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Case Study

A Case Study on Epstein-Barr Virus Infection Induced Haemophagocytic Lymphohistiocytosis

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I N F O

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A B S T R A C T

One of the effects of Epstein-Barr virus (EBV) infection is a condition known as Haemophagocytic Lymphohistiocytosis (HLH). Unrestrained immune system activation, which results in unrestricted cytokine release and macrophage activation, is the cause of the fatal uncommon condition known as HLH. EBV infection can cause systemic lymphadenopathy, cytopenia, and fulminant constitutional symptoms. Here, we have discussed a case of a 69-year-old man with neurological issues who also had HLH caused by EBV and beta cell lymphoma.

Keywords: Haemophagocytic Lymphohistiocytosis, Epstein-Barr Virus, FLH, sHLH

Introduction

A double-stranded DNA-containing herpes virus called the Epstein-Barr virus (EBV) infects 95% of people worldwide.[1] Memory B cells operate as a reservoir for EBV, which primarily infects B lymphocytes as a result of contact between the infectious polypeptide gp350 and CD21 receptor. EBV is capable of infecting T as well as NK cells in addition to B cells. Reactive disorders and lymphoma are examples of EBV-associated lymphoproliferative disorders (LPDs).[2] Most EBV-associated lymphomas exhibit type II EBV latency.[3] The main sites of Epstein-Barr virus (EBV) infection are human B cells. Due to a strong host immune response, EBV infection is typically asymptomatic; nonetheless, some people have self-limiting infectious mononucleosis whereas some have EBV-associated lymphoma or epithelial malignancies.[4] The severe hyper-inflammatory disease known as Haemophagocytic Lymphohistiocytosis (HLH) is affected by the prolonged, improper activation of lymphocytes and macrophages.[5] Familial HLH (FLH) and Secondary HLH (sHLH) are the types of HLH. FHL generally manifests in newborns and early childhood and is brought on by genetic abnormalities that affect the activity of lymphocytes with cytotoxic effects and natural killer (NK) cells. sHLH is more prevalent in adolescence and adulthood and is brought on by illnesses, neoplasms, and autoimmune disorders.[6]

Case Report

A 61-year-old man from Rajkot, Gujarat diagnosed with HLH with EBV positive and B cell lymphoma admitted to the hospital. Symptoms include disoriented, slurring of speech, decreased eye movement, drowsiness and generalised weakness. The patient had a history of hypertension and transurethral resection of the prostate (TURP) operation. He was on a mixed diet and had no significant family or personal history. He had no social history of alcohol consumption and smoking.

On examination, we discovered body swelling and yellow-

coloured sclera. Serology testing performed during laboratory examinations revealed the presence of EBV antibodies and a ferritin level of 53550 ng/ml (the normal range is 22–32 ng/ml), which indicates HLH. Other tests that were found to be abnormal included the white blood cell (WBC) count (2100 per mcL), red blood cell (RBC) count (2.21 million/mm^3), haemoglobin (6.4 g/dl), C-reactive protein (CRP) (167.9 mg/dl), serum creatinine (6.32 mg/dl), blood urea (449.4 mmol/L), blood urea nitrogen (210 mmol/L), ammonia (81 mol/L), and gamma-glutamyl transpeptidase (GGT) (109 IU/L).

Bone marrow aspiration showed relatively increased erythropoiesis, adequate iron stores, megakaryocytes, and haemophagocytes. Glucose–6–Phosphate Deficiency (G6PD) report shows low G6PD kinetics (7.2 g/dl) and high G6PD quantitative blood kinetics 22.78 (units/gram of haemoglobin).

Treatment included a 2-gram stat dose of inj. meropenem followed by 500 mg twice a day, 100 mg of inj. doxycycline twice a day, 100 mg of inj. fluconazole once a day, 550 mg of tab. rifaximin twice a day, 40 mg of inj. dexamethasone twice a day and 20 g of inj. IVIG (intravenous immunoglobulin).

In order to control abnormal stimulation of the immune system, HLH protocol-2004 was used. Then full recovery was achieved.

