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Chronic active Epstein-Barr disease in a 57 year old woman: A case report

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Abstract

Infectious Mononucleosis (IM) caused by the Epstein-Barr virus (EBV) is prevalent in the adolescent and young adult population. Common symptoms include fatigue, sore throat, swollen glands, and fever.

We present a case of a 57 year old female patient with fatigue and low energy for 6 months. She has a past medical history of systemic scleroderma and hypothyroidism, controlled on medications and managed by her primary care physician. Her physical exam revealed very mild erythema of the soft palate and mild anterior and posterior cervical lymphadenopathy. Initial laboratory workup for fatigue was negative and symptoms worsened despite antibiotic treatment. New laboratory tests revealed elevated EBV IgM and IgG antibodies and the patient was managed both conservatively and pharmacologically. Follow-up months later revealed a persistent EBV IgM level and the patient was referred to an Infectious Disease specialist where a PCR assay was performed to quantify her EBV viral load.

The intention of this case report is to raise awareness of the rare manifestations of Infectious Mononucleosis caused by the Epstein-Barr virus; and to suggest that there may be a relationship between chronic active EBV and patients with autoimmune disorders.

Keywords

Chronic fatigue syndrome; EBV; epstein-barr; exhaustion; glandular fever; kissing disease; infectious mononucleosis; low energy

Abbreviations

EBV: Epstein-barr virus; IgM: Immunoglobulin M; IgG: Immunoglobulin G; IM: Infectious mononucleosis; PCR: Polymerase chain reaction

Introduction

Fatigue is a common complaint in an outpatient setting, as approximately 5-7% of patients will complain of low energy and tiredness [3]. Some of the most common causes of fatigue include lack of sleep due to poor sleep hygiene, sleep apnea, anemia, major depression, hypovolemia or volume depletion, and thyroid disorders. Outpatient diagnostic testing for patients with a chief complaint of fatigue include drawing labs for a complete blood count, c-reactive protein, erythrocyte sedimentation rate, comprehensive metabolic panel, thyroid function panel, urinalysis, and urine pregnancy if patient is of reproductive age. Laboratory tests for IgM and IgG antibodies towards the Epstein-Barr virus are not routinely drawn, unless there is an indication to do so.

The Epstein-Barr virus is a member of the herpesvirus family and is known as Human Herpesvirus 4 (HHV-4). Approximately 90% of adults are positive for EBV by the age of 35, with the highest prevalence between ages 6-19 [1]. This virus, which causes Infectious Mononucleosis and infects both epithelial and B-cells, is transmitted quickly through saliva and has consequently been nicknamed "The Kissing Disease". The most common symptoms associated with an EBV infection are fever, sore throat, swollen glands, and fatigue. Common findings on physical exam include exudative pharyngitis, erythema of the soft palate with petichae, and prominent posterior cervical lymphadenopathy.

Case Presentation

MA if a 57 year old Hispanic female patient who presented to our urgent care with a chief complaint of overwhelming fatigue, body aches, and intermittent headaches for the past 2 weeks. She has a history of both systemic scleroderma and hypothyroidism and takes 25mcg of Liothyronine daily. She described the fatigue as "overpowering, causing me to sleep 13 hours per day" and it does not improve after napping. The fatigue began about 6 months ago, but she attributed it to her underactive thyroid. She stated that "the body aches may be from my scleroderma, but something just doesn't feel right". She described her headache as "a dull ache once in a while and a feeling of haziness". When asked about associated symptoms, she mentioned "a very mild sore throat once in a while".

MA has a past medical history of Hypothyroidism, Essential Hypertension, and Systemic Scleroderma with Reynaud's Syndrome. Current medications include Liothyronine 25mcg daily, Hydrochlorothiazide 25mg daily, and Telmisartan 40mg daily; the latter which covers both her high blood pressure and Reynaud's Syndrome. She has no surgical history and a noncontributory family history. She lives at home with her husband and does not drink or smoke. She denied any recent travel. She also denied cough, confusion, neck pain, changes in vision, weight changes, dyspnea, chest pain, lightheadedness, weakness, numbness, or new skin changes.

