# Severe Complications From Infectious Mononucleosis After Prolonged Steroid Therapy

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**Abstract:** Infectious mononucleosis (IM) is a disease common among adolescents in the United States. Frequently, symptoms include sore throat, malaise, fevers, lymphadenopathy, and abdominal pain. Severe complications have been reported such as splenic rupture, acute upper airway obstruction, hepatitis, acute renal failure, and hematological and neurological complications. The mainstay of treatment is supportive care. Steroids are recommended for impending airway obstruction and hematological complications. However, steroids are commonly used in uncomplicated cases of IM, with insufficient evidence on the efficacy of steroids for symptom control. Furthermore, there is a lack of research on the adverse effects and long-term complications of steroid use for IM. We present a case of an adolescent boy who presented to his primary care physician with symptoms consistent with uncomplicated IM that was treated with a prolonged course of steroids. Subsequently, he developed worsening symptoms, including fevers, headache, vomiting, and left-sided facial swelling. He presented to a pediatric emergency department in decompensated septic shock as a result of polymicrobial bacteremia. During his hospital course, he developed pulmonary septic emboli, a sinus thrombus, an empyema, and orbital cellulitis complicated by Pott puffy tumor. In this case report, we summarize the current literature on steroid treatment of uncomplicated IM and highlight how our case addresses the use and possible complications of prolonged steroid use in uncomplicated IM.

**Key Words:** steroids, infectious mononucleosis, complications, bacteremia

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Infectious mononucleosis (IM) is a common manifestation of primary Epstein-Barr virus (EBV). Several studies estimate that EBV infects at least 90% of the population worldwide.[1,2] In the United States, there are 500 cases of IM per 100,000 persons per year, with most cases occurring in people between 15 and 24 years of age.[2] Common symptoms include sore throat, malaise, fevers, lymphadenopathy, and abdominal pain. Most patients with IM recover within 1 month without sequelae.[2] However, in approximately 1% of patients with IM, severe complications have been reported, including splenic rupture, acute upper airway obstruction, cholestatic hepatitis, acute renal failure, Lemierre syndrome, and hematological and neurological complications.[1–5] The recommended treatment of uncomplicated IM is supportive care with acetaminophen, nonsteroidal anti-inflammatory agents, and adequate fluid intake. Steroid treatment is only recommended in patients with marked tonsillar inflammation with impending airway obstruction, massive splenomegaly, hemolytic anemia, or hemophagocytic lymphohistiocytosis.[6] However, steroids are often used for symptom relief. A recent Cochrane review concluded that there is insufficient evidence on the efficacy of steroids for symptom control and a lack of research on adverse effects and long-term complications.[7] Furthermore, it is unknown how steroid use may contribute to EBV complications.

This article presents a case of an adolescent boy who was diagnosed as having IM and treated with a prolonged course of steroids. He developed worsening symptoms after his steroid course leading to admission to the hospital for septic shock. Subsequently, he was found to have polymicrobial bacteremia with resulting pulmonary septic emboli, pleural empyema, and epidural abscess with adjacent dural sinus thrombosis. This case highlights the recent literature surrounding corticosteroid use in treatment of IM and the complications that may occur with the prolonged use of steroids.

## CASE

A 15-year-old boy presented to a pediatric emergency department with a chief complaint of myalgias, cough, and vomiting. He was seen by his pediatrician 2 weeks prior for sore throat, neck pain, fevers, and weight loss. A strep culture was negative at that time. Epstein-Barr virus serologies and a monospot were both positive. He was treated with a 10-day course of prednisone for symptom control. He received prednisone 60 mg daily for 5 days, with a tapered dosage of 40 mg daily for 2 days, then 20 mg daily. He initially improved but subsequently developed fevers, vomiting, diarrhea, cough, headache, and left-sided facial swelling on the last day of his steroid course. He had not taken any other medications. He had a repeat visit with his pediatrician and was referred to the pediatric emergency department because of dehydration and concern for sinusitis.

