adults: A systematic scoping review. *Blood Rev* 2016; **30**: 411-420 [PMID: 27238576 DOI: 10.1016/j.blre.2016.05.001]

- 3 **Song Y**, Wang JS, Wang YN, Wang Z. Hemophagocytic Lymphohistiocytosis during the Postpartum Stage of Pregnancy: A Report of Eight Cases. *Acta Haematol* 2019; **141**: 55-60 [PMID: 30537757 DOI: 10.1159/000493879]
- 4 **Liu L**, Cui Y, Zhou Q, Zhao H, Li X. Hemophagocytic lymphohistiocytosis during pregnancy: a review of the literature in epidemiology, pathogenesis, diagnosis and treatment. *Orphanet J Rare Dis* 2021; **16**: 281 [PMID: 34154616 DOI: 10.1186/s13023-021-01790-9]
- 5 **Yildiz H**, Vandercam B, Thissen X, Komuta M, Lanthier N, Debieve F, Dahlqvist G. Hepatitis during pregnancy: A case of hemophagocytic lymphohistiocytosis. *Clin Res Hepatol Gastroenterol* 2018; **42**: e49-e55 [PMID: 29239849 DOI: 10.1016/j.clinre.2017.10.007]
- 6 **Lee J**, Pham B, Karanjawala ZE, Adesina O. Postpartum fevers, a rare presentation of secondary hemophagocytic lymphohistiocytosis. *Clin Case Rep* 2023; **11**: e7070 [PMID: 36941837 DOI: 10.1002/ccr3.7070]
- 7 **Ibarra Stone KA**, Solis JG, Blanco-Lemus E, Malagón-Rangel J, Gordillo-Perez G. Spotted Fever: An Undercover Cause of Hemophagocytic Lymphohistiocytosis in the Immediate Postpartum. *Case Rep Infect Dis* 2022; **2022**: 3348393 [PMID: 35273815 DOI: 10.1155/2022/3348393]
- 8 **B Rathna R**, Dhali A, Varghese AK, H Balakrishnan C. Rare association of haemophagocytic lymphohistiocytosis (HLH) and antiphospholipid syndrome (APS) in postpartum period: a considerable overlap? *BMJ Case Rep* 2022; **15** [PMID: 35110287 DOI: 10.1136/bcr-2021-247376]
- 9 **Kim YR**, Kim DY. Current status of the diagnosis and treatment of hemophagocytic lymphohistiocytosis in adults. *Blood Res* 2021; **56**: S17-S25 [PMID: 33935031 DOI: 10.5045/br.2021.2020323]
- 10 **Jaffe R**. The histiocytoses. *Clin Lab Med* 1999; **19**: 135-155 [PMID: 10403078]
- 11 **Bergsten E**, Horne A, Aricó M, Astigarraga I, Egeler RM, Filipovich AH, Ishii E, Janka G, Ladisch S, Lehmsberg K, McClain KL, Minkov M, Montgomery S, Nanduri V, Rosso D, Henter JI. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: long-term results of the cooperative HLH-2004 study. *Blood* 2017; **130**: 2728-2738 [PMID: 28935695 DOI: 10.1182/blood-2017-06-788349]
- 12 **Henter JI**, Samuelsson-Horne A, Aricó M, Egeler RM, Elinder G, Filipovich AH, Gadner H, Imashuku S, Komp D, Ladisch S, Webb D, Janka G; Histiocyte Society. Treatment of hemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. *Blood* 2002; **100**: 2367-2373 [PMID: 12239144 DOI: 10.1182/blood-2002-01-0172]
- 13 **Henter JI**, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J, Janka G. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2007; **48**: 124-131 [PMID: 16937360 DOI: 10.1002/pbc.21039]
- 14 **Ramos-Casals M**, Brito-Zerón P, López-Guillermo A, Khamashta MA, Bosch X. Adult haemophagocytic syndrome. *Lancet* 2014; **383**: 1503-1516 [PMID: 24290661 DOI: 10.1016/S0140-6736(13)61048-X]