Vital signs were as follows: T: 100.4F, P: 68-90 (range), BP: 132-139/73-75 (range), RR: 10, O2: 97.

Physical examination presented an alert and oriented female in moderate distress that appeared pale and fatigued. She was febrile and orthostatic as per her vital signs, as well as significantly volume

depleted. Head was normocephalic and atraumatic and eye exam showed pupils that were equal, round, and reactive to light. Fundoscopic exam was normal. Examination of the throat revealed very mild erythema of the soft palate, but not pharynx; and showed no tonsillar enlargement or exudates. Patient's neck was supple with full range of motion with both anterior and posterior cervical lymphadenopathy. Abdominal exam was without any splenomegaly. Neurologic examination was normal and cranial nerves 2 through 12 were intact.

Based on the Centor Criteria, the patient scored a 3 out of 4; which is an indication for a rapid streptococcal antigen test (she was given 1 point for the following: tender anterior cervical lymphadenopathy, history of fever, absence of cough; she was given 0 points for tonsillar exudate) [2]. However, the rapid test was performed and was negative. Though, the throat culture was sent to the lab along with blood work including a CBC, ESR, and CRP. The patient was subsequently hydrated with 3 full liters of Ringer's lactate solution and given broad spectrum antibiotics intravenously. She was eventually discharged and treated with Augmentin (Amoxicillin-Clavulanate) 500mg twice a day given symptoms. The decision to treat the patient was based on her clinical symptoms, as well as the 75-90% sensitivity of the rapid streptococcal antigen test and high rate of false negative tests [4].

MA returned to the urgent care approximately 2 weeks after her initial visit with persistent symptoms including "pain with difficulty swallowing" despite oral antibiotics. All laboratory workup was within normal limits and her throat culture was negative for Group A Strep. At this time, a more extensive laboratory workup was initiated including ANA, serum ferratin, serum B12, liver function testing with viral hepatitis, HIV antigen/antibody screening, and EBV Capsid IgM and IgG testing.

The following laboratory tests were positive:

	NAME	VALUE	REFERENCE RANGE
F	EBV CAPSID Ag.Ab/IgM	>160.0 A	<36.0 (U/mL)
F	EBV CAPSID Ag.Ab/IgG	152.0 A	<18.0 (U/mL)

Figure 1A: Serologic testing showing antibody levels towards the Epstein-Barr virus. The patient's EBV demonstrates a recent infection given the increased values of both IgM and IgG antibodies. A value of 160 is expressed as the inverse of the greatest dilution which still yields a positive result (1:160).

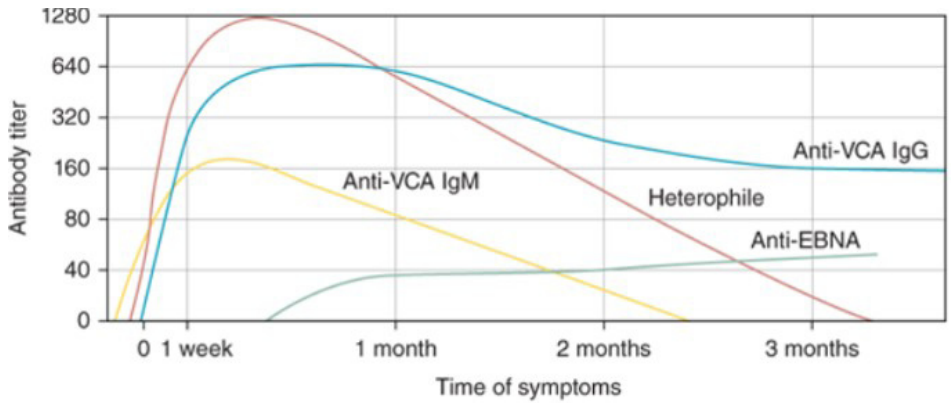
	NAME	VALUE	REFERENCE RANGE
F	WBC	9.30	4.00-10.10 (x10(3)/uL)
F	RBC	4.11	3.58-5.19 (x10(6)/uL)
F	HGB	12.3	11.0-15.5 (gm/dL)
F	HCT	37.1	31.5-44.8 (%)
F	MCV	90.3	78.0-98.0 (fL)
F	MCH	29.9	25.2-32.6 (pg)
F	MCHC	33.2	31.0-34.7 (gm/dL)
F	RDW	16.8 H	12.0-15.5 (%)
F	POLYS	68.2	37.1-78.1 (%)
F	LYMPHS	20.8	13.7-50.9 (%)
F	MONOS	9.4	3.0-11.9 (%)
F	EOS	1.2	0.0-5.0 (%)
F	BASOS	0.3	0.0-1.0 (%)
F	IMMATURE GRANULOCYTES	0.1	0.0-1.0 (%)
F	PLATELET COUNT	396	140-425 (x10(3)/uL)
F	MPV	9.1	8.6-12.1 (fL)