His vital signs at presentation were as follows: temperature, 99.5°F; pulse, 125 beats/min; respiratory rate, 28 breaths/min; blood pressure, 83/37 mm Hg; and pulse oximetry, 100% on room air. He was ill appearing, with generalized myalgias and tenderness over his left forehead and neck. His physical examination was also significant for scleral icterus, cervical lymphadenopathy, abdominal tenderness, and mild hepatosplenomegaly. There were no meningeal signs. Laboratory results were notable for the following: white blood cell count, 16,500/μL (reference range, 4500–13,000/μL); platelet, 60,000/μL (reference range, 135,000–466,000/μL); sodium, 131 mmol/L (reference range, 136 to 145 mmol/L); creatinine, 2.53 mg/dL (reference range, 0.46–1.00 mg/dL); direct bilirubin, 5.8 mg/dL (reference range, 0.0–0.3 mg/dL); aspartate aminotransferase, 80 U/L (reference range, 10–36 U/L); alanine transaminase, 66 U/L (reference range, 12–49 U/L); lactate, 3.9 mmol/L (reference range, 1.0–2.4 mmol/L); and procalcitonin, >200 ng/mL (reference range, ≤0.50 ng/mL). His activated partial thromboplastin time was 49.3 seconds (reference range, 22.9–36.0 seconds), and his prothrombin time was 15.0 seconds (reference range, 9.6–11.6 seconds). His international normalized ratio was normal. His rapid flu test showed a negative result. Chest x-ray showed a right multifocal pneumonia. His head/facial computed tomography (CT) showed left frontal, maxillary, and anterior ethmoid sinusitis. An abdominal ultrasound showed splenomegaly, biliary sludge, and diffuse hypoechoic liver echogenicity. He received 2 L of normal saline with subsequent improvement of his tachycardia and blood

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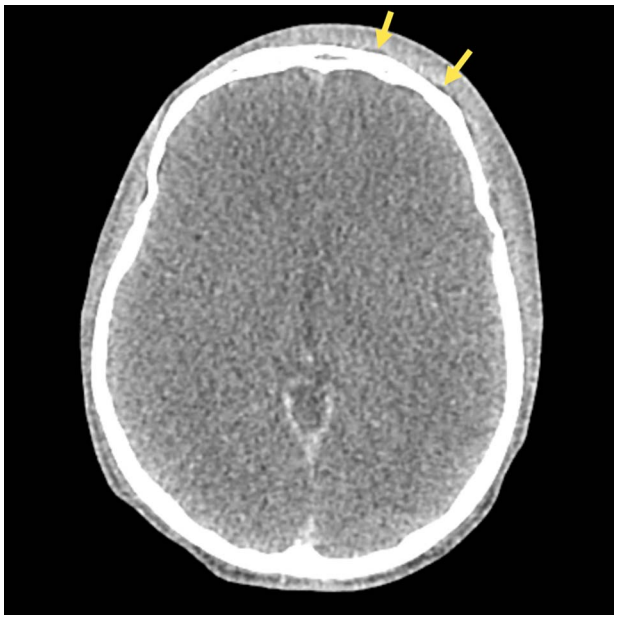

**FIGURE 1.** Axial CT of the orbits and sinuses demonstrates a thin subperiosteal collection along the outer table of the left frontal bone (yellow arrows). There was extensive paranasal sinus opacification, including the frontal sinuses, which are partially visualized. There is overlying soft tissue edema. This appearance is consistent with frontal bone osteomyelitis and Pott puffy tumor.

pressure. A blood culture was obtained. He received intravenous ceftriaxone and was admitted to the pediatric intensive care unit (PICU) for further management.

On admission to the PICU, the patient required aggressive fluid resuscitation and brief vasopressor support with norepinephrine for septic shock. The result from his echocardiogram was normal. He briefly required bilevel positive airway pressure because of increased work of breathing from fluid overload. Laboratory work was consistent with disseminated intravascular coagulation on admission. Initial blood culture was positive for *Streptococcus anginosus* and *Fusobacterium necrophorum*, and the patient was treated with ceftriaxone, clindamycin, and vancomycin. Stress dose steroids were given for the first 6 days of hospital admission. The patient developed left eye edema on day 6 of admission. A CT scan of the orbits and sinuses showed left orbital cellulitis and extensive paranasal sinus disease with subperiosteal collections along the outer table of the left frontal bone suspicious for frontal bone osteomyelitis (Figs. 1, 2). Computed tomographic scan of the chest showed multifocal consolidation with multiple areas of cavitation, an appearance consistent with pulmonary septic emboli (Figs. 3A, B). Antimicrobial coverage was further broadened with Flagyl. The patient was taken to the operative room on hospital day 7 for a left lateral orbitotomy, sinus wash-out and culture, drainage of the subperiosteal abscess, and subgaleal drain placement. He improved after drainage and was transferred to the general hospital floor on hospital day 9.

