An Uncommon Cause of Severe Upper Airway Obstruction in a Toddler

Carlos Castillo, MD1, and Carston Ruffo, MD2

Received August 11, 2017. Accepted for publication August 28, 2017

Case Report
A previously healthy 3-year-old boy is evaluated for a 3-day history of fever and swelling on both sides of his neck. He was found to have acute otitis media and was started on amoxicillin by his pediatrician. Since 2 days ago, the patient presents drooling, loud snoring, noisy breathing, hoarseness, inability to eat solids, and persistence of fever. There is no history of rash, weight loss, night sweats, neck stiffness, sick contacts, recent travel, or exposure to animals.

Physical examination reveals an alert, sick-looking child. His temperature is 39.6°C, heart rate is 130 beats per minute, respiratory rate is 28 breaths per minute, blood pressure is 96/54 mm Hg, and oxygen saturation is 99% on room air. He has nasal congestion, bilaterally enlarged tonsils with mild erythema, and white exudates. The uvula is not deviated. There are multiple 2- to 3-cm mobile, nonerythematous, nontender anterior cervical lymph nodes bilaterally. The remainder of his physical findings is unremarkable.

His initial laboratory results show a hemoglobin level of 12.6 g/dL (126 g/L); white blood cell count of 14.2 × 10^3/µL (14.2 × 10^9/L) with 37% neutrophils, 52% lymphocytes; and platelet count of 208 × 10^3/µL (208 × 10^9/L). His serum electrolyte values are within normal range. His aspartate transaminase level is 38 U/L, alanine transaminase level is 50 U/L, and C-reactive protein level is 17.17 mg/dL. Rapid strep test is negative. A neck ultrasound (Figure 1) reveals multiple lymph nodes ranging from 1.8 to 3.6 cm over the right subauricular and left subauricular regions without fluid collection. Neck computed tomography without contrast (Figure 2) ruled out any retropharyngeal mass and confirmed level II and level V lymphadenopathy.

The patient is admitted and additional tests reveal the diagnosis.

Hospital Course
Due to increasing respiratory distress, the patient was transferred to the pediatric intensive care unit from inpatient service for cardiorespiratory monitoring. He was treated with racemic epinephrine, intravenous (IV) steroids, IV hydration, and IV antibiotics. Respiratory distress responded to initial treatment. However, despite broad spectrum antibiotics, the patient remained persistently febrile. Repeated complete blood count tests revealed the presence of 19% atypical cells. Subsequent serologic studies showed Epstein-Barr virus (EBV) viral capsid antigen IgM negative/IgG positive and cytomegalovirus (CMV) IgM positive/IgG positive. Antibiotics were discontinued on serology results and with negative blood cultures. The patient continued on conservative therapy and was discharged after 5 days.

Final Diagnosis
Cytomegalovirus infection

Introduction
Cytomegalovirus infection is endemic in the community. The majority of children acquire CMV after joining daycare and 80% of children get infected by the age of 2 years.1 Ninety percent of cases are asymptomatic, and symptomatic patients may present with anything from a flu-like illness to an infectious mononucleosis (IM) like syndrome.2,3 Severe upper airway obstruction (UAO) is as rare as 1% to 3.5% among patients with IM-like syndrome.4

Pathophysiology
Cytomegalovirus, or HHV-5, is a member of the betaherpesvirus group and is ubiquitous within the population. Transmitted horizontally through most bodily fluids (including saliva, urine, and genital secretions),

1Lincoln Medical and Mental Health Center, New York, NY, USA
2Saint George’s University, True Blue, Grenada

Corresponding Author:
Carlos Castillo, Lincoln Medical and Mental Health Center, Department of Pediatrics, 234 E 149th St, Bronx, New York, NY 10451, USA.

Email: ccastilopinto@gmail.com
CMV has a predilection for infecting the mucosal surface of both the upper respiratory and genital tracts. CMV can also be transmitted vertically from mother to infant, through blood transfusions and organ transplantation. Viremia has been indicated as the likely mechanism for systemic dissemination, with those cells infected displaying a classic “owl’s eye” nucleus on histology, as a result of nuclear viral replication. Once infected, individuals begin to shed the virus at 4 to 6 weeks and may continue to do so up to several months postinfection. Cessation of viral shedding does not necessarily indicate complete resolution, as latent infections may reactivate with recurrent viral excretion.

**Epidemiology**

Increased rates of primary CMV infection are typically associated with the perinatal period, enrollment in daycare, and during the reproductive age in adolescents (the start of sexual activity), due to the increase in body fluid exposure at these times. Studies have indicated that active viral shedding among those in US daycare centers can range anywhere from 9% to as high as 69%, with the vast majority of those infected remaining asymptomatic.

While an analysis of the total population indicates EBV to be the most common cause of those presenting with symptoms characteristic of either IM or IM-like syndromes, a 1994 study of 124 children with such symptomatology demonstrated that CMV may be the leading cause for those under 4 years of age.

**Signs and Symptoms**

While CMV infections in immunocompetent children are typically asymptomatic, the development of

---

**Figure 1.** Neck ultrasound shows several enlarged lymph nodes in subauricular areas bilaterally. The largest one was 3.6 × 2.8. No fluid collection.

