

A Tale of Two Mononucleosis Syndromes

Cytomegalovirus and Epstein-Barr Virus for the Primary Care Provider



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KEYWORDS

- Herpes virus • Mononucleosis syndromes • Fevers • Malaise • Pharyngitis
- Splenomegaly • Viremia • Immunocompetent host

KEY POINTS

- Mononucleosis syndromes can present nonspecifically with malaise, fever, and pharyngitis.
- These can be difficult to diagnose in primary care clinics with vague presenting symptoms, laboratory results that can be challenging to interpret, and only supportive treatment as the remedy.
- Epstein-Barr virus (EBV) is the most common virus causing mononucleosis in immunocompetent patients.
- Cytomegalovirus causes severe disease primarily in immunocompromised patients, including those with hematologic malignancies and transplants.
- Heterophile antibody testing is most specific for EBV but can be falsely negative early in the course of infection and falsely positive in inflammatory conditions.

CASE REPORT

A previously healthy 22-year-old man presents to a neighborhood primary care clinic with complaints of malaise, fever, and pharyngitis for the past 3 days. He describes extreme fatigue, and that his neck “feels swollen.” Physical examination does indeed show cervical adenopathy with complete blood count (CBC) remarkable for atypical lymphocytosis. A heterophile antibody test is negative.

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INTRODUCTION

Mononucleosis typically describes a constellation of symptoms, including fever, malaise, and pharyngitis. They are common presentations to primary care clinics, yet are often left undiagnosed or misdiagnosed: the differential is broad, the symptoms are nonspecific, and the treatment is often supportive. Even in the immunocompetent patient, however, the sequelae of infection can lead to significant morbidity. This review provides practical information, including evaluation and treatment of mononucleosis syndromes for the primary care provider.

EPSTEIN-BARR VIRUS

Introduction

Primary infection with Epstein-Barr virus (EBV) in the immunocompetent host can cause heterophile-antibody-positive mononucleosis that is characterized most commonly by fever, pharyngitis, and lymphadenopathy. Transferred primarily by saliva, it is known colloquially as the “kissing disease,” although in certain populations it can lead to lymphoma, lymphoproliferative disorders, and squamous cell carcinoma.¹

Pathology and Presentation

EBV infects B cells and the mucosal cells of the nasopharynx. The antibody response to infection is robust, including nonspecific antibodies that can be picked up by the “heterophile antibody” test for use in diagnosis. The immune system provides lifelong control but does not eradicate EBV. If this immunity is significantly impaired, rarely lymphoproliferative disorders or lymphoma can occur.¹

Adolescents (10–19 years of age) are most likely to develop symptomatic primary EBV infection.^{2–5} The typical incubation period is 30 to 50 days. Presentation can include pharyngitis, fever, and lymphadenopathy. Some patients may present with a diffuse maculopapular rash after the administration of amoxicillin. CBC shows atypical lymphocyte predominance with or without thrombocytopenia.^{1,3} Resolution of infection should be within 1 to 3 weeks, although it can take months for the malaise and fatigue to resolve. Chronic mononucleosis (with detectable virus in blood) has uncommonly been described, persisting as long as 6 to 12 months beyond the initial infection.⁶ Transmission of EBV is typically through saliva, which is the most infectious bodily fluid and may remain infectious even after the patient is asymptomatic, up to 6 months.² EBV also has been isolated in cervical cells and seminal fluid, suggestive of possible sexual transmission.^{7,8} The major risk factor for transmission, however, has been found to be via saliva (such as with kissing) due to the high number of viral particles found in saliva.^{2,5}

Complications

Splenic rupture

Splenomegaly occurs in approximately 50% of EBV-associated mononucleosis syndromes; splenic rupture is an uncommon but serious complication, occurring in 0.1% to 0.2% of cases.^{9,10} Because an enlarged spleen is often palpable in only half of cases and rupture is not always associated with trauma, it is recommended that all patients with confirmed EBV avoid contact sports for at least 3 weeks after presentation.¹¹ There are case reports of splenic rupture occurring as late as 8 weeks, however, so clinicians should thoroughly carefully counsel patients of the risks associated with contact sports. Interestingly, there is no correlation between hematologic abnormalities, disease severity, and splenic rupture.^{9,10,12,13}

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