# Pleuropneumonia as the Sole Manifestation of Epstein-Barr Virus-Associated Infectious Mononucleosis

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The most frequent manifestations of Epstein-Barr virus-associated infectious mononucleosis in children are fever, pharyngitis, hepatosplenomegaly and lymphadenopathy. Severe pulmonary involvement of this infection in an immunocompetent host has rarely been described [1]. We report an immunologically normal child who presented with pneumonia complicated by large pleural effusion, which constituted the sole manifestation of EBV infection.

## Patient Description

A previously healthy 16 month old girl presented in the Pediatric Emergency Department with cough and fever that had begun 3 days prior to admission. Physical examination revealed a moderately sick child with mild respiratory distress. Her body temperature was 40.2°C, respiration rate 50/minute, heart rate 120/minute, and oxygen saturation in room air 96%. There was a diminished breath sound and bronchial breathing at the upper part of the left lung. No pharyngotonsillitis, lymphadenopathy or hepatosplenomegaly were noted and the rest of the physical examination was unremarkable.

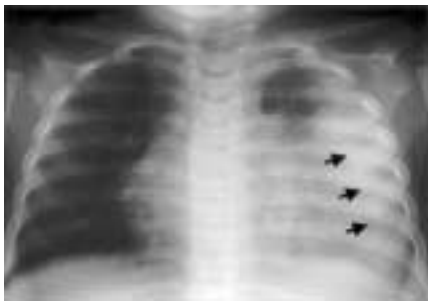
Initial laboratory investigation revealed an erythrocyte sedimentation rate of 44 mm/hour, hemoglobin 9.0 g/dl, reticulocyte count 1%, platelet count 175,000/mm$^3$, and white blood cell count 4,380/mm$^3$ with a differential of 8% bands, 4% neutrophils, 69% lymphocytes (of which only few were atypical), and 17% monocytes. Serum electrolytes, renal and liver functions were within normal limits. Two sets of blood cultures were sterile. A chest X-ray revealed a left upper lobe consolidation. Intravenous therapy with cefuroxime 75 mg/kg/day was started.

On day 3 of admission the child remained febrile and her respiratory distress worsened. The physical examination was unchanged and the oxygen saturation in room air was over 96%. Chest X-ray and chest ultrasound performed on that day demonstrated expansion of the left lung consolidation with large pleural effusion [Figure]. Additional laboratory investigations revealed hemoglobin 8.4 g/dl, reticulocytes 1%, platelets 248,000/mm$^3$, and WBC 5,630/mm$^3$ with a differential of 2% bands, 7% neutrophils, 51% lymphocytes, 10% atypical lymphocytes, 22% monocytes and 8% eosinophils. Liver and renal enzymes were within normal limits.

The patient was transferred to the Pediatric Intensive Care Unit. A diagnostic thoracocentesis on day 4 yielded 90 ml of mildly cloudy fluid. Examination of the fluid revealed pH 7.21, glucose 57 mg/dl, protein 4.4 g/dl, and lactate dehydrogenase 1,350 units/L. The white cell count was 2,000/mm$^3$ with a differential of 50% neutrophils and 50% lymphocytes. No malignant cells were detected on cytologic examination of the fluid. Gram and Ziehl-Neelsen stains were negative. Aerobic and anaerobic bacterial cultures and culture for *Mycobacterium tuberculosis* were sterile. A second thoracocentesis was performed on day 5, yielding 50 ml of fluid with similar chemistry and WBC contents as before.

Therapy with intravenous erythromycin 40 mg/kg/day was added on day 4, and the antibiotic regimen was changed to oral clarithromycin 15 mg/kg/day on day 10. Further studies demonstrated normal immunoglobulin levels, negative Mantoux test and negative nasopharyngeal cultures for influenza A, influenza B, parinfluenza 1,2 and 3, respiratory syncytial virus, and adenovirus. Serology tests for infection with *Mycoplasma pneumoniae*, *Coxiella burnetti*, cytomegalovirus, and *Toxoplasma* were all negative. However, Epstein-Barr serology obtained on day 4 of admission and performed by enzyme-linked immunosorbent assay was reported on day 10 to be conclusive for recent infection, by positive IgM and negative IgG to viral capsid antigen. Liver function tests that were obtained on day 7 were mildly elevated, with aspartate aminotransferase 105 U/L (normal 0–37) and alanine aminotransferase 142 U/L (normal 0–43).

