Rhabdomyolysis after cerebral perfusion pressure-guided management in severe head injury

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Abstract

Intravenous infusion of norepinephrine is usually effective and safe to maintain adequate cerebral perfusion pressure for the management of posttraumatic intracranial hypertension. We report the case of a 17-year-old woman who suffered from traumatic intracranial bleeding and hypotension; she developed rhabdomyolysis, myoglobinuria and acute renal failure after receiving high dose norepinephrine postoperatively. Hemodialysis was begun 3 days after the onset of myoglobinuria when acute renal failure was noted, despite aggressive fluid supplementation and alkaline diuresis. After aggressive treatment and dialysis, the patient’s myoglobinuria and rhabdomyolysis gradually declined. Her kidneys eventually regained normal function. We consider that systemic hypotension may have been the leading cause for development of rhabdomyolysis, and vasoconstrictors such as norepinephrine aggravated this. We emphasise the potentially devastating consequences of rhabdomyolysis when a large dose of norepinephrine is given for the treatment of hypotension during cerebral perfusion pressure-guided management.

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Keywords: Cerebral perfusion pressure; Rhabdomyolysis; Acute renal failure

1. Introduction

Induced hypertension to raise cerebral perfusion pressure (CPP) to 70 mmHg has become a popular and effective treatment for severe head injury. Vasopressors such as norepinephrine and/or dopamine, heavy sedation with propofol, muscle relaxation with atracurium besylate, vascular volume expansion with albumin, and osmotic diuresis with mannitol are widely used in these patients.1,2 In this report, we describe a rare case of rhabdomyolysis and acute renal failure after cerebral perfusion pressure (CPP)-guided treatment with norepinephrine. We investigate the etiology of rhabdomyolysis and its diagnosis and treatment.

2. Case report

A 17-year-old, 45 kg female patient who was previously in good health was brought to the emergency room in a drowsy state (Glasgow Coma Scale score 10) after a traffic accident. There were no obvious associated injuries include extremity fractures or crush injury on physical examination. The patient’s serum alcohol level was <10 mg/dL (normal <10 mg/dL). Brain computed tomography (CT) showed a left traumatic subarachnoid hemorrhage. She was admitted to the neurosurgery intensive care unit (ICU) for conservative treatment. Unfortunately, the next day her conscious level deteriorated to coma and her left pupil dilated. Emergency brain CT scan showed a delayed left acute subdural hemorrhage (SDH) of approximately 50 mL in volume, with severe mass effect. She immediately underwent a left craniotomy to remove the SDH. An intracranial pressure (ICP) monitor was placed in the ipsilateral frontal parenchyma. The duration of surgery was approximately 95 minutes.

On return to the ICU, she received CPP-guided management, with the aim of CPP support at 70 mmHg. The patient was sedated with propofol, given vascular volume expanders (hydroxyethyl starch and albumin), systemic vasopressors (norepinephrine and dopamine) and mannitol. Concurrent additional drugs included phenytoin, metoclopramide, cefazoline, potassium chloride, morphine, ranitidine and acetaminophen.

On hospital day 3, the patient developed tea-colored urine. A positive urine myoglobin and myoglobinemia were identified. Serum creatine phosphokinase (CPK) was 54,620 IU/L (normal 22–198 IU/L). During the initial 2 days of CPP-guided management, propofol was continuously maintained at a mean of 3.73 ± 1.17 mg/kg/h (range, 2.4–4.6 mg/kg/h). The continuous dose of atracurium was 0.14 ± 0.06 mg/kg/h (range, 0.07–0.22 mg/kg/h). The continuous dose of norepinephrine was 0.25 ± 0.14 μg/kg/min (range, 0.10–0.40 μg/kg/min) and that of dopamine was 3.9 ± 1.0 μg/kg/min (range, 2.9–4.9 μg/kg/min). Mannitol (every 4 h and as needed) was given at an average dose of 110 ± 30 g/day (range, 80–140 g/day).
Hypoxemia was not evident on admission, resuscitation or subsequent care. The patient’s core temperature was not excessive and there was scant shivering. Unexpected hypotension was noted several times after drug (mannitol, propofol and codeine) bolus infusions and the patient suffered from cardiac arrhythmia during the initial 2 days of CPP-guided management. Resuscitation with intravenous fluid was started immediately and the dose of norepinephrine was adjusted simultaneously.

Unfortunately, intermittent hypotension and persistent high ICP developed following myoglobinuria. The CPK level progressively elevated to a peak of 274,080 IU/L on hospital day 6 (Fig. 1). The patient began hemodialysis on admission day 5 when acute renal failure and pulmonary edema were noted despite aggressive fluid supplementation and alkaline diuresis.

Table 1 and 2 show the drugs administered and daily fluid input and output before hemodialysis. During dialysis, the patient’s limbs and trunk became extraordinarily swollen. The patient’s maximum body weight gain compared to her admission weight was 31 kg on hospital day 14. A plastic surgeon was consulted for compartment syndrome. No fasciotomy was recommended at that time. Dialysis was discontinued when renal function recovered at 36 days after acute renal failure onset. Table 3 shows the changes in laboratory data during dialysis.

