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Case Report

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Epstein-Barr Virus Infectious Mononucleosis in a Splenectomized Patient

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Abstract

The clinical picture in infectious mononucleosis (IM) consists primarily of pharyngitis, fever, and lymphadenopathy. IM is a common clinical syndrome. However, little attention has been paid to a clinical feature of IM that can occur in a previously splenectomized subject. Indeed, the clinical features of splenectomized patients with IM have not yet been fully described. Especially, in Epstein-Barr virus (EBV), to our knowledge, there is no report in the English language literature. We describe here an atypical IM case; an asplenic but healthy male presented with acute primary EBV infection. He was afebrile, there was an absence of lymphadenopathy, and there was relatively marked lymphocytosis in his peripheral blood. This case illustrates that an asplenic state can distort the typical clinical picture of EBV mononucleosis.

Keywords: Epstein-Barr virus; Infectious mononucleosis; Post-splenectomy

Introduction

The clinical picture in infectious mononucleosis (IM) consists mainly of the classic triad: pharyngitis, fever, and lymphadenopathy [1, 2]. Common laboratory findings in patients with IM include marked lymphocytosis with atypical lymphocytes [2]. Additionally, elevation of aminotransferase levels often occurs in 50-80% of patients with IM [3], especially in older children and adults. Epstein-Barr virus (EBV) is most commonly associated with IM, while other viruses, such as cytomegalovirus (CMV), human immunodeficiency virus (HIV), and human herpesvirus 6, can also cause IM [4].

IM is a common clinical syndrome. However, little attention has been paid to the clinical picture of IM in a splenectomized patient. Indeed, the clinical features in splenectomized patients with IM have not yet been fully described. Especially with EBV, to our knowledge, no published report is currently available in the English language literature.

Although rare, several reports of CMV-IM in splenectomized patients have been published. Han et al [5] reported two cases with post-splenectomy CMV mononucleosis. In their report, the clinical features highlighted were prolonged fever, marked lymphocytosis in the peripheral blood, an impaired IgM response to CMV, and clonal T-cell proliferation, with T-cell receptor γ gene rearrangements. Furthermore, based on a literature review, Han et al argued that post-splenectomy CMV mononucleosis was a distinct clinicopathological syndrome because they noticed that CMV-IM in an asplenic state had some unique clinical characteristics [6].

Here, we report an atypical IM case in a splenectomized patient who presented with a primary EBV infection, focusing on its unique clinical features.

Case Report

A 37-year-old Japanese male was seen in our outpatient clinic because of headache and fatigue. The patient had been well until 2 weeks earlier. Headache and malaise developed, associated with pharyngeal discomfort and slight loss of appetite, but with no weight loss or night sweats. He denied having fever, although he had not measured his temperature. His spleen was removed surgically because of a previous accident: major trauma in connection with snow skiing at the age of 22. He worked at a research institute and was an immunology researcher. He was single and heterosexual, with no risk factor for HIV. He had no history of illicit drug use, recent travel, hypersensitivity to mosquito bites, or known allergies. He had not had any disease that could be indicated for splenectomy, such as immune-induced thrombocytopenic purpura, myeloproliferative diseases, lymphomas, he-

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Table 1. Laboratory Data

	Reference range, Adults	On presentation	3 weeks after presentation	4 weeks after presentation	6 weeks after presentation	8 weeks after presentation	14 weeks after presentation	1 year after presentation
Anti-EBNA IgG	< 1:10	< 1:10			< 1:10	< 1:10	< 1:10	1:80
EBV anti-VCA IgG	< 1:10	1:1,280			1:1,280	1:1,280	1:640	1:320
EBV anti-VCA IgM	< 1:10	1:160			1:80	1:80	1:20	< 1:10
CMV IgM	Negative	Negative			Negative	Negative	Negative	
CMV antigenemia assay	Negative				Negative			
Screening test for HIV	Negative	Negative						Negative
White-cell count (per mm^3)	3,500-8,500	27,400	17,840	7,880	6,830	4,100	6,740	
Lymphocytes		15,618	12,844	6,304	4,781	2,665	2,628	
Atypical lymphocytes		7,946	1,427	394	204	0	0	
Aspartate aminotransferease (U/L)	13 - 23	212	140	53	25	21	33	
Alanine aminotransferase (U/L)	8 - 42	274	289	95	30	23	29	
Lactate dehydrogenase (U/L)	119 - 229	534	526	345	252	191	182	
Alkaline phosphatasse (U/L)	115 - 359	788	875	537	346	299	268	

reditary spherocytosis, or sickle cell disease.

On examination, his temperature was 36.8 °C, blood pressure was 116/76 mmHg, pulse was 58 beats per min, and oxygen saturation was 98% while breathing ambient air. His neck was not significantly swollen; posterior cervical lymphadenopathy was not seen. His throat had pharyngeal erythema and swelling, a tonsillar exudate, and edematous uvulas. His chest was clear on auscultation, and heart sounds were regular with no murmur. No significant hepatomegaly was noted. The examination was otherwise normal.