His hospital course was further complicated by a left epidural abscess with adjacent nonocclusive superior sagittal sinus thrombus, right pleural effusion, and a left-sided empyema, which required repeat admission to the PICU. Throughout the remainder of his course, he had resolution of the sinus thrombus on repeat imaging, as well as improvement of his subperiosteal and epidural abscess while receiving intravenous antibiotics. He was discharged home on hospital day 34 and continues to follow with Infectious Disease, Neurosurgery and Ophthalmology.

## DISCUSSION

Steroid treatment as symptomatic care for patients with IM has been widely debated. Current guidelines recommend considering steroids in patients with marked tonsillar inflammation with impending airway obstruction, massive splenomegaly, hemolytic anemia, or hemophagocytic lymphohistiocytosis.[6] For this subset of patients, the recommended dosage of prednisone is 1 mg/kg daily for 7 days with subsequent tapering. Despite these strict recommendations on when to prescribe corticosteroids, research has shown that most patients with IM who receive corticosteroids do not meet these criteria. Thompson et al[8] evaluated practice patterns at a single tertiary center in New York City. Most patients were adolescents and young adults who presented to the emergency department with symptoms consistent with IM. They found that over a 5-year period, 44% of patients were treated with systemic corticosteroids, of which greater than 90% did not have symptoms of airway obstruction or hematological complications. Although most patients do not have severe symptoms, younger children may be more likely to have severe complications.[9] Therefore, understanding the proper use of steroids in this population is especially important to pediatric emergency providers.

Most patients with IM have tonsillopharyngeal symptoms, which can be painful and last for 5 to 7 days.[10] Patients often present with these symptoms to their primary physician or the emergency department in search of pain relief. Although IM is a self-limited disease, physicians may be inclined to treat with steroids to help reduce symptoms. A recent systematic review and meta-analysis showed that a single low dose of corticosteroids provides pain relief among patients with sore throat without serious adverse effects; however, patients with IM were excluded.[11] Prior studies have shown different outcomes in efficacy of symptom relief for patients with IM who are treated with steroids. Some studies have shown no difference in symptoms.[7] Four studies to date have shown improvement in pharyngitis within 1 to 4 days of steroid treatment but not

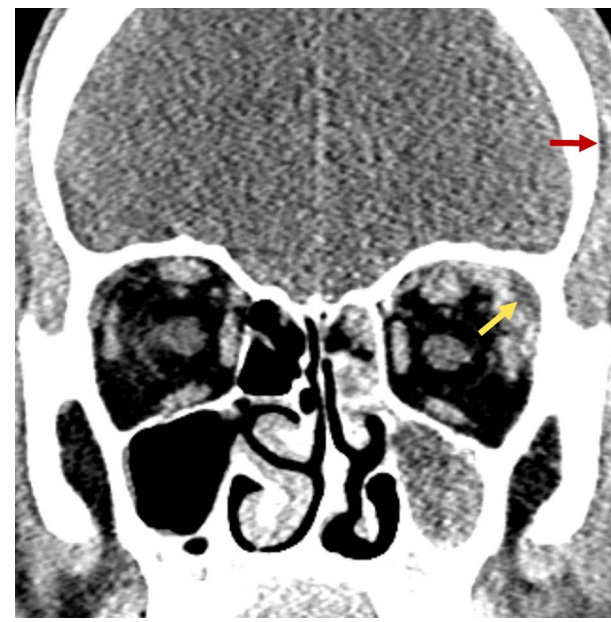

**FIGURE 2.** Coronal contrast-enhanced CT of the sinuses and orbits demonstrates a subperiosteal collection in the superior-lateral left orbit (yellow arrow). Also seen is a small portion of a subperiosteal collection along the outer table of the left frontal bone (red arrow). The left maxillary sinus is completely opacified, and partially opacified ethmoid air cells are seen.