The patient was weaned off the mechanical ventilator on hospital day 48. After 54 days of ICU care, she was transferred to the ordinary ward with clear consciousness and bilateral lower extremity weakness. A muscle biopsy at this time revealed chronic inflammation. A nerve conduction velocity study showed bilateral peroneal palsies; nerve entrapment was suspected. She was discharged from the hospital 12 weeks after admission with normal renal function and having lost a great amount of weight.

3. Discussion

Rhabdomyolysis is a potentially life-threatening syndrome resulting from the breakdown of skeletal muscle fibers, with leakage of muscle contents into the circulation. These intracellular contents include myoglobin, CPK, potassium, phosphate and other muscle enzymes. The diagnosis is confirmed by serum elevation of intracellular proteins unique to myocytes, specifically CPK and myoglobin. In our patient, the clinical diagnosis of rhabdomyolysis was made after the patient developed dark urine. Urinalysis was positive for blood by analysis with reagent strips, likely secondary to the passage of myoglobin through the glomeruli. The serial measurement of CPK revealed persistent and increasing serum CPK activity, which suggests ongoing myocyte damage.

The most serious complication of rhabdomyolysis is acute renal failure. The incidence of renal failure is increased in patients with high CPK levels (>15,000 IU/L), but only myoglobin, not CPK or other intracellular contents, has been demonstrated to be directly nephrotoxic. The reason for myoglobin toxicity to the kidney is precipitation of myoglobin within the kidney tubules, particularly in an acidic environment. Therefore, alkalinization of the urine to a pH of greater than 6.5 is recommended to prevent impairment of renal function. However, this management technique failed in our patient despite aggressive treatment with forced alkaline diuresis. This may have been due to the greatly elevated CPK (maximum, 274,080 IU/L) and the ongoing pathologic insult. CPK levels such as this are reported to peak in 24-48 h with aggressive hydration. In our patient, the CPK peaked between hospital days 5 and 6. We suppose that the rhabdomyolysis may have occurred between hospital days 3 and 4, while the pathologic insult was ongoing.

The most common cause of rhabdomyolysis is mechanical damage to muscle occurring in trauma patients. Other causes include muscle compression due to prolonged surgery, hyperthermia, intense shivering, seizure, prolonged administration of propofol, high-dose administration of glucocorticoids and atracurium.
An intravenous infusion of norepinephrine is frequently used in the management of posttraumatic intracranial hypertension to maintain adequate cerebral perfusion pressure. In 1995, Rosner et al. recommended that norepinephrine, at a dose of 0.2–0.4 μg/kg/min, was effective and safe to maintain adequate cerebral perfusion pressure. In our patient, the average continuous dose of norepinephrine administration on hospital day 3 before myoglobinuria developed was 0.35 μg/kg/min (range, 0.30–0.42). The high norepinephrine dose was given to manage high ICP (36.6 ± 10.6 mmHg) and unexpected hypotension in our patient. Vasoconstrictor use and hypotension have been multifactorial. We consider that systemic hypotension was the leading cause of rhabdomyolysis, and a vasoconstrictor, norepinephrine, aggravated it. We want to emphasize the potentially devastating consequences of rhabdomyolysis when large doses of norepinephrine are given during hypotension and CPP-guided ICP management. Only with early recognition of rhabdomyolysis and aggressive treatment, is the prognosis good for rhabdomyolysis complicated by acute renal failure.

4. Conclusion

The causes of rhabdomyolysis in our patient may have been multifactorial. We consider that systemic hypotension was the leading cause of rhabdomyolysis, and a vasoconstrictor, norepinephrine, aggravated it. We want to emphasise the potentially devastating consequences of rhabdomyolysis when large doses of norepinephrine are given during hypotension and CPP-guided ICP management. Only with early recognition of rhabdomyolysis and aggressive treatment, is the prognosis good for rhabdomyolysis complicated by acute renal failure.

References

Leptomeningeal infiltration as the presenting manifestation of a malignant glioma


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Abstract

Infiltration of the leptomeninges by a malignant glioma typically occurs with recurrent supratentorial tumors, but patients may present with leptomeningeal gliomatosis before the primary tumor is diagnosed. This report describes two patients who presented with headache and signs of multifocal neurological disease. One of the patients had neurofibromatosis type I. In both patients the primary tumor was small, and the diagnosis was not confirmed until autopsy.

Keywords: Astrocytoma; Chronic meningitis; Cerebrospinal fluid; Neurofibromatosis

1. Introduction

In post-mortem series, leptomeningeal gliomatosis is present in 15–27% of patients with gliomas. Most of these patients have a rapidly growing supratentorial tumor. Symptomatic leptomeningeal gliomatosis is found in only 2–7% of patients with supratentorial malignant gliomas. The diagnosis of leptomeningeal gliomatosis is straightforward unless the patient presents when the primary tumor is asymptomatic, or not visible on imaging. In these patients leptomeningeal gliomatosis may be difficult to distinguish from other causes of chronic meningitis. We report two patients who presented with multifocal neurological disease caused by leptomeningeal metastases. In both patients the primary tumor was small, and the diagnosis was not confirmed until autopsy.