

Pediatric Myocardial Infarction After Racemic Epinephrine Administration

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ABSTRACT. Myocardial infarction is a previously unreported complication of treatment with racemic epinephrine that is used commonly in the emergency department for severe respiratory distress in bronchiolitis or croup syndrome. We describe a pediatric patient who presented with the croup syndrome and severe respiratory distress that required multiple doses of nebulized racemic epinephrine in the emergency department. The patient developed ventricular tachycardia and mild chest discomfort during one treatment, which resolved spontaneously on discontinuation of the nebulization. Persistently abnormal electrocardiograms and elevated creatine phosphokinase MB isoenzyme (CPK-MB) levels suggested a myocardial infarction had occurred. Subsequent echocardiography, cardiac catheterization, and angiography revealed an anatomically normal heart with normal coronary circulation; however, a stress nuclear study showed a small myocardial infarct. The significance of this previously unreported complication of racemic epinephrine is discussed, along with recommendations for proper use in the emergency department. *Pediatrics* 1999; 104(1). URL: <http://www.pediatrics.org/cgi/content/full/104/1/e9>; *racemic epinephrine, croup, myocardial infarction, ischemia, arrhythmia.*

ABBREVIATION. EKG, electrocardiogram.

Nebulized racemic epinephrine is used commonly in the emergency department to treat severe respiratory distress in patients presenting with croup syndrome or bronchiolitis.¹ Croup syndrome, characterized by a bark-like cough, inspiratory stridor, and respiratory distress, is caused commonly by acute laryngotracheobronchitis (viral croup), epiglottitis, or bacterial tracheitis.² Racemic epinephrine reduces upper airway obstruction by reducing tracheobronchial mucosal edema.² It is a potent adrenergic agonist and has potential cardiovascular side effects including hypertension, tachycardia, bradycardia, and syncope.^{3,4} We report a case of myocardial infarction after the administration of

racemic epinephrine to a pediatric patient who presented with croup syndrome.

CASE REPORT

An 11-year-old prepubertal, Hispanic male was in his usual state of good health until 4 days before admission when he developed progressive congestion, cough, fever, and chills. He presented on the day of admission to the emergency department in severe respiratory distress with tachypnea, respiratory retractions, nasal flaring, stridor, barking cough, hoarse voice, and a room air oxygen saturation of 80%. His oxygen saturation normalized after he received oxygen by mask. Because of continued respiratory distress, treatments with nebulized racemic epinephrine (0.5 mL diluted with 3 mL 0.9% saline) were initiated, and he received three treatments over the next 55 minutes. During the initial treatment, his heart rate increased to 152 beats per minute, then stabilized and decreased to 101 beats per minute. His respiratory status improved, although stridor and retractions persisted. Oxygen saturations remained >92% throughout his emergency department course. During the third treatment with racemic epinephrine, the patient developed premature ventricular complexes that rapidly progressed to ventricular tachycardia (Fig 1), and the nebulization was discontinued immediately. During this arrhythmia, the patient remained alert and hemodynamically stable but complained of mild chest tightness. The ventricular tachycardia spontaneously resolved within 5 minutes, and a 12-lead electrocardiogram (EKG) showed sinus tachycardia with anterolateral ST segment elevation and inferior reciprocal changes (Fig 2). The patient's chest discomfort resolved ~20 minutes later, and a second 12-lead EKG showed resolution of the ST segment elevations. A chest radiograph showed narrowing of the glottic region strongly suggesting the possibility of croup and no infiltrates, and a lateral neck film revealed a normal epiglottis and trachea.

