Coma, myalgia and hypoxia

Paul RA Froomes, John Haddad, David Harding

A 32-year-old man who had recently commenced oral methadone presented semiconscious, after a two-day history of myalgias, weakness and dyspnoea. On examination, he was drowsy, localising to pain, eye opening to speech and verbalising to pain. He had a respiratory rate of 10 min, a blood pressure of 135/80 mmHg and was febrile (38.1°C). There was tenderness over proximal muscle groups with marked muscle weakness of his legs and arms. Laboratory findings are presented in box 1. He was given supplemental oxygen, intravenous hydration with alkaline diuresis and antibiotics. His conscious state improved rapidly after intravenous naloxone.

Over the next few days his hypoxia resolved, conscious state returned to normal, urine output and hydration remained stable. His muscle pains resolved and the muscle weakness greatly improved. He then complained of a painful, swollen right arm that was warm, tender and oedematous on examination.

<table>
<thead>
<tr>
<th>Laboratory investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>arterial pH 5.0</td>
</tr>
<tr>
<td>partial pressure oxygen 84 (on 10 litres/min O₂)</td>
</tr>
<tr>
<td>partial pressure carbon dioxide 41</td>
</tr>
<tr>
<td>blood urea nitrogen 7.0 mmol/l</td>
</tr>
<tr>
<td>serum creatinine 91 μmol/l</td>
</tr>
<tr>
<td>white blood cells 10 x 10⁹/l</td>
</tr>
<tr>
<td>serum bilirubin 18 μmol/l</td>
</tr>
<tr>
<td>urine: appearance: dark brown; haem pigment 3+, protein 1+, red cells 2/high power field</td>
</tr>
<tr>
<td>X-ray (chest, abdomen): normal</td>
</tr>
<tr>
<td>serum electrolytes, glucose, liver enzymes: normal</td>
</tr>
</tbody>
</table>

Box 1

Questions

1. What is the most likely diagnosis of his initial presentation and what diagnostic tests should be performed?
2. Suggest possible causes.
3. How do drugs predispose to muscle damage?
4. What are the possible explanations of his hypoxia and what tests should be performed?
Answers

QUESTION 1
The most likely diagnosis is drug-induced nontraumatic rhabdomyolysis and coma. In this case methadone was the culprit drug. The presentation is characteristic with drowsiness, diffuse myalgias, muscle weakness and dark urine. However, the usual setting is that of an acute overdose of intravenous narcotic, not physician administered oral methadone. The diagnostic tests performed include blood and urine drug screen for narcotics and sedatives (positive), dark urine that is positive for haemoglobin and measurement of serum creatine phosphokinase (3415 U/l), and lactic dehydrogenase (326 U/l).

QUESTION 2
Traumatic rhabdomyolysis occurs in the setting of burns, crush syndromes, prolonged convulsions and heat stroke. It is now recognised that nontraumatic rhabdomyolysis is responsible for the majority of cases, this is known to occur after drug overdose and during systemic infections. Some series have implicated drugs in as many as 81% of cases of rhabdomyolysis. Drug-induced rhabdomyolysis can be either a primary problem or secondary to seizures, hypothermia, prolonged coma or muscle compression as a result of the overdose. In our patient methadone was associated with nontraumatic, nonseptic rhabdomyolysis confirmed by elevated creatine kinase and myoglobinuria. However, unlike the other cases described, acute renal failure did not occur and rhabdomyolysis occurred after commencing oral methadone in a supervised programme. Drugs associated with primary rhabdomyolysis are listed in box 2.

QUESTION 3
The mechanism for rhabdomyolysis in response to narcotics was previously thought to be due to muscle damage from pressure necrosis due to profound sedation but this was unlikely in our patient due to the suddenness of his presentation. Other authors have observed primary rhabdomyolysis after chronic administration of methadone and hypothesised a direct myotoxic action that interferes with myocyte ATP metabolism. Other suggested mechanisms include inhibition of calcium metabolism by the sarcoplasmic reticulum, disruption of muscle cell membranes and altered carbohydrate metabolism.

Box 2

Drugs causing primary rhabdomyolysis

alcohol
amphetamines
amphotericin B
antihistamines
barbiturates
benzodiazepines
cimetidine
cocaine
colchicine
cotrimoxazole
isoniazid
lithium
monoamine oxidase inhibitors
narcotics
phenothiazines
simvastatin
streptokinase
theophylline

Final diagnosis
Rhabdomyolysis and respiratory failure following oral methadone.

Keywords: drug-induced rhabdomyolysis, respiratory failure, methadone.

Coma, myalgia and hypoxia.

P. R. Froomes, J. Haddad and D. Harding

doi: 10.1136/pgmj.72.852.629

Updated information and services can be found at:
http://pmj.bmj.com/content/72/852/629.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/