



## Infectious mononucleosis with *Staphylococcus aureus* pharyngitis co-infection

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**Summary** Epstein-Barr virus (EBV), a member of the herpesvirus family, is one of the most common human viruses affecting more than 90% of the world's population. The most common manifestation of primary infection is a self-limited clinical syndrome that most frequently affects adolescents and young adults. The incidence of clinical infectious mononucleosis is not well documented because reporting is not obligatory in most states. The available data have been derived from special surveys such as the community survey in Olmstead County, Minnesota, which includes the Mayo Clinic, where a rate of 200 per 100,000 patients had a positive heterophile test.<sup>1</sup> Once a diagnosis of mononucleosis is confirmed, treatment is supportive because there is no specific treatment for the disease. Mononucleosis is rarely fatal but some complications include central nervous system involvement, splenic rupture, upper airway obstruction, and bacterial super infections. The following clinical case is of a patient diagnosed with acute infectious mononucleosis with *Staphylococcus aureus* pharyngitis co-infection. © 2010 Elsevier Inc. All rights reserved.

### Case presentation

#### History of present illness

D.D., an 18-year-old female dance student in Philadelphia presented with a three-day history of fever of 101 °F, night sweats, sore throat, upper respiratory congestion, swollen glands, abdominal pain, nausea, and fatigue. A rapid strep test was performed in the office and was negative; however, a throat culture was sent out for analysis. In addition, blood work was ordered for a mono spot heterophile antibody test, Epstein-Barr Virus (EBV) panel, complete blood count, and complete metabolic profile.

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### Focused physical examination

The patient had posterior pharyngeal erythema and exudates with enlarged tonsils. Enlarged posterior and anterior cervical lymph nodes were also noted. The abdomen was soft with minor nonlocalized tenderness on palpation. The spleen and liver were examined for enlargement and tenderness, both were unremarkable. The remainder of the physical examination was unremarkable.

### Laboratory and cultures

Laboratory studies revealed an elevated white blood cell count of 13.8, absolute lymphocytes of 9.5, and absolute monocytes of 1.2. Neutrophils were 21% and lymphocytes were 69%, with 23% atypical lymphocytes. Liver function test revealed elevated total bilirubin of 2.1 mg/dL, alkaline phosphatase of 321, AST of 241, and ALT of 312.

**Table 1** Symptoms and signs of infectious mononucleosis

Symptoms of infectious mononucleosis	Signs of infectious mononucleosis
Sore throat (75%)	Lymphadenopathy (95%)
Malaise (47%)	Fever (93%)
Headache (38%)	Pharyngitis and tonsillitis (82%)
Abdominal pain, nausea, and vomiting (17%)	Splenomegaly (51%)
Chills (10%)	Hepatomegaly (11%)
	Rash (10%)
	Periorbital edema (13%)
	Palatal exanthem (7%)
	Jaundice (5%)

Percentages indicate the likelihood that a person with infectious mononucleosis will present with the described sign or symptom. Data taken from Ref. 16.

## Treatment

At the conclusion of the office visit, the patient was instructed to complete a course of amoxicillin 875 mg twice daily for 10 days to treat suspected group A beta-hemolytic streptococci (GABHS). In addition, the patient was instructed to use over-the-counter guaifenesin for congestion. A few days later, the lab results returned and a diagnosis of acute infectious mononucleosis with hepatitis was made. In addition, the throat culture results were positive for *Staphylococcus aureus* and yeast.

The patient was called and informed to refrain from physical activity, to drink plenty of fluids, and to rest. She was informed of danger signs that might prompt a visit to the emergency department (e.g., abdominal pain, odynophagia, dysphonia). The patient was instructed to return to the office in one month for a follow-up and to have her laboratory values rechecked. The patient was prescribed a one-day course of fluconazole (1 tablet, 150 mg) for the isolated yeast on the throat culture, and sulfamethoxazole and trimethoprim double strength, one tablet by twice daily for 10 days to treat the *Staphylococcus aureus* pharyngitis.

## Follow-up visit

At follow-up, the patient had completed the course of fluconazole and trimethoprim/sulfamethoxazole and stated that she felt much improved and was regaining her energy. She denied any abdominal pain, chest pain, shortness of breath, nausea, vomiting, or diarrhea. Upon physical exam-

ination, her nasal mucosa and turbinates were found to be normal. Her posterior pharynx showed no signs of exudate. Her abdomen was soft and nontender with normal bowel sounds. Liver and spleen palpation showed no signs of enlargement or nodularity. Minor anterior cervical adenopathy was present. The patient was instructed to return to the office six weeks later to recheck her laboratory values, particularly her liver function tests, and to receive permission to return to school and resume dancing.

## Discussion

Infectious mononucleosis is usually caused by the Epstein-Barr virus (EBV; or human herpesvirus 4). More than 90% of adults worldwide are seropositive for EBV. Infectious mononucleosis may be seen at any age but usually occurs sporadically or epidemically in persons in the United States between the ages of 10 and 35 years. EBV is transmitted by close human contact, frequently with the saliva during kissing. In certain instances it can be associated with certain lymphomas and nasopharyngeal carcinomas. Infectious mononucleosis is characterized by generalized lymphadenopathy, splenomegaly, pharyngeal erythema and exudate, and the appearance of atypical activated T lymphocytes (CD8+ T cells) in the blood.<sup>2,3</sup> Table 1 lists the symptoms and signs of infectious mononucleosis.

