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A Typical Presentation of Epstein: Barr Virus (EBV) Induced Infectious Mononucleosis with literature Review

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ABSTRACT

Epstein-Barr Virus (EBV) is a human gammaherpesvirus known for causing infectious mononucleosis (IM) and implicated in various cancers and autoimmune diseases. We present a case of atypical IM in a 43-year-old male. Initial symptoms included fever, sore throat, and malaise, with persistent fever despite antibiotic treatment. Diagnostic testing revealed positive EBV IgM antibodies, confirming IM. The patient experienced prolonged lymphocytosis, reflecting the immune response to EBV. Although symptoms improved over months, complete blood parameter normalization took over 9 months. This case underscores the importance of considering IM in prolonged fever and lymphocytosis, especially in adults with atypical presentations. It emphasizes the protracted course of IM and highlights the need for comprehensive follow-up. The study aims to enhance IM diagnosis, focusing on long-term outcomes and proactive management strategies, including potential EBV vaccination to prevent associated cancers. Recognition of IM's significance in adults and monitoring hematologic parameters until full recovery is crucial for optimal patient care.

INTRODUCTION

Epstein Bar Virus (EBV) belongs to the human gammaherpesviruses family, comprising four subfamilies. It serves as the prototype of the Lymphocryptovirus genus[1]. With a genomic length of roughly 170 kilobase pairs, EBV is a linear and a double-stranded DNA virus[2]. It is the primary cause of infectious mononucleosis (IM), also known as glandular fever, a condition marked by fever, sore throat, swollen lymph nodes and general discomfort, mostly affecting B cells and epithelial cells[3,4]. Approximately 70% of teenagers and young adults in affluent nations contract infectious mononucleosis (IM) due to EBV infection, which affects over 95% of the global population[5]. As the first human tumor virus, EBV is also known to play a major role in the development of a number of lymphoid and epithelial cancers, such as gastric cancer (GC), nasopharyngeal carcinoma (NPC), post-transplant lymphoproliferative disease (PTLD), Burkitt lymphoma (BL) and Hodgkin lymphoma (HL)[6,7,8,9]. Many studies also suggest the involvement of EBV in the onset of multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis and Sjogren's syndrome, among other autoimmune diseases[10,11]. EBV commonly spreads through saliva and is acquired during infancy in developing nations, contrasting with its typical acquisition during adolescence in developed countries[12,13]. In this report we present an unusual case with an atypical presentation of prolonged deranged Lymphocytosis in blood picture in a 43-year-old patient who is also the corresponding author of present article.

MATERIALS AND METHODS

Case Presentation: A 43-year-old male, developed sudden onset fever that was mild to moderate accompanied with night sweats, continuous in nature with associated symptoms of sore throat, malaise, anorexia and body ache for 7 days following which the patient visited the clinician for further evaluation. On physical examination, the patient had no inflamed lymph nodes in the neck and tonsils were normal. His temperature was 101°F. Routine blood investigations were done to exclude typhoid, malaria and Dengue. The typhi dot test was negative for IgM antibody to salmonella typhi. Peripheral blood smear was negative for malarial parasite. Dengue serology NS1 Antigen along with IgM and IgG were negative. There were no chills, rigors, loose stools, cough or vomiting at presentation. The physical examination was otherwise normal. Patient reported that he sought medical help only because he was having persistent fever. The first investigations done on day 7 (Table 1). The clinician prescribed 1gm BD ceftriaxone i.v injection for 7 days but there was no relief in pattern and nature of fever. Throughout this course there was associated complaint of lethargy, fatigue, body ache and severe sore throat. The investigations were repeated on day 10 (Table 2). After 2 weeks of illness the detailed investigation (Table 3) including the viral markers were performed as the fever continued even after 7 days of i.v Ceftriaxone and the diagnosis of viral fever was suspected. On day 14, the presence of positive IgM (VCA) antibodies for Epstein-Barr virus and IgG antibodies for cytomegalovirus (CMV) confirmed the diagnosis of Infectious Mononucleosis (IM). There was mild elevation of liver enzymes also initially during presentation but subsided in a month of illness. The fever persisted for almost 2 months with a consistent pattern, remaining mild to moderate continuous, without chills or rigors. Symptoms such as malaise, lethargy, body aches and throat pain gradually improved after about 1 month, while the fever persisted. Subsequently, repeat blood tests, including peripheral blood smear and cell counts, revealed reactive lymphocytosis suggestive of viral etiology without any abnormal cells (Table 4). Further blood investigations were repeated at 2 months (Table 5), 3 months (Table 6), 8 months (Table 7) and lastly after 9 months and 2 weeks (Table 8).

RESULTS AND DISCUSSIONS

Epstein-Barr virus (EBV) is a member of the herpes virus family, known for replicating mainly in ß-lymphocytes. Additionally, it can replicate in epithelial cells of the pharynx and parotid duct[14]. The primary mode of transmission is through saliva, with an incubation period ranging from four to eight weeks. In a study involving 500 confirmed cases of infectious mononucleosis, nearly all patients (98%) exhibited symptoms such as sore throat, lymph node enlargement, fever and tonsillar enlargement. Other prevalent physical signs included pharyngeal inflammation (85%) and transient palatal petechiae (50%). This clinical presentation is commonly observed in adolescents. However, older adults are less prone to experiencing sore throat and adenopathy but are more susceptible to hepatomegaly and jaundice[15]. The majority of symptoms typically resolve within 10 days, but fatigue and cervical lymphadenopathy may persist for about 3 weeks on average. Additionally, less common findings, observed in less than 20% of cases, encompass abdominal pain, hepatomegaly, splenomegaly, nausea, vomiting, palatal petechiae, periorbital and eyelid edema, as well as rash[16].

