Case Report

Rhabdomyolysis due to parainfluenza 3 virus infection: Case report and review of literature

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Case Report

ABSTRACT

Influenza virus is the most frequently reported viral cause of rhabdomyolysis and case reports of rhabdomyolysis associated with parainfluenza virus are rare. We describe a seven month old child with Parainfluenza type 3 infection associated with rhabdomyolysis.

Key words: Rhabdomyolysis, Parainfluenza

Introduction

Rhabdomyolysis is characterized by muscle pain or tenderness, elevated creatine phosphokinases levels, acute kidney injury and/or myoglobinuria. It may occur due to various causes like viral illness, trauma, metabolic or autoimmune illness.1 While influenza, coxsackie and dengue viruses are known to cause rhabdomyolysis, there are few reported cases of rhabdomyolysis associated with parainfluenza.

Case Report

A seven month old girl was admitted with cough for 2 days, loose stool, decreased oral intake and fever for 1 day. Urine output was decreased.

She was fed formula by bottle in appropriate dilution. There was no significant past medical or family history. She is the second child of non-consanguinous parents.

On admission she was febrile (103°F) and irritable with HR 160/min, palpable peripheral pulses, cool extremities, and dry oral mucosa. The rest of her systemic examination was within normal limits. Her weight and height were appropriate for age. Our initial clinical impression was acute gastroenteritis with dehydration. Fluid rehydration was started and lab parameters were sent.

Initial reports showed normal anion gap metabolic acidosis with hypernatremia, hypokalemia and AKI (pH-7.2, HCO3-7.2, pCO2-15.6, Na-165 meq/l, Cl-129 meq/l, k-2.8 meq/l, BUN 21 mg/dl and creatinine 1.1 mg/dl). Her lactate level was normal.

Over the next 24 hours she developed tachypnea that progressed to respiratory failure needing mechanical ventilation. Her chest x-ray showed bilateral infiltrates. She was started on Injection Ceftriaxone.

On day 3 she remained febrile with dropping platelet count. Her sodium level gradually normalized. Her liver enzymes were elevated (SGOT 958, SGPT 252 U/L) with normal coagulation profile. As she had dark coloured urine with normal urine microscopy and SGOT > SGPT with normal INR, Creatinine Phosphokinase (CPK) levels were sent which came high (28160 U/L, Normal: up to 250 U/L). Urine Myoglobin level was >30000 mcg/L. She was started on hyperhydration therapy.

Nasopharyngeal aspirate tested for respiratory pathogens by polymerase chain reaction assay (Film Array, Respiratory Panels, Biofire Diagnostics Inc, Salt Lake City, UT, USA) was positive for Parainfluenza 3; per was negative for respiratory syncytial virus, influenza a and B, parainfluenza types 1, 2 and 4, adenovirus, rhinovirus, metapneumovirus, bordetella pertussis, mycoplasma pneumonia, chlamydia pneumonia, and corona virus. Blood culture was negative. On day 4 she had a focal seizure with secondary generalization. Serum calcium, magnesium, sodium, blood glucose, EEG and MRI were normal. The child’s condition gradually improved. Her CPK level gradually came

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down (table 1). She was extubated on day 5 and transferred to the ward on day 9.

Discussion

In the setting of multi-organ dysfunction, elevated SGOT more than SGPT with normal coagulation profile should prompt one to check CPK levels. Rhabdomyolysis is characterized by muscle necrosis with release of creatine kinase, myoglobin, phosphorous and potassium. While some authors define rhabdomyolysis as Creatinine Phosphokinase levels more than 5 times the upper limit of normal, others define it as elevated CPK with acute renal failure with or without myoglobinuria.

Table 1: Laboratory investigations during hospital stay

<table>
<thead>
<tr>
<th>Day of illness</th>
<th>SGOT/SGPT (U/L)</th>
<th>CPK (U/L)</th>
<th>Total counts (X10⁹/L)</th>
<th>Platelets (X10⁹/L)</th>
<th>BUN/Creatinine (mg/dl)</th>
<th>pH/HCO₃ (meq/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>51/38</td>
<td>7340</td>
<td>1.5lakhs</td>
<td>21/1.1</td>
<td>7.2/7</td>
<td>7.2/7</td>
</tr>
<tr>
<td>D3</td>
<td>958/262</td>
<td>28160</td>
<td>9890</td>
<td>91000</td>
<td>14/0.8</td>
<td>7.27/11.4</td>
</tr>
<tr>
<td>D5</td>
<td>645/376</td>
<td>24270</td>
<td>5680</td>
<td>80000</td>
<td>15/0.7</td>
<td>7.3/20</td>
</tr>
<tr>
<td>D6</td>
<td>444/356</td>
<td>12200</td>
<td>4500</td>
<td>76000</td>
<td>11/0.6</td>
<td>7.4/24</td>
</tr>
<tr>
<td>D9</td>
<td>348/353</td>
<td>8400</td>
<td>5250</td>
<td>86000</td>
<td>5/0.3</td>
<td>7.47/25</td>
</tr>
<tr>
<td>D15</td>
<td>98/137</td>
<td>4080</td>
<td>11250</td>
<td>100000</td>
<td>4/0.4</td>
<td>7.28/27</td>
</tr>
</tbody>
</table>

