Postoperative rhabdomyolysis: a completely localised and symmetrical phenomenon?

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SUMMARY

The aim of this case report is to describe an unusual case, where rhabdomyolysis was completely confined to both anterior tibial muscles, with sparing of the posterior compartments (no involvement of gastrocnemii). The patient had undergone a 3 h craniotomy and was weaned from ventilator support on postoperative day 1. All haemodynamic and vital parameters were within normal limits. However, severe pain (8/10 on the visual analogue scale) was felt in lateral-anterior tibial compartments bilaterally; creatine kinase (CK) value was found to be abnormally high. An MRI of both tibial regions was performed, that showed very particular findings. The patient complained of foot drop and pain worsening during standing; he recovered completely within 2 months following the surgery, with serum CK dropping considerably within this period.

BACKGROUND

Non-traumatic rhabdomyolysis is a heterogenous syndrome, arising from a panoply of factors, among which drugs, perioperative medication, and propofol are probably the most important of an iatrogenic nature.¹ The major complication related to the non-traumatic rhabdomyolysis is the creation of a compartment syndrome, occasionally requiring surgical treatment, such as fasciotomy.²⁻³ Several disorders may be the underlying cause of rhabdomyolysis, among which inherited diseases, mitochondrial myopathies and other muscular diseases sustaining the myolytic process; but toxins, muscle compression or vigorous exercise and other inflammatory events are important aetiological factors.⁴ Even the list of probable causative medications is not complete and is continuously updated, with antipsychotics, lipid-lowering drugs ('statins'), colchicine, newer antidepressants such as selective-serotonin reuptake inhibitors and lithium being widely implicated.⁴⁻⁵ When discussing the probability of a specific drug towards causing rhabdomyolysis, however, the causal link between rhabdomyolysis and the implicated medication is generally presumed but rarely, if ever, definitely proven. An incontestable causality is difficult to show, if suspected medication is a mixture of active components (like cough-treating products), An incontestable causality is difficult to show, if suspected medication is a mixture of active components (like cough-treating products), or when the event is completely isolated or unusual or when the event is completely isolated or unusual.⁶⁻⁷

The character of a potentially life-threatening disorder has been emphasised.⁵ The same authors suggest that a drop in myoplasmic ATP paralleled with sustained elevations in cytosolic calcium concentration represents a common signature of rhabdomyolysis.⁵ Interestingly, cardiac muscle is usually spared. When

there is cardiac involvement, this is mainly related to some of the complications of rhabdomyolysis, such as acidosis and electrolytic imbalances.⁸

CASE PRESENTATION

A young Caucasian man, aged 34 years, underwent a craniotomy in the supine position for the removal of a brain tumour. General anaesthesia was induced with midazolam, fentanyl and maintained with isoflurane; vecuronium was used to facilitate the endotracheal intubation. Propofol was administered immediately postoperatively and inside the intensive care unit, during the first 2 