International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AS A COMPLICATION OF VIRAL INFECTION IN A CHILD- CASE REPORT
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3913
RECEIVED	26 July 2025
ACCEPTED	23 September 2025
PUBLISHED	30 September 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS AS A COMPLICATION OF VIRAL INFECTION IN A CHILD- CASE REPORT

Marianna Chmiel *(Corresponding Author, Email: marianna.anna.chmiel@gmail.com)*
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0001-9571-9477

Artur Tumiński
Regional Specialized Hospital in Wrocław, ul. Kamieńskiego 73A, 51-124 Wrocław, Poland
ORCID ID: 0009-0001-3646-7142

Gabriela Kapłon
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0005-1985-318X

Weronika Perczyńska
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0000-0002-2487-2650

Julia Szczotka
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0009-7619-9259

Gabriela Szpila
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0008-5105-1189

Aleksandra Sokół
District Health Center in Otwock, ul. Stefana Batorego 44, 05-400 Otwock, Poland
ORCID ID: 0009-0000-9431-4366

Anna Kamieniak
University Clinical Hospital No. 4 in Lublin, ul. Doktora Kazimierza Jaczewskiego 8, 20-954 Lublin, Poland
ORCID ID: 0009-0006-1217-0658

Karolina Glajcar
University Clinical Hospital in Wrocław, Borowska 213, 50-556 Wrocław, Poland
ORCID ID: 0009-0007-2496-0793

Remigiusz Flakus
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0008-7890-3521

Żaneta Kania
4th Military Clinical Hospital with Polyclinic in Wrocław, ul. Rudolfa Weigla 5, 50-981 Wrocław, Poland
ORCID ID: 0009-0001-6058-0866

Dominika Gieroba
Stefan Cardinal Wyszyński Provincial Specialist Hospital SPZOZ in Lublin, al. Kraśnicka 100, 20-718 Lublin, Poland
ORCID ID: 0009-0006-3454-1595

ABSTRACT

Introduction and objective: Haemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome that may follow viral infections. We present a case of a 12-month-old boy who developed disseminated intravascular coagulation (DIC) and fulfilled HLH diagnostic criteria following influenza A virus infection. Extensive diagnostics excluded a genetic cause. Treatment based on the HLH-2018 protocol led to full recovery. This case emphasizes the importance of considering HLH in infants with severe systemic inflammation and coagulopathy, even in the absence of EBV infection. Early recognition and appropriate therapy are essential to improve outcomes.
Results. This case report describes a 12-month-old boy with haemophagocytic lymphohistiocytosis (HLH) and disseminated intravascular coagulation (DIC) following influenza A infection. Despite negative genetic testing, the patient met HLH diagnostic criteria. Treatment per HLH-2018 protocol was successful. The case underscores the importance of early recognition of HLH in viral infections beyond Epstein-Barr virus.

KEYWORDS

Haemophagocytic Lymphohistiocytosis, HLH, Disseminated Intravascular Coagulation, DIC, Influenza a Virus

CITATION

Marianna Chmiel, Artur Tumiński, Gabriela Kapłon, Weronika Perczyńska, Julia Szczotka, Gabriela Szpila, Aleksandra Sokół, Anna Kamieniak, Karolina Glajcar, Remigiusz Flakus, Żaneta Kania, Dominika Gieroba. (2025) Haemophagocytic Lymphohistiocytosis as a Complication of Viral Infection in a Child – Case Report. *International Journal of Innovative Technologies in Social Science.* 3(47). doi: 10.31435/ijitss.3(47).2025.3913

Introduction

Haemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition characterised by hyperactivation of the immune system in the form of uncontrolled activation of cytotoxic lymphocytes and macrophages which secrete cytokines that cause tissue damage [7]. The disease may be primary (genetic basis) or secondary (complication of infection, malignancy or autoimmune disease) [9]. The most common infectious agent triggering HLH is Epstein-Barr Virus (EBV), but other pathogens are also known to cause the disease, mainly viruses [2]. A dangerous condition that can accompany this syndrome is disseminated intravascular coagulation (DIC), which involves activation of the coagulation system, leading to intravascular fibrin formation and subsequent closure of small and medium-sized blood vessels [14].

Case report

A 12-month-old infant was referred to the Department of Pediatrics, Haematology and Oncology for coagulation disorders and thrombocytopenia. The boy had had a history of vomiting and fever and symptoms of upper respiratory tract infection for several days prior to admission. Due to confirmation of influenza in 2 family members, outpatient treatment with oseltamivir was recommended. On day 3 of the fever, the parents went to hospital due to the child's weakness and massive swelling of the right upper limb. On admission, the boy was in a severe general condition, wheezing, and sleepy. On physical examination, pale skin, generalised oedema, significantly increased in the right upper limb, oedema of the fifth finger of the left hand with its bruising, petechiae on the left upper limb, accelerated breathing, tachycardia, hepatosplenomegaly were found. Laboratory tests performed on admission showed high inflammatory markers (C-Reactive Proteine (CRP) 286.69mg/dl, Procalcitonin (PCT) 239.82ng/dl, IL-6 2420pg/dl), reduced haemoglobin levels (8.3g/dl), significantly decreased thrombocyte count (6x10^3/ul), decreased antithrombin III activity (29%), prolonged activated partial thromboplastin time (APTT) (50.9s), prolonged prothrombin time (16.4s), decreased fibrinogen (187mg/dl), markedly elevated D-dimers (13523ng/mL), elevated lactate concentration (1.55mmol/l), elevated Lactate Dehydrogenase (LDH) activity (608U/l), reduced total protein concentration (4.2g/dl), hypoalbuminaemia (2.2g/dl), hyponatraemia (133.7mmol/l), hyperferritinaemia (1999ug/l), elevated urea (69.2mg/dl) and Blood urea nitrogen (BUN) (32.3mg/dl)). Blood and urine cultures were sterile. On the basis of the clinical condition and laboratory abnormalities, DIC was diagnosed as a generalized inflammatory