In this case report, the patient presented with signs and symptoms suggestive of GABHS pharyngitis or infectious mononucleosis. An EBV panel verified infectious mononucleosis and the results are shown in Tables 2 and 3. Heterophile antibodies are 40% positive in patients with infectious mononucleosis in the first week, and initial tests may be negative. In addition, throat culture swab results indicated a *S. aureus* pharyngitis infection (Table 4). The significance of this finding is that infectious mononucleosis with *S. aureus* pharyngitis co-infection is not commonly encountered in the clinical setting. In general, the studies we encountered showed that GABHS is the most common bacterial cause of pharyngitis.<sup>4,5</sup> Three studies to date illustrate a relationship between infectious mononucleosis and GABHS pharyngitis co-infection. In one study of 500 patients with infectious mononucleosis, 30% had GABHS.<sup>6</sup> Two other studies reported that rates were between 3% to 4% in more than 100 patients.<sup>7,8</sup> As a result of these findings, the true rate most likely falls somewhere between 3% and 30%.

**Table 2** Patient's EBV panel results

	Heterophil Ab	VCA-IgM	EA-IgG	VCA-IgG	NA-ABS
Acute infection	Negative	Positive, 472 au/mL	Negative, 76 au/mL	Positive, 2822 au/mL	Negative, 73 au/mL

VCA-IgM, viral capsid antigen-immunoglobulin M; EA-IgG, early antigen diffuse complex; VCA-IgG, viral capsid antigen-immunoglobulin G; NA-ABS, nuclear antigen-antibodies.

**Table 3** EBV interpretation chart from lab

	VCA-IgM	EA-IgG	VCA-IgG	NA-Abs
Susceptible	Negative	Negative	Negative	Negative
Acute Infection	Positive	Positive or negative	Positive	Negative
Convalescent phase	Positive or negative	Positive or negative	Positive	Positive
Chronic or reactivated phase	Negative	Positive	Positive	Positive or negative
Old infection	Negative	Negative	Positive or negative	Positive

VCA-IgM, viral capsid antigen-immunoglobulin M; EA-IgG, early antigen diffuse complex; VCA-IgG, viral capsid antigen-immunoglobulin G; NA-Abs, nuclear antigen-antibodies.

*S. aureus* infections, on the other hand, are better known for causing skin lesions and cellulitis, in addition to osteomyelitis, pneumonia after an influenza infection, endocarditis, food poisoning, and toxic shock syndrome.<sup>3</sup> *S. aureus* pharyngitis infections are possible but are not nearly as prevalent as GABHS pharyngitis infections. Studies in the past have been documented to investigate the relationship and mechanism between oropharyngeal bacterial colonization during a viral illness. Two studies in the 1980s demonstrated that adherence of *S. aureus* to pharyngeal cells is increased during upper respiratory infections.<sup>9,10</sup> In addition, epidemiological studies have shown a prevalence of *S. aureus* in the United States. However, these studies monitored nasal colonization of *S. aureus* as opposed to pharyngeal colonization.<sup>11,12</sup> A recent study in 2006 by Nilsson and Ripa illustrated that *S. aureus* throat colonization is more frequent than nasal colonization. They concluded that *S. aureus* carriage in the anterior nares in most cases indicates the presence of the organism in the throat.<sup>13</sup> Admittedly, in this study the individuals were healthy so it remains to be seen whether the frequency of infection would change when comparing throat colonization to anterior nares colo-

nization in persons who are also concomitantly infected with a viral illness. Questions still remain as to what is the best source for detecting *S. aureus*. According to an article by Mertz et al., throat swabs are necessary to more accurately detect carriers of *S. aureus*.<sup>14</sup> All carriers of *S. aureus* are not identified by nasal swabs alone. The study showed that 30% of persons in the population are carriers of *S. aureus* in the anterior nares and an additional 12.8% are pharyngeal carriers alone.<sup>14</sup> With the rising occurrence of methicillin-resistant *Staphylococcus aureus* (MRSA) in the United States, determining which patients are pharyngeal asymptomatic carriers from patients who have an acute *S. aureus* pharyngitis infection may help to reduce the occurrence of MRSA infections in the future. Current screening programs for MRSA do not call for pharyngeal swabs, but the standard of care may change during the upcoming years as we continue to see an increase in the prevalence of MRSA in the health care setting.<sup>14,15</sup>

In conclusion, the patient was treated with antibiotics for infectious mononucleosis with *S. aureus* pharyngitis co-infection. We acknowledge that the patient may have been an asymptomatic carrier and more research should be directed towards investigating the percentage of the population who are pharyngeal-asymptomatic carriers of *S. aureus* versus those with an active *S. aureus* pharyngitis infection. We must be careful because treatment of asymptomatic carriers may promote antimicrobial resistance. It may not be necessary for physicians to treat patients who are previously found to be asymptomatic carriers with antibiotics, thus helping to prevent antimicrobial resistance, particularly that to MRSA.

**Table 4** Throat culture analysis

Results	
Heavy growth of oxacillin sensitive <i>Staphylococcus aureus</i>	
Yeast isolated	
Antimicrobial susceptibility	
Heavy growth of oxacillin sensitive <i>Staphylococcus aureus</i>	S
Clindamycin	S
Erythromycin	S
Gentamicin	S
Levofloxacin	S
Linezolid	S
Oxacillin	S
Penicillin	R
Rifampin	S
Tetracycline	S
Trimethoprim/sulfa	S
Vancomycin	S

S, sensitive; R, resistant.

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