**Figure 2.** Neck computed tomography shows right levels II and V lymphadenopathy.
heterophil Ab-negative IM, or IM-like syndrome, is a possible consequence of the infection. IM-like syndrome is characterized by a vague panel of symptoms including fever, malaise, headache, and fatigue. Symptoms have been shown to persist for an average of ~7 weeks in symptomatic, immunocompetent adults infected with CMV. While less common, CMV IM-like syndrome may progress to a more severe presentation, which can include hepatitis, hepatomegaly, splenomegaly, thrombocytopenia, hemolytic anemia, myocarditis, gastrointestinal ulcerations, and UAO. Of those displaying signs of infection, those with compromised immune systems (such as premature neonates, those co-infected with HIV, and transplant recipients) are at a greater risk of developing severe, life-threatening presentations. Mortality among those with IM-related UAO is extremely low due to the effectiveness of airway management and self-limiting nature of these infections. Death due to asphyxiation, however, can occur if cases are improperly managed, such as in the instance documented by Boglioli and Taff, involving an 18-year-old girl with EBV IM.

Diagnosis

The symptomatology of IM-like syndrome, including the potential for UAO, is identical to that of EBV-associated IM and requires laboratory workup to differentiate. A negative monospot test, in combination with a positive CMV IgM and negative EBV IgM, is highly indicative of an acute CMV infection. In children under 4 years of age, the monospot test is often falsely negative, so serological tests are typically relied upon for diagnosis.

Treatment

Patients admitted with IM-like symptoms who display signs of stridor, tachypnea, cyanosis, nasal flaring, dyspnea, intercostal and supracostal retractions, as well as the use of accessory respiratory muscles, should be placed on high suspicion of severe UAO. In these cases, prompt management and continued observation is required to ensure the condition does not progress to asphyxiation. Also recommended is that clinical severity and choices of intervention should be judged based on general appearance of the patient rather than clinical measurements such as respiratory rate, pulse, and blood gas analysis. While established treatment guidelines for CMV-related UAO are currently pending future research, Chan and Dawes have proposed a series of management steps for EBV-related UAO in children, which coincides with current clinical practice. Their regimen includes airway observation (looking for any of the previously mentioned key signs), in combination with recordable pulse oximetry to measure the baseline, frequency, duration, and severity of all desaturations. They also recommend systemic corticosteroids on admission, and possible airway intervention should the condition progress. Airway management should ideally involve a nasopharyngeal stent as first choice; however, endotracheal intubation or acute tracheostomy may be required in the most severe cases. For IM UAOs that fail to respond to corticosteroids, an acute tonsillectomy can be used to relieve obstruction; however, should only be used as a last resort due to the risk of bacteremia and postoperative hemorrhage. Last, while the benefits certainly outweigh the risks, the use of immune suppressing corticosteroids should include close monitoring, as both CMV and EBV are oncogenic viruses.

Conclusion

While instances of pediatric (UAO) associated with EBV infectious mononucleosis (IM) have been well documented, current clinical presentation shows that primary CMV infections that progress to an IM-like syndrome can also manifest in a similar form of respiratory distress. Recognizing the potential for primary CMV to present in this way will allow clinicians to better predict and treat these uncommon cases.

Acknowledgments

Magda Mendez, Department of Pediatrics, Lincoln Medical and Mental Health Center, affiliated with Weill Cornell Medical College.

Author Contributions

CC: Contributed to conception and design; drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
CR: Contributed to acquisition, analysis, or interpretation; critically revised the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

References
1. Adler SP. Cytomegalovirus transmission among children in day care, their mothers and caretakers. Pediatr Infect Dis J. 1988;7:279-285.
2. American Academy of Pediatrics. Cytomegalovirus infection. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. Elk Grove, IL: American Academy of Pediatrics; 2015:317-322.
3. Klemola E. Cytomegalovirus infection in previously healthy adults. Ann Intern Med. 1973;79:267-268.
4. Glynn FJ, Mackle T, Kinsella J. Upper airway obstruction in infectious mononucleosis. Eur J Emerg Med. 2007;14:41-42.
5. Robert F. Cytomegalovirus. In: Long SS, Pickering LK, Prober CG, eds. Principles and Practice of Pediatric Infectious Disease. 4th ed. London, England: Saunders; 2012:1044-1052.
6. Ferri F, ed. Cytomegalovirus infection. In: Ferri’s Clinical Advisor 2016: 5 Books in 1. Amsterdam, Netherlands: Elsevier; 2015:391-391.
7. Jenson HB. Acute complications of Epstein-Barr virus infectious mononucleosis. Curr Opin Pediatr. 2000;12:263-268.
8. Sahai S. Lymphadenopathy. Pediatr Rev. 2013;34:216-227. doi:10.1542/pir.34-5-216.
9. Lajo A, Borque C, Del Castillo F, Martin-Ancel A. Mononucleosis caused by Epstein-Barr virus and cytomegalovirus in children: a comparative study of 124 cases. Pediatr Infect Dis J. 1994;13:56-60.
10. Luzuriaga K, Sullivan JL. Infectious mononucleosis. N Engl J Med. 2010;362:1993-2000. doi:10.1056/NEJMcp1001116.
11. Wohl DL, Isaacson JE. Airway obstruction in children with infectious mononucleosis. Ear Nose Throat J. 1995;74:630-638.
12. Boglioli LR, Taff ML. Sudden asphyxial death complicating infectious mononucleosis. Am J Forensic Med Pathol. 1998;19:174-177.
13. Tsaparas YF, Brigden ML, Mathias R, Thomas E, Raboud J, Doyle PW. Proportion positive for Epstein-Barr virus, cytomegalovirus, human herpesvirus 6, toxoplasma, and human immunodeficiency virus types 1 and 2 in heterophile-negative patients with an absolute lymphocytosis or an instrument-generated atypical lymphocyte flag. Arch Pathol Lab Med. 2000;124:1324-1330.
14. Chan SC, Dawes PJ. The management of severe infectious mononucleosis tonsillitis and upper airway obstruction. J Laryngol Otol. 2001;115:973-977.