The patient remained febrile and tachypneic for 12 days although supplement of oxygen was deemed not to be necessary. The fever subsided on day 13 and she was discharged home the next day in good



**[A]** Chest X-ray on day 3 of admission demonstrates the left lower lobe infiltrate and a large size pleural effusion (arrows).

EBV = Epstein-Barr virus

WBC = white blood cells

Ig = immunoglobulin

condition. Repeat chest X-ray one day before discharge demonstrated no pleural fluid and an improvement of the left lung consolidation.

## Comment

This case is unique in that the only manifestation on presentation of EBV infection was pleuropneumonia, while other stigmata of infectious mononucleosis were noted later during the hospitalization. EBV infection was suspected because of the atypical presentation and the finding of marked mononuclear cells and atypical lymphocytes in the blood smear. The diagnosis was confirmed by the combination of positive serology and exclusion of other infections that might have caused similar disease.

Serology remains the gold standard for the diagnosis of EBV-associated pneumonia [1]. As mentioned below, EBV virus was isolated and/or EBV DNA was found by polymerase chain reaction in peripheral blood and bone marrow lymphocytes, saliva and also in the lung tissue in patients with acute infectious mononucleosis-associated pulmonary involvement [2,3]. Our patient had anemia that worsened during the hospitalization. Hemolytic anemia is a severe but rare complication of acute EBV infection in children, which is caused by production of heterophil antibodies. The test for heterophil antibodies (e.g., mono test) is rarely positive in children under the age of 4 years [1]. Also, the low reticulocyte level does not support hemolytic anemia, which was most probably part of the acute disease.

We did not isolate the EBV virus in nasopharyngeal cultures. Unfortunately, the PCR technique is not yet available for daily use. Other infections should be considered in the differential diagnosis, and excluded. The pulmonary histopathology seen in patients who died from infectious mononucleosis revealed perivascular and interstitial mononuclear infiltrate and is similar to other viral pneumonias. Additionally, X-ray findings in such patients are usually indistinguishable from those of other atypical or viral pneumonias [1,2]. Moreover, some patients with pneumonia and serologic evidence of current or recent EBV infection also showed a rise in antibody to some other known respiratory pathogens (e.g., *Mycoplasma pneumoniae*, adenovirus, etc.) [1,3]. Perhaps EBV acts as a co-pathogen or alternatively, by inducing a state of temporary immunosuppression, may actually predispose a patient to another infection. Since EBV-associated symptomatic lung involvement is extremely rare, attribution of a primary lesion to the virus should be made only after other pathogens are carefully excluded, as in our case.

According to the literature, systematic radiographic studies of pediatric patients with infectious mononucleosis revealed pulmonary involvement in 5–10% of the cases [1]. However, these findings appear to be clinically insignificant and self-limited. Reports of severe EBV symptomatic lung involvement are rare and have mostly been described in immunosuppressed adults. They include adult respiratory distress syndrome, lymphocytic interstitial pneumonitis, unilateral or bilateral pulmonary patchy infiltrates, hilar and/or mediastinal lymphadenopathy, and pleural effusion. Although most of these patients typically suffered from moderate to severe hypoxemia, most were completely cured. In some of these patients EBV was isolated from the lung tissue, saliva or sputum [1,4]. A Medline search of the English-language medical literature from 1965 to December 2000 disclosed only four reports of severe lung involvement in EBV infection in immunocompetent children. In contrast to our patient, all exhibited other stigmata of infectious mononucleosis at presentation, such as cervical adenopathy, pharyngitis, splenomegaly, swollen eyelids, atypical lymphocytes, etc. Three children [4,5] suffered from respiratory distress and interstitial pneumonitis, and one [3] from bilateral lower lobe consolidation and effusion complicated by hemoptysis.