Rhabdomyolysis due to parainfluenza 3 virus infection

There is considerable overlap with benign acute childhood myositis where CPK levels more than 4000 U/L have been reported.²

Rhabdomyolysis may occur due to various causes such as trauma, drugs, infection and inherited disorders (Table 2). Viral infections are among the most commonly reported causes of rhabdomyolysis in children while trauma and drugs are the commonest in adults. In a case series of 191 children¹, the commonest symptoms were fever (45%), muscle pain (40%) and symptoms of viral infection (38%). In infants, such as in our case, muscle pain and weakness may be difficult to recognize. The classic triad of muscle pain, weakness and dark urine may be seen in less than 10% of children.

Muscle injury due to various causes may finally lead to ATP depletion or sarcolemmal rupture, both of which cause increased intracellular ionized calcium. This causes abnormal interaction between actin myosin with hypercontractility, mitochondrial dysfunction, increased cellular permeability and release of potassium, phosphorous, myoglobin, creatine kinase into the circulation. Myoglobin has a half life of 2-3 hours and appears in the urine when serum concentration exceeds 1.5 mg/dl. Urine colour change usually occurs only when urine myoglobin concentration exceeds 100-300mg/dl. Myoglobin levels peak by 12 hours and return to baseline by 24 hours after injury. Serum CPK levels rise 6-12 hours after muscle injury, peak by day 3 and return to baseline over the next 3-5 days once muscle injury resolves. Thus, depending on the day of testing CPK levels may be elevated with absent myoglobin. Persistent elevation of CPK beyond 7-10 days may be due to compartment syndrome or ongoing rhabdomyolysis.

Renal damage occurs due to vasoconstriction, direct toxicity of myoglobin, tubular ischaemia, cytokine release, and free radical injury. Pigmented casts may result due to myoglobin combining with Tamm Horsfall protein; this is enhanced by low pH. Urine dipstick positive for blood with absence of hematuria on microscopy may indicate
Early complications of rhabdomyolysis include hyperkalemia, hypocalcemia, arrhythmias and cardiac arrest. Renal failure or DIC may occur after 24-36 hours. Renal injury has been reported in 10-55 % of cases. There is no correlation between myoglobin levels or initial CPK and AKI or mortality. A study of 28 children with acute renal failure and rhabdomyolysis showed that while there was no correlation between admission or peak CPK levels and need for renal replacement therapy; all the 11 children who needed RRT had CPK levels > 5000 U/L. Our patient had a peak CPK value of 28,000 but did not develop renal failure.

Management comprises treatment of underlying cause, hydration and monitoring and treatment of complications. Hydration should ideally be started within 6 hours of onset of injury. As myoglobin toxicity is enhanced in acidic urine, it was thought that maintaining urine pH >6.5 would reduce the risk of acute kidney injury, however there is currently no evidence for alkalization of urine. Mannitol therapy has been tried but literature does not support its use. Parainfluenza virus is a single stranded RNA virus of the paromyxoviridae family. Parainfluenza virus 1 and 2 commonly cause croup while para influenza virus 4 causes bronchiolitis or pneumonia. Non-respiratory complications such as rhabdomyolysis are rare.

Muscle injury may occur due to direct invasion or immune mediated mechanisms such as elevated Interferon α. Benign acute myositis due to parainfluenza as well as rhabdomyolysis have been reported (Table 3). To date there are 5 reported cases of children with parainfluenza infection with elevated CPK and myoglobinuria or renal failure. The children ranged in age from 2 to 10 years. 3 children developed renal failure, 1 had compartment syndrome and 1 died. Rhabdomyolysis has been reported due to hyponatremia and hypernatremia. Our patient had hypernatremia at admission. However the occurrence of lung, GI and CNS involvement make it more likely that the rhabdomyolysis was due to parainfluenza.

**Conclusion**

In infants with viral infections, a high index of suspicion is needed to detect rhabdomyolysis. In older children, myalgia is commonly reported in infections caused by parainfluenza virus and worsening pain, tenderness or muscle swelling should prompt further investigations to detect possible rhabdomyolysis, even in the absence of dark urine. Rhabdomyolysis further leads to acute kidney injury, electrolyte disturbances, and compartment syndrome. Although influenza is the most frequently reported viral cause of rhabdomyolysis, appropriate use of laboratory methods such as multiplex polymerase-chain reaction assays may lead to enhanced recognition and characterization of rhabdomyolysis associated with parainfluenza or other pathogens. Viral testing...
although expensive may help limit antibiotic use and prove cost-effective in the long run.

There is need for a standardised definition for rhabdomyolysis as well as further study on ways to reduce acute kidney injury.

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