The white-cell count was 27,400/mm^3, with a differential count of 14% neutrophils, 57% lymphocytes, and 29% atypical lymphocytes. The chemistry panel showed aspartate aminotransferase of 212 U/L, alanine aminotransferase of 274 U/L, and alkaline phosphatase of 788 U/L. Levels of a total bilirubin, renal function, albumin, C-reactive protein, glucose, and electrolytes were normal. Laboratory test results are shown in the Table 1.

The symptoms, such as his characteristic pharyngeal findings, marked leukocytosis and lymphocytosis, and significant hepatitis with elevated alkaline phosphatase, led us to consider a mononucleosis-like condition, especially IM with primary EBV infection. The serum viral immunoassay was positive for EBV viral capsid antigen (VCA) IgM and negative for anti-EBV nuclear antigen (EBNA) IgG. Additionally, tests of both CMV IgM and HIV antibodies were negative. IM with EBV primary infection was strongly suspected because of the clinical picture and suggestive result of the EBV panels. Moreover, his symptoms had improved gradually with observation in the outpatient clinic. At the eighth week after disease onset, liver enzymes were significantly decreased, with normalization of the white cell count, while the VCA IgM titer decreased gradually. At the 1-year follow-up, the patient was reported being symptom-free. No other disease occurred. EBNA IgG was positively converted and his HIV status was again negative (Table 1).

Discussion

We describe a case of acute EBV primary infection, presenting as atypical IM, in a patient who had been well since a splenectomy was performed for blunt trauma. We think that, as seen in patients with CMV-IM [5], the asplenic state may distort the typical clinical picture of EBV-IM. In fact, our patient manifested some atypical symptoms.

First, no febrile state was confirmed from the medical interview or physical examination, while fever is one of the classic IM triad. Second, lymphadenopathy was not prominent. Third, he was relatively old. IM most commonly affects people who have primary EBV infection during or after the second decade of life [4], even in developed countries. Finally, total lymphocytes and atypical lymphocytes seemed increased relatively versus typical EBV mononucleosis. Ventura and Hudnall [7] described in their paper that mean white cell and lymphocyte count in patients with heterophile antibody-positive IM were 11,400 ± 5,400/μL and 4,000 ± 3,200/μL, respectively. However, generally, a wide range of atypical lymphocytosis is well-known [2] and accounts for up to 30% of the differential count [8]. The laboratory data suggested that our patient's cell count was elevated, but not extremely so.

The spleen is a replication site of early immunity against viral infection [6]. For eusplenic people, primary viral infection can elicit an early IgM response. On the other hand, viral clearance in an asplenic patient is compromised, which may accelerate the anti-viral immune response in another site, the bone marrow. As a result, leukocyte, lymphocyte, and atypical lymphocyte counts in peripheral blood may be increased markedly.

Next, we discuss the validity of the diagnosis of EBV-IM in this case. Three major grounds supported the diagnosis of EBV-IM. First, all of the serological EBV panel indicated a primary infection, based on the serological course and conversion. EBNA IgG was negative during the early phase of the disease, and finally seroconverted, while the titer of VCA IgM decreased slowly for negative conversion according to clinical disease activity. Second, two major typical manifestations were noted in our patient: significant hepatitis without other etiology and positive pharyngeal findings, compatible with an acute primary EBV infection, often seen as a mononucleosis. These symptoms recovered spontaneously, indicating that the pathological etiology in our patient was acute viral infection, not a bacterial or malignant neoplastic process. Finally, other diagnostic hypotheses seemed unlikely. Repeated HIV screening was negative. Because he was generally in good medical condition previously with no special therapy or medication, a hematological malignancy that could cause marked atypical lymphocytosis seemed unlikely. In addition, the indication for the splenectomy was accidental trauma to his thorax, not a disease [9, 10]. Accordingly, although atypical, we conclude that our patient indeed had a primary EBV infection, which resulted in a mononucleosis-like condition.

On the other hand, our analysis has certain limitations and our case some uncertainties. First, we have no direct evidence of EBV infection; EBV viral load was not measured. However, we believe that even possible mononucleosis does not warrant routine measurement of EBV viral load. In principle, typical IM with a primary EBV infection is a benign syndrome and can be self-limiting, except a fulminant course in viral-associated hemophagocytic lymphohistiocytosis or a neurological complication [8]. Next, hematological neoplastic conditions, such as lymphoma, leukemia, and lymphoproliferative disease, could not be completely ruled out. We did not obtain a bone marrow specimen. However, if IM is suspected clinically and the patient does not appear to have a serious condition or be physically exhausted, clinicians

usually choose "watchful waiting" and hold back from an intensive work-up in the outpatient setting in departments of general internal medicine. Unfortunately, flow cytometric assessment of blood lymphocytes was not performed. Thus, the clonality of the increased lymphocytes in his blood sample remains unknown. Additionally, no Southern blot analyses of marrow aspirate were performed; therefore, we had no information on our patient's T-cell receptor γ gene rearrangements.

In summary, we suggest that the immune system in a splenectomized patient can distort the clinical picture of EBV-IM, although the underlying mechanism remains to be elucidated. Our case involved several atypical issues. Although the possibility of individual variation cannot be excluded, the atypical factors we describe here may characterize the clinical features of EBV-IM in asplenic patients.

Declaration

No financial support or other benefits from commercial sources for the work reported on in the manuscript (All authors).

Conflict of Interest

None (All authors).

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