Because of the events noted above, in the face of persistent respiratory distress, the patient was transported to the operating room for endotracheal intubation by an otolaryngologist. On direct laryngoscopy, only slight edema and erythema of the epiglottis were noted. The vocal cords revealed minor swelling and slight exudates. A No. 4.5 endotracheal tube was the largest tube that could be passed and produced an air leak at 25 cm H₂O. The patient was treated empirically with cefotaxime, but blood cultures remained negative. Cultures of the subglottic area and tracheal aspirate grew few colonies of group A streptococci, coagulase-negative staphylococcus, and oral flora. The patient was extubated within 24 hours of admission with only mild stridor, which resolved over the subsequent 4 days. He had no additional chest pain or other cardiac-related symptoms during a 5-day hospitalization. Creatine phosphokinase levels were followed and peaked on day 1 at 1236 IU/liter (normal range 3–190) with 4.4% MB fraction (normal range 0–2.4%; Table 1). The patient was discharged after 5 days with instructions to follow-up with pediatric cardiology because of persistent EKG changes consisting of T wave inversions across the precordial leads (Fig 3).

He was seen in a pediatric cardiology clinic 9 days after his emergency department presentation. At that time, physical examination was completely normal. A transthoracic echocardiogram showed a structurally normal heart with normal coronary arteries and no wall motion abnormalities. Because of continued T wave inversions on his EKG, an exercise stress thallium perfusion study was performed; it showed a fixed filling defect in the posterior wall of the left ventricle consistent with myocardial infarction. A

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Fig 1. Wide complex tachycardia observed during third nebulized racemic epinephrine treatment.

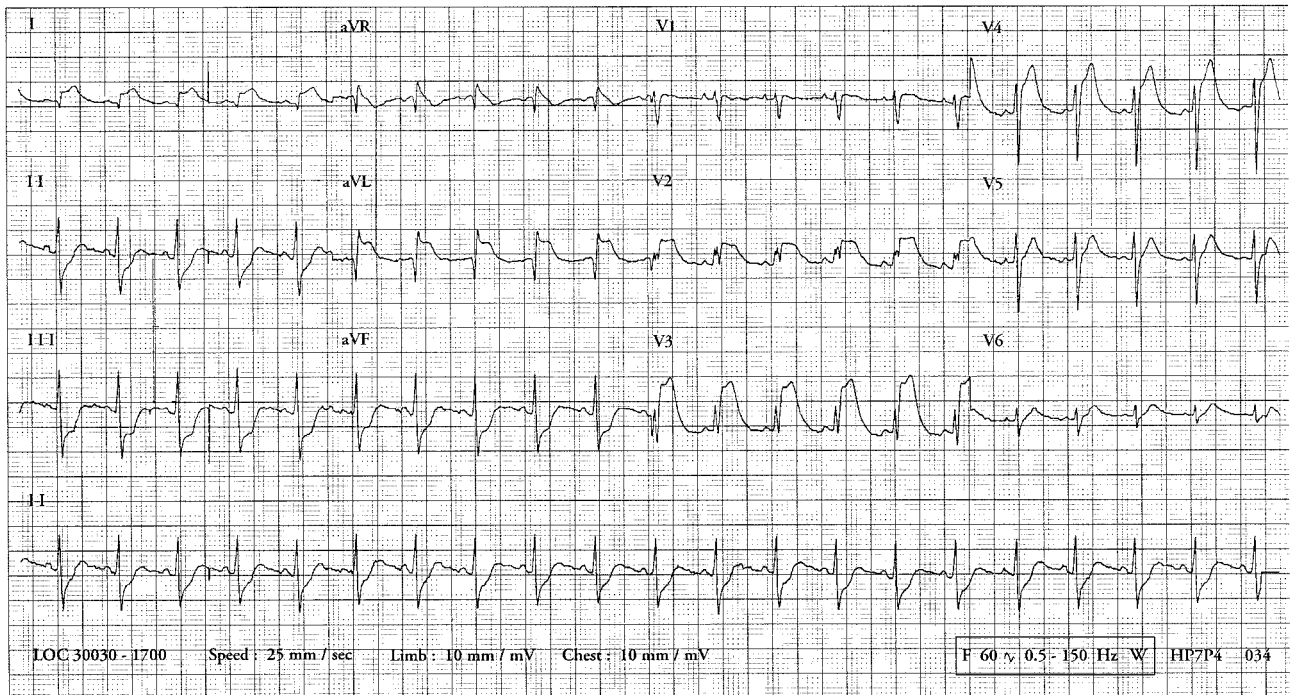
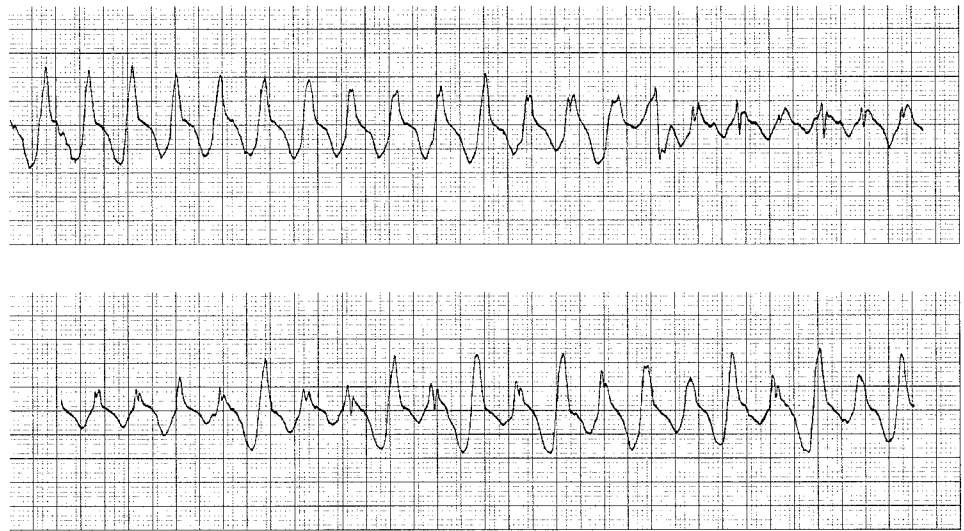