- 15 **Jamy O**, Nunnery S, Giri S, Wiedower E, Johnson B, Yaghamour G, Martin MG. Under-recognition of hemophagocytic syndrome in United States' rural, non-teaching hospitals. *Leuk Lymphoma* 2016; **57**: 2911-2913 [PMID: 27087428 DOI: 10.3109/10428194.2016.1169407]
- 16 **Groer ME**, Jevitt C, Ji M. Immune changes and dysphoric moods across the postpartum. *Am J Reprod Immunol* 2015; **73**: 193-198 [PMID: 25227158 DOI: 10.1111/aji.12322]
- 17 **Jordan MB**, Allen CE, Greenberg J, Henry M, Hermiston ML, Kumar A, Hines M, Eckstein O, Ladisch S, Nichols KE, Rodriguez-Galindo C, Wistinghausen B, McClain KL. Challenges in the diagnosis of hemophagocytic lymphohistiocytosis: Recommendations from the North American Consortium for Histiocytosis (NACHO). *Pediatr Blood Cancer* 2019; **66**: e27929 [PMID: 31339233 DOI: 10.1002/pbc.27929]
- 18 **Pasvolsky O**, Leader A. Postpartum Hemophagocytic Lymphohistiocytosis: A New Entity Is Born. *Acta Haematol* 2019; **141**: 61-62 [PMID: 30537710 DOI: 10.1159/000495340]
- 19 **Shah AJ**, Kapoor N, Cooper RM, Crooks GM, Lenarsky C, Abdel-Aziz H, Wu SQ, Wilson K, Weinberg KI, Parkman R, Kohn DB. Pre- and post-natal treatment of hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2009; **52**: 139-142 [PMID: 18819128 DOI: 10.1002/pbc.21778]
- 20 **Wang Y**, Huang W, Hu L, Cen X, Li L, Wang J, Shen J, Wei N, Wang Z. Multicenter study of combination DEP regimen as a salvage therapy for adult refractory hemophagocytic lymphohistiocytosis. *Blood* 2015; **126**: 2186-2192 [PMID: 26289641 DOI: 10.1182/blood-2015-05-644914]
- 21 **Jin JG**. Fludarabine is effective in treating refractory hemophagocytic lymphohistiocytosis with brucellosis. *Int J Rheum Dis* 2017; **20**: 2256-2257 [PMID: 28378406 DOI: 10.1111/1756-185X.12995]
- 22 **Raschke RA**, Garcia-Orr R. Hemophagocytic lymphohistiocytosis: a potentially underrecognized association with systemic inflammatory response syndrome, severe sepsis, and septic shock in adults. *Chest* 2011; **140**: 933-938 [PMID: 21737492 DOI: 10.1378/chest.11-0619]
- 23 **Sibai BM**. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstet Gynecol* 2004; **103**: 981-991 [PMID: 15121574 DOI: 10.1097/01.AOG.0000126245.35811.2a]
- 24 **Park HS**, Kim DY, Lee JH, Kim SD, Park YH, Lee JS, Kim BY, Jeon M, Kang YA, Lee YS, Seol M, Lee YJ, Lim YS, Jang S, Park CJ, Chi HS, Lee KH. Clinical features of adult patients with secondary hemophagocytic lymphohistiocytosis from causes other than lymphoma: an analysis of treatment outcome and prognostic factors. *Ann Hematol* 2012; **91**: 897-904 [PMID: 22147006 DOI: 10.1007/s00277-011-1380-3]
- 25 **Jin YK**, Xie ZD, Yang S, Lu G, Shen KL. Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis: a retrospective study of 78 pediatric cases in mainland of China. *Chin Med J (Engl)* 2010; **123**: 1426-1430 [PMID: 20819601]
- 26 **Campo M**, Berliner N. Hemophagocytic Lymphohistiocytosis in Adults. *Hematol Oncol Clin North Am* 2015; **29**: 915-925 [PMID: 26461151 DOI: 10.1016/j.hoc.2015.06.009]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