Discussion

The herpes virus family includes the Epstein-Barr virus (EBV), commonly referred to as human herpes virus 4. It is one of the most prevalent viruses in people. The EBV virus may be found anywhere. The majority of people get EBV at some time in their life. EBV is most frequently transmitted by body fluids, particularly saliva. Infectious mononucleosis, usually known as mono, and other diseases can be brought on by EBV.[7]

The Epstein-Barr virus (EBV) is a lifelong illness that affects the majority of people. Although the majority of infections are long-lasting and asymptomatic, the virus is linked to numerous potentially fatal side effects, including lymphoma, interstitial pneumonia, and viral-associated haemophagocytic syndrome. Pancytopenia, hepatosplenomegaly, lymphadenopathy, and fever can all be symptoms of EBV-positive lymph proliferative disease (EBV-LPD).[7,8]

Clinical symptoms of EBV-HLH include fever, splenomegaly, and cytopenia along with histological evidence of haemophagocytosis, which results in abnormally high serum levels of ferritin, lactate dehydrogenase, and soluble CD25. EBV-HLH is a clinicopathological syndrome that encompasses a dramatically dysregulated immune response and hypercytokinaemia. EBV-HLH has a significant death rate, often from multiorgan failure, in the absence of early and efficient treatment. The increase in survival rates has been facilitated by recently developed diagnostic and treatment recommendations. East Asian study centres have produced the majority of the descriptive papers on EBV-HLH, the majority of which concentrated on primary EBV infection in kids or teenagers. Haemophagocytic syndrome, on the other hand, is typically caused by factors other than EBV infection in adults. Even though there have been few occurrences of adult EBVHLH recorded in people of various ethnicities, the bulk of those affected have been people of East Asian descent.[9]

HLH often affects newborns and young children. Adults may also experience it. The condition often passes down to children. Adults can develop HLH from a wide range of illnesses, such as cancer and infections. If you have HLH, the immune system, which acts as your body's defence mechanism, fails. White blood cells of the histiocyte and lymphocyte varieties attack your own other blood cells. The dysfunctional blood cells that accumulate there cause your liver and spleen to enlarge.[10]

HLH was first characterised in 1939. Primary or hereditary HLH and secondary HLH are two subtypes of HLH that can be distinguished. On the basis of symptoms, the secondary form is comparable to the primary form of an inflammatory disease. The majority of instances of primary HLH (70%) occur in infants younger than one year of age, although it can also happen to adults in extremely rare circumstances (mutations in the Perforin gene have been found in people with primary HLH). In individuals with primary HLH, five different gene mutation types have been found. For instance, Type 2 is caused by mutations in genes 21–22, while Type 5 is caused by mutations in MUNC18–20, which may be accompanied by hypogammaglobulinaemia. The patient's hypogammaglobulinaemia was not verified since it was unable to check for mutations (the relevant tests were sent to Germany to look into the type 5 illness).[11] Hypogammaglobulinaemia may also occur together with EBV for a brief time.[11]

Secondary HLH is linked to immunologic stimulation brought on by bacterial or congenital infections as well as cancer. Viral infections caused by EBV, CMV, ProB19, and HIV are the most frequent causes of secondary HLH. Any age can get secondary HLH brought on by EBV. Patients with healthy immune systems may potentially develop a secondary type of HLH. However, people with immune system problems may also experience it. EBV infection is known to cause secondary HLH, especially in those with x-linked lymphoproliferative disorder. One in one million male babies has the X-linked lymphoproliferative condition.[12]

Conclusion

Although a severe EBV infection does not always indicate a condition that is life-threatening, our case study

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requires immediate medical attention. The presence of secondary HLH is disputed in individuals who have hepatosplenomegaly, pancytopenia, coagulopathy, and long-term EBV infection. The diagnosis will be verified using a BMA as well as the serum ferritin level. The HLH-2004 protocol method is appropriate for the first treatment for individuals with secondary HLH. When HLH and EBV are present, the immune response can be suppressed by rituximab, which is the primary goal of treatment in order to lower the risk of death in HLH patients.

Conflict of Interest: None

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