Fig 2. Twelve-lead EKG performed immediately after the nebulization was turned off, showing sinus tachycardia with anterolateral ST segment elevation and inferior reciprocal changes.

TABLE 1. Creatine Phosphokinase Levels

Hours After Arrhythmia	CPK (IU/L) (Normal: 3-190)	CPK-MB Fraction (Normal: 0-2.4%)
0	173	Not measured
8	1236	4.4%
16	1040	4.4%
30	660	3.3%

diagnostic cardiac catheterization demonstrated normal hemodynamics, and selective angiography revealed normal coronary architecture with no blockages. Two years after the event, the patient is well and has had no additional cardiac or respiratory symptoms.

DISCUSSION

This patient's clinical course, persistent EKG changes, and stress thallium results are consistent

with a myocardial infarction. The etiology of his myocardial infarction remains unclear, although it is likely that the administration of racemic epinephrine was a contributing factor. Racemic epinephrine (a 1:1 mixture of *d* and *l* isomers of epinephrine) is a potent agonist of both α and β adrenergic receptors. α -adrenergic stimulation can result in coronary vasospasm which, if it is severe enough, can deprive the myocardium of adequate oxygen delivery. In addition, vasospasm can lead to stress-induced disruption of the vascular endothelium causing acute vessel thrombosis.^{5,6} Both of these pathophysiologic events have been described with other adrenergic agents including cocaine, ephedrine, pseudoephedrine, and intravenous epinephrine.⁷⁻¹⁰ An alternative explanation is that sys-

