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CLINICAL VIGNETTE

Severe Pharyngitis due to Primary Acute Epstein-Barr Virus (EBV) and Cytomegalovirus (CMV) Coinfection

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Introduction

Mononucleosis (or mono) is a common infection of children, teenagers, and young adults classically presenting with the constellation of fever, swollen lymph node, and fatigue. It is typically caused by either Epstein-Barr Virus (90%) or cytomegalovirus (5%) infections. While very common in pediatrics, acute mono is much less common in general adult medicine practices, especially in hospitalized patients. In the hospitalist role, acute mononucleosis in an immunocompetent patient is rare, but can have severe consequences.

Case Presentation

A 20-year-old male presented to the ED with hoarse voice, throat tightness, and fever. About ten days prior, he developed sore throat and rash on the right forearm and left thigh and was seen at student health where rapid strep was positive and he was prescribed amoxicillin and methylprednisolone. Symptoms initially improved, but several days later he developed diffuse, pruritic rash on upper trunk, and the following day noticed swollen nodes in his neck with subjective fever, chills, and throat tightness. Initial exam prompting ED eval was significant for tachycardia, palpable cervical lymph nodes, hoarse speech, and enlarged tonsils. He received normal saline, ketorolac, and dexamethasone, and was counseled to follow-up in student health. He felt better, but over the next two days, was unable to tolerate solids or liquids and returned to the ED.

At re-presentation, his voice was markedly hoarse, and his tonsils were erythematous and touching. He had a leukocytosis of 16K and unremarkable chemistries. CT revealed bilateral adenoid and tonsil enlargement without fluid collection. He denied prior mononucleosis, new sexual partners or recent travel. His only sick contact was his girlfriend who had multiple recent "strep throat" infections over the preceding month. He was admitted for close observation and continued on IV steroids. He initially received ampicillin/sulbactam until procalcitonin returned negative. Significant studies included peripheral smear with reactive lymphocytes, negative HIV, negative HHV 6 IgM, positive Monospot, positive CMV IgM and negative IgG, and positive EBV IgM and negative IgG consistent with acute infectious mononucleosis. He improved and was discharged after three days tolerating POs. One month later, he was seen in ENT clinic and offered bilateral tonsillectomy.

Discussion

With the triad of fever, sore throat, and palpable neck lymphadenopathy, acute mono pharyngitis should be strongly considered, especially in the usual at-risk population of adolescents and young adults. Approximately ~95% of cases are due to either EBV or CMV with HHV6 and HIV being other less common diagnostic considerations.¹ It is difficult to clinically differentiate the viral etiologies of mono, but typically, a positive heterophile antibody test such as the Monospot with these symptoms is diagnostic of mono due to EBV.² Viral mononucleosis is common, but severity leading to hospitalization in adolescents/adults is rare, and this case is instructive for both diagnostic and therapeutic reasons. From the diagnostic side, acute primary coinfection with EBV and CMV is relatively rare in adults with only a few case reports in the literature.^{3,4} While more common in children, only 6/190 in a retrospective study of hospitalized children with suspected mono tested serologically positive for primary coinfection.⁵ Assuming both viruses are considered, the diagnosis may still be confused due to high cross-reactivity of common tests, reported up to 49%.⁶ Additionally, CMV can disrupt the immune system through modulation of interleukin synthesis, allowing EBV to reactivate, leading to an incorrect/incomplete diagnosis.⁷ In this case, the EBV IgG was negative (94% sensitivity), implying no prior infection.⁸ Severe mono leading to hospitalization as in this case is atypical, but may occur if someone has prominent tonsils at baseline.

In regards to therapy after diagnosis, prescribing steroids for mononucleosis remains controversial. A systematic review was equivocal for benefit of steroid treatment and expert opinion is mixed.³ Supportive care is the primary therapy once the correct diagnosis is made, including adequate hydration and airway management with intubation or tonsillectomy if necessary in extreme cases. There are a number of important sequelae to be aware of in mononucleosis. Fatigue commonly follows the initial infection, however, there have been rare cases of associated acute transverse myelitis.⁹ A more well-known sequelae is splenic infarction, which occurs rarely, and is likely due to EBV's effects on the coagulation cascade, including reduction in Protein S and increase in Factor VIII.¹⁰ Associations between EBV and the development of nasopharyngeal carcinoma, Burkitt's lymphoma, Hodgkin lymphoma, gastric carcinoma, and lymphoma especially in the immunocompromised patients, have been the impetus to explore vaccination.¹¹ This is of particular interest at UCLA where a

significant proportion of our inpatients are immunocompromised. It is critical to consider these viruses as when they relate to the clinical situation and broaden our differential.

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