reaction syndrome secondary to influenza virus infection. Hydration and forced diuresis, empirical broad-spectrum antibiotic therapy, antithrombin was administered, coagulation abnormalities were balanced, and red blood cell and platelet concentrates were transfused. The study confirmed influenza A virus infection and excluded infection with influenza B virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Respiratory Syncytial Virus (RSV), Epstein-Baar Virus (EBV), Cytomegalovirus (CMV), Human Immunodeficiency Virus 1 (HIV-1), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV). An elevated COVID-19 IgG antibody level of 230.0 BAU/ml (normal <33.8) was demonstrated. A computed tomography scan of the head showed no features of bleeding, a chest radiograph showed no inflammatory changes in the lungs. Cerebrospinal fluid examination ruled out meningitis, but showed macrophages with features of phagocytosis. After the boy's condition stabilised, the fever recurred on day 5 of hospitalisation, laboratory tests showed worsening anaemia , thrombocytopenia, increasing ferritinaemia, hypofibrinogenemia. The patient met 5 of the 8 of the HLH diagnosis criteria according to the HLH-2018 protocol, so treatment was implemented according to the protocol.

Table. 1. The comparison of the patient's clinical presentation with criteria for the diagnosis of HLH [5]

Criteria for diagnosis of HLH	Laboratory test results
Fever ≥38.5°C	present
splenic enlargement	present
peripheral blood cytopenias ≥2 of 3 lines (haemoglobin <9 g/dl, platelets <100 000/µl, neutrophils <1000/µl)	haemoglobin 8.3g/dl platelets 17000/ul
hypertriglyceridaemia (fasting ≥3 mmol/l [265 mg/dl]) and/or hypofibrinogenemia (<1.5 g/l)	absent
hyperferritinaemia ≥500 µg/l	hyperferritinaemia 1999ug/l
haemophagocytes in bone marrow, cerebrospinal fluid or lymph nodes	haemophagocytes in cerebrospinal fluid
reduced or absent NK cell activity	absent
sCD25 concentration ≥2400 U/ml	sCD25 concentration 3473U/ml

Genetic testing by Next Generation Sequencing (NGS) revealed no typical mutations for the congenital form of HLH. In accordance with the treatment protocol, an evaluation was performed at week 9 of treatment finding a good response to treatment, which allowed the completion of treatment for the secondary, non-familial form of HLH.

Discussion

According to the literature, EBV is the most common pathogen complicating the course of HLH and, in children, the most important initiating factor of this disease process [9,6,15]. EBV infection was not confirmed in the presented patient. In the case described, the likely trigger for the excessive immune response leading to the development of HLH symptoms was a viral infection. Influenza was confirmed by an antigen test in the child's parents a few days before the onset of symptoms, and at the same time the child had high levels of anti COVID-19 IgG, so it is conceivable that one or both viruses may have been involved in the pathogenesis of the child's disease.

To date, few cases of haemophagocytic lymphohistiocytosis associated with influenza virus have been described [6,4]. There are known cases of children in whom the causative agent of HLH was influenza virus. A case of a 10-month-old child with HLH secondary to influenza B virus infection, which was confirmed by PCR, has been described. The child presented with fever and cough for 6 days, two episodes of convulsions, in addition to splenomegaly, anaemia, thrombocytopenia, hypertriglyceridaemia, hyperferritinaemia, among others. Lymphohistiocytosis secondary to influenza B virus infection was diagnosed. Due to the absence of recurrence and the child's good development, primary HLH was not excluded [10].

Another case describes a 4-year-old boy with fever, myalgia, malaise, cough, respiratory distress and diffuse petechiae. The patient was diagnosed with H1N1 influenza virus infection by Polymerase chain reaction (PCR). Due to persistent fever, severe pancytopenia, hyperferritinaemia, hypertriglyceridaemia,

hepatosplenomegaly and hypofibrinogenemia, HLH was diagnosed. In addition, a bone marrow aspiration was performed and the results showed haemophagocytosis [4].