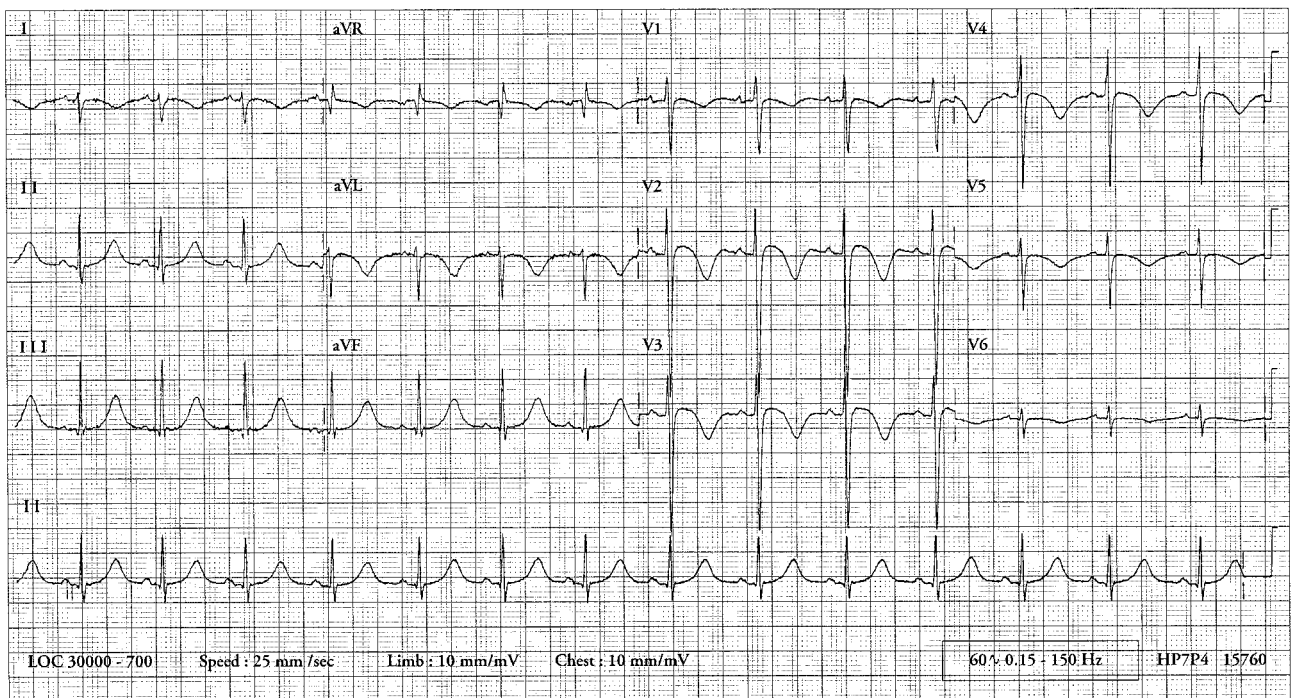


Fig 3. Twelve-lead EKG performed around the time of discharge, showing normal sinus rhythm with inverted T waves across the precordial leads.

temically absorbed epinephrine, in the presence of severe respiratory distress, possible hypercarbia, and an already stressed heart, caused an imbalance between myocardial oxygen consumption and oxygen delivery leading to ischemia and myocardial necrosis. This phenomenon has been encountered in pediatric patients with severe asthma given intravenous isoproterenol and may also account for some adverse cardiac sequelae after cocaine abuse.¹¹⁻¹³ We were unable to find alternative explanations for this patient's myocardial infarction. Selective coronary angiography demonstrated normal caliber coronary vessels and no abnormalities in their origin. We did not do an ergonovine challenge to look for Prinzmetal's or variant angina, but this entity is rarely observed in the pediatric age range.^{14,15} The EKG did not reveal any conduction defects, and we did not perform any invasive electrophysiologic tests.

Nebulized epinephrine has long been considered standard treatment for severe upper airway obstruction, and is now used commonly in infants with bronchiolitis as well.¹ Although its side effect profile is consistent with its sympathomimetic activity, racemic epinephrine has generally been considered a safe treatment modality. This is the first report describing myocardial infarction in the pediatric age range associated with nebulized racemic epinephrine administration. Given the numerous reports of myocardial ischemia with other sympathomimetic agents, it is possible that subclinical ischemia occurs more frequently with racemic epinephrine than is suspected. Based on our experience with the above patient, we concur with previous recommendations that the administration

of nebulized epinephrine, if given more frequently than every 1 to 2 hours, requires continuous heart rate and electrocardiographic monitoring.¹⁶ In addition, continued work is needed to explore the efficacy of alternative therapies, such as nebulized budesonide,^{2,17,18} for the acute treatment of croup and bronchiolitis.

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