Figure 1B: Complete blood count (CBC) showing a slightly elevated red blood cell distribution width (RDW) in bold red; that of which is a measurement of the size of the patient's red blood cells. Many disorders may cause a variation of red blood cell size. There was no increase in the patient's overall white blood cell count, as one may expect with a diagnosis of Infectious Mononucleosis.

The patient was diagnosed with Infectious Mononucleosis given positive antibody levels towards the capsid of the Epstein-Barr virus (Figure 1A). The elevated RDW with borderline high MCV may be attributed to iron, B12, or folate deficiency; however subsequent laboratory tests appeared normal (Figure 1B). At this time, the patient was managed with supportive care including analgesics for symptomatic relief, fluids for adequate hydration, limited activity throughout the day, and avoidance of strenuous activity. The patient was also given (1) a 60mg Prednisone six-day taper given persistent dysphagia and odynophagia and (2) antiviral Valacyclovir 500mg three times per day to reduce the frequency of EBV-infected B cells [5].

Discussion/conclusion

The acute phase of Infectious Mononucleosis usually lasts for a median of 10 days. MA continued to follow-up at our clinic on a regular basis, as she had persistent symptoms for months; despite increases in the dose of Valacyclovir (500mg to 1 gram) and duration of treatment. Laboratory tests were repeated after 6 months and IgM antibodies towards the EBV viral capsid remained >160 U/ml. We would expect her Anti-VCA IgM antibody level to have decreased by the 3 month mark (Figure 2). At this time, she was referred to an Infectious Disease specialist for viral load PCR testing given that was still experiencing symptoms.



Source: D.L Kasper, A.s. Fauci, S.L. Hauser, D.L. Longo, J.L.Jameson, J. Loscalzo: Harrison's Principals of Internal Medicine, 19th Edition www.accessmedicine.com

Figure 2: This chart represents the progression of viral capsid antibodies (VCA) to the Epstein-Barr virus in patients with Infectious Mononucleosis. Following the onset of MA's symptoms, we would expect a full decrease in Anti-VCA IgM antibodies after 2.5 months.

While most symptoms associated with EBV resolve in a matter of months, a rare complication manifests after 6 months in the form of chronic active EBV [6]. Patients with chronic active EBV experience persistent symptoms including persistent sore throat, fever, lymphadenopathy, and fatigue. Early reports attributed chronic active EBV to a rare strain of the virus which has a deletion in the viral genome [7]. A patient in a chronic immunocompromised state may go on to develop progressive cellular and humoral immunodeficiencies and is at risk for opportunistic infections.

In this case, MA may be predisposed for a disseminated EBV infection given her immunocompromised

state in the first place. Systemic scleroderma represents of group of autoimmune diseases which, on their own, play a role in the activation and destruction of the immune system. There may be a link between MA's immunocompromised state leading to a chronic Epstein-Barr infection; that of which will be beneficial to study in more detail.

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