Haemophagocytic lymphohistiocytosis can also be caused by SARS-CoV2, but the majority of cases described are in adults [13]. These diseases may overlap, and additionally may co-occur with coagulation disorders, including DIC [3]. However, a case is described of a 2-year-old boy who was confirmed to be infected with SARS-CoV-2 virus by Reverse transcription polymerase chain reaction (RT-PCR) test. Two weeks after the negative SARS-CoV-2 virus test, the patient's condition worsened, with decreased haemoglobin, thrombocytopaenia, hyperferritaemia, bone marrow aspirate showed features of phagocytosis, in addition to increased D-dimers. The H-score estimated from the 2014 H-score was 239, indicating a 98%-99% probability of HLH [12].

DIC can be a condition secondary to infection, especially in the course of severe sepsis (approximately 30-60%)[1]. There are known cases of DIC in the course of influenza virus [5]. Disseminated intravascular coagulation may co-occur with HLH [11].

Conclusions

In summary, viral infections can give rise to rare complications, such as haemogagocytic lymphohistiocytosis or disseminated intravascular coagulation. These are life-threatening conditions, so early detection and implementation of appropriate treatment is important. Influenza or COVID-19 vaccination appears to be an appropriate prophylaxis for such conditions.

REFERENCES

1. Adelborg K, Larsen JB, Hvas A-M. Disseminated intravascular coagulation: epidemiology, biomarkers, and management. *Br J Haematol* 2021;192:803–18. https://doi.org/10.1111/bjh.17172.
2. Al-Samkari H, Berliner N. Hemophagocytic Lymphohistiocytosis. *Annual Review of Pathology: Mechanisms of Disease* 2018;13:27–49. https://doi.org/10.1146/annurev-pathol-020117-043625.
3. Chu R, van Eeden C, Suresh S, Sligl WI, Osman M, Cohen Tervaert JW. Do COVID-19 Infections Result in a Different Form of Secondary Hemophagocytic Lymphohistiocytosis. *Int J Mol Sci* 2021;22:2967. https://doi.org/10.3390/ijms22062967.
4. Demircioğlu F, Kazancı E, Genç DB, Erdoğan H, Bilir Göksügür S, Bekdaş M. H1N1 Infection-Related Hemophagocytic Lymphohistiocytosis in a Child. *Turk J Haematol* 2013;30:426–8. https://doi.org/10.4274/Tjh.2013.0022.
5. Fukunaga S, Ishida C, Nakaoka A, Ito T. A case of acute kidney injury and disseminated intravascular coagulation associated with influenza B viral infection. *CEN Case Rep* 2014;4:95–100. https://doi.org/10.1007/s13730-014-0147-9.
6. Gao J, Pasion J, Sanchez-Petitto G, Law J. Influenza virus B-associated hemophagocytic lymphohistiocytosis. *Hematol Rep* 2019;11:8268. https://doi.org/10.4081/hr.2019.8268.
7. Griffin G, Shenoi S, Hughes GC. Hemophagocytic lymphohistiocytosis: An update on pathogenesis, diagnosis, and therapy. *Best Pract Res Clin Rheumatol* 2020;34:101515. https://doi.org/10.1016/j.berh.2020.101515.
8. Hayden A, Park S, Giustini D, Lee AYY, Chen LYC. Hemophagocytic syndromes (HPSs) including hemophagocytic lymphohistiocytosis (HLH) in adults: A systematic scoping review. *Blood Reviews* 2016;30:411–20. https://doi.org/10.1016/j.blre.2016.05.001.
9. Imashuku S, Morimoto A, Ishii E. Virus-triggered secondary hemophagocytic lymphohistiocytosis. *Acta Paediatr*2021;110:2729–36. https://doi.org/10.1111/apa.15973.
10. Jayashree K, Rao S, Kamath N. Influenza B Virus Triggering Macrophage Activation Syndrome in an Infant. *Indian J Crit Care Med* 2017;21:802–3. https://doi.org/10.4103/0972-5229.218137.
11. Padhi S, Varghese RGB, Ramdas A, Phansalkar MD, Sarangi R. Hemophagocytic lymphohistiocytosis: critical reappraisal of a potentially under-recognized condition. *Front Med* 2013;7:492–8. https://doi.org/10.1007/s11684-013-0292-0.
12. P K, D L, B D, J M, B B, H B. Secondary Hemophagocytic Lymphohistiocytosis in Post-COVID-19 Patients: A Report of Two Cases. *Cureus* 2021;13. https://doi.org/10.7759/cureus.17328.
13. Retamozo S, Brito-Zerón P, Sisó-Almirall A, Flores-Chávez A, Soto-Cárdenas M-J, Ramos-Casals M. Haemophagocytic syndrome and COVID-19. *Clin Rheumatol* 2021;40:1233–44. https://doi.org/10.1007/s10067-020-05569-4.
14. Valade S, Azoulay E, Galicier L, Boutboul D, Zafrani L, Stepanian A, et al. Coagulation Disorders and Bleedings in Critically Ill Patients With Hemophagocytic Lymphohistiocytosis. *Medicine (Baltimore)* 2015;94:e1692. https://doi.org/10.1097/MD.0000000000001692.
15. Xu L, Guo X, Guan H. Serious consequences of Epstein-Barr virus infection: Hemophagocytic lymphohistocytosis. *International Journal of Laboratory Hematology* 2022;44:74–81. https://doi.org/10.1111/ijlh.13736.