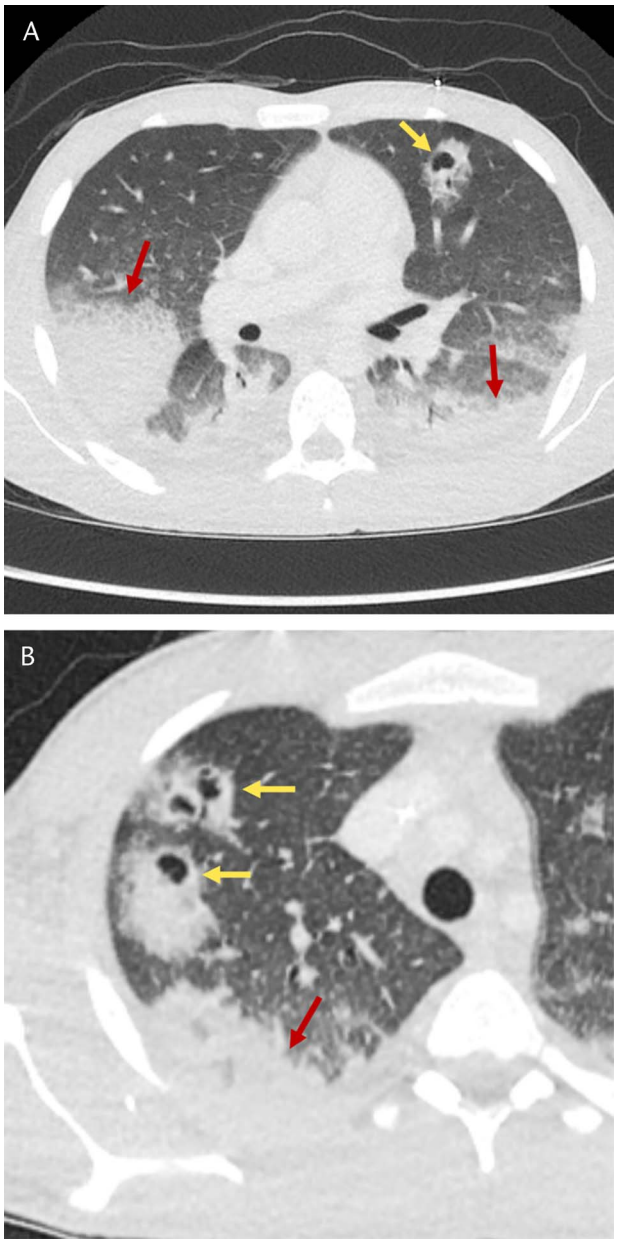


**FIGURE 3.** A and B, Axial contrast-enhanced CT of the chest shows areas of consolidation (red arrows) as well as peripheral nodular areas of consolidation with central cavitation (yellow arrows). There are also bilateral pleural effusions.

afterward.[10,12] Only one prior study evaluated the side effects of steroid treatment with no reported adverse outcomes, but these patients also received antiviral therapies.[13] Thus, exactly how steroid monotherapy and subsequent length of treatment may contribute to adverse outcomes in patients with IM is still unknown.

Certain complications of IM are well known in the literature. Patients with IM who are being treated with corticosteroids may proceed to develop otolaryngological complications, such as peritonsillar abscesses, and other deep space neck infections.[9,14–17] These cases have led to speculation that steroids may be related to the development of these complications. Prior case reports involving patients with severe IM complications have received varying lengths of steroid courses. A recent article presented an adolescent girl with atypical symptoms of Lemierre syndrome after being diagnosed as having IM and had been previously treated with 9 days of steroids.[18] The only other case report somewhat similar to our patient in both steroid treatment course and morbidity was more than 30 years ago. This case described a 16-year-old boy with IM who developed sinusitis, orbital cellulitis, and polymicrobial septicemia after receiving 7 days of steroids for symptom control.[19]

Studies involving other disease processes have evaluated outcomes in patients treated with steroids and suggest that systemic corticosteroids may be associated with repression of genes responsible for adaptive immunity.[20] Prior research has shown that steroids may delay formation of certain EBV antibodies.[21] These processes may have been involved with our patient, as he developed bacteremia, sinusitis, and empyema. Corticosteroids may have prolonged the bacteremia in this patient, leading to his severe complications.

There has not been a case report to date that has shown all known IM complications to occur within the same patient with a prolonged steroid course. Our patient was treated with a 10-day course of steroids and subsequently developed severe complications due to his IM. Steroids are often used for symptom relief despite the disease being self-limited. Research has not consistently shown a significant improvement in symptoms in patients treated with a prolonged course of steroids, and it may suppress their immunity. This case highlights the need for pediatric emergency providers to evaluate the risks and benefits of treating a patient with IM with steroids given the possibility of severe complications. It is our recommendation that physicians strongly consider avoiding the use of prolonged steroids in patients for symptom control and instead reserve prolonged steroid use for those with severe airway or hematological sequelae.

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