The pathophysiology of EBV-associated lung infection in immunocompetent hosts is not fully understood. EBV-infected lymphocytes can infiltrate the lung during acute infectious mononucleosis. EBV DNA was detected by PCR in lung tissue of a patient with EBV-associated lymphocytic interstitial pneumonitis. However, it remains unclear whether pulmonary involvement in EBV infections is the result of direct viral invasion of lung tissue or whether it represents an immunologic reaction (as with hemolytic anemia) [1,2].

The exact therapeutic approach to EBV-associated pneumonitis is supportive. Whether antiviral agents (such as acyclovir) or steroids would be beneficial remain to be determined [1].

Our case and others should alert physicians who are attending children with pneumonia to the possibility of EBV infection if the clinical and laboratory manifestations are compatible with this disease.

PCR = polymerase chain reaction

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*He that does you a very ill turn will never forgive you*

*English proverb*

Epstein-Barr Virus and Infectious Mononucleosis. National Center for Infectious Diseases. Centers for Disease Control and Prevention.Â  This suggests that intentional early primary exposure could potentially be used as a method of preventing the later onset of mononucleosis. Impacts and Issues. The statistics show that inevitably, at some stage of their life, almost the entire world population will be exposed to, contract, and harbor the Epstein-Barr virus. However, the majority of people who encounter infection during early childhood will not even develop mononucleosis. It is the omnipresence of EBV that prevents the eradication of the infection. What Tests Diagnose Epstein-Barr Viral Infections? The diagnosis of mononucleosis starts with a detailed history and physical examination. The doctor will look for fever, an inflamed or sore throat, swollen lymph nodes in the neck, and an enlarged spleen. Red dots (petechiae) may be seen on the palate.Â  Which Types of Doctors Treat Epstein-Barr Virus? You may be treated by a primary care provider (PCP), such as a family practitioner, an internist, or a child's pediatrician, for Epstein-Barr virus. If the symptoms of EBV become chronic, you may be referred to an infectious-disease specialist or an immunologist (also called an allergist/immunologist). You may need to see a neurologist for EBV-related neurological complications. Epstein-Barr is the virus that causes mononucleosis. You might know this disease better by its nickname, "mono." It's also called the "kissing disease" because of one way you can spread it to someone else. Even though Epstein-Barr virus (EBV) isn't a household name, you've probably been infected without knowing it. Lots of people carry the virus but don't get sick. Symptoms. Once you're infected with EBV, symptoms can take 4 to 6 weeks to show up. When they do, they're often mild, especially in young children. Kids' symptoms may be more like those of a cold or flu. Teens often have more obvious symptoms of mono. If you do get symptoms, most likely you'll have clinical syndrome associated with primary infection with Epstein-Barr virus (EBV), commonly presenting with fever, pharyngitis, and lymphadenopathy1,2,3. infectious mononucleosis (IM) is rare when primary infection acquired in childhood, but arises in up to 70% of adolescents and adults1,2,3. illness is typically self-limited, resolving within 1-2 months in most patients1,2,3. Also Called. mononucleosis. mono. monocytic angina. manifestation epstein-barr. 4. pleuropneumonia sole. 4. sole manifestation. 4. mononucleosis. 1. pleuropneumonia. 1. manifestation. 1. infectious. 1. epstein-barr. 1. virus--associated. 1. Member Articles.Â  Please type a message to the paper's authors to explain your need for the paper. Paper: Pleuropneumonia as the sole manifestation of Epstein-Barr virus--associated infectious mononucleosis. To: Dan Miron, Yoseph Merzel, Amiram Lev, Jean-Jack Meir, Yoseph Horowitz. From (Name): E-mail: Only shared with authors of paper. Please enter a personalized message to the authors. More detailed explanations for your need are more likely to get a response.