Infectious mononucleosis holds medical significance due to the severity and prolonged duration of the acute illness. Additionally, it carries long-term implications, notably an increased risk of developing specific cancers and autoimmune disorders. The imperative to develop an EBV vaccine has persisted due to the substantial disease impact of both acute and chronic EBV infections. Researchers in the field have prioritized this endeavor for years. The National

Table 1. The blood picture on day 7 of illness.

Parameter	Reported Value
RBC	4.21 x 10^6/mm3
HGB	12.6 g/dl
WBC	4.9 x 10^3/mm3
Differential Count	N-25%, L-72%, M-02%,E-01%
Platelets	172 thou/mm^3

Table 2. The blood picture on day 10 of illness.

Parameter	Reported Value
RBC	3.90 x 10^6/mm3
HGB	11.7 g/dl
WBC	10.1 x 10^3/mm3
Differential Count	N-21%, L-69%, M-10%,E-00%
Platelets	176 thou/mm^3

Table 3. The blood picture at day 14 of illness.

Parameter	Reported Value
RBC	4.55 x 10^6/mm3
HGB	13.3 g/dl
WBC	12 x 10^3/mm3
Differential Count	N-16.4%, L-74.80 %, M-8.1%,E-0.4%
Platelets	256 thou/mm^3
ESR	19/mm in Ist hour
Lactate Dehydrogenase	359 U/L
EBV(VCA) IgM	0.39
CMV IgG	>250 IU/ml
CMVIgM	0.72

Table 4. The blood picture at 1 month of illness.

Parameter	Reported Value
RBC	4.71 x 10^6/mm3
HGB	13.6 g/dl
TLC	8.30 x 10^3/mm3
Differential Count	N-37.20%, L-56.10%, M-3.1%, E-2.8%, B-0.80%
Platelets	154 thou/mm^3

Table 5. The blood picture at 2 month of illness.

Parameter	Reported Value
RBC	4.43 x 10^6/mm3
HGB	12.80 g/dl
TLC	5.96 x 10^3/mm3
Differential Count	N-40.30%, L-49.70%, M-3.5%, E-5.70%, B-0.80%
Platelets	120 thou/mm^3

Table 6. The blood picture at 3 month of illness.

Parameter	Reported Value
RBC	4.50 x 10^6/mm3
HGB	12.80 g/dl
TLC	6.87 x 10^3/mm3
Differential Count	N-39.80%, L-51.50%, M-3.8%, E-4.20%, B-0.70%
Platelets	178 thou/mm^3

Table 7. The blood picture at 8 months of illness

Parameter	Reported Value
RBC	4.29 x 10^6/mm3
HGB	12.70 g/dl
TLC	6.56 x 10^3/mm3
Differential Count	N-40.90%, L-50.50%, M-3.4%,E-4.30%,B-0.90%
Platelets	181 thou/mm^3

Table 8. Blood picture at 9 months and 2 weeks of illness.

Parameter	Reported Value
RBC	4.43 x 10^6/mm3
HGB	12.80 g/dl
TLC	6.92 x 10^3/mm3
Differential Count	N-52.7%, L-35.8%, M-7.7%,E-2.9%,B-0.90%
Platelets	188 thou/mm^3

Cancer Institute has advocated for further clinical trials to evaluate the safety and effectiveness of a vaccine aimed at preventing both infectious mononucleosis and EBV-associated cancers[3]. The presented case illustrates a prolonged and atypical manifestation of infectious mononucleosis (IM) in a 43-year-old medical doctor. The initial symptoms, including fever, sore throat and malaise, were suggestive of a viral infection. However, the persistence of symptoms despite antibiotic treatment raised suspicion for an underlying viral etiology. Subsequent investigations revealed positive IgM antibodies for Epstein-Barr virus (EBV) and Ig G antibodies for cytomegalovirus (CMV) indicative of past infection, thus confirming the diagnosis of infectious mononucleosis. Throughout the course of the illness, the patient experienced reactive lymphocytosis, characterized by elevated lymphocyte counts and atypical lymphocyte morphology that was more pronounced in the early part of illness where lymphocytes were seen as large clump of cells in peripheral blood picture. This phenomenon is commonly observed in IM and reflects the immune response to EBV infection. Despite gradual resolution of symptoms over several months, complete normalization of blood parameters, including total leukocyte count and lymphocyte distribution, took more than 9 months. This case underscores the importance of considering IM in the differential diagnosis of prolonged fever and lymphocytosis, especially in adult patients presenting with atypical clinical features. Additionally, it highlights the protracted course of IM and the need for comprehensive follow-up to monitor hematologic parameters until complete recovery is achieved.

CONCLUSION

The objective of this report and literature review is to enhance the differential diagnosis of Infectious Mononucleosis (IM), aiming to advance patient care and facilitate management strategies, particularly focusing on long-term outcomes. By synthesizing existing knowledge and evidence, the goal is to offer healthcare professionals valuable insights into distinguishing IM from other similar conditions, thereby enabling more accurate diagnoses. Special attention is dedicated to understanding the long-term implications of IM, in order to develop proactive strategies for mitigating associated risks and optimizing patient health in the extended term. In our current scenario, total leucocyte count returned to normal at 2 months of illness but lymphocytosis persisted and it took nearly 9 months for the percentage of lymphocytes in differential blood cell counts to normalize after the infectious mononucleosis episode, contrasting with the usual duration of 1-2 months for mononucleosis. Thus our case report highlights the significance of recognizing infectious mononucleosis (IM) as a potential cause in adults with prolonged fever and lymphocytosis, particularly when atypical symptoms are present. Furthermore, it emphasizes the extended duration of IM and the necessity for

thorough monitoring of hematologic indicators until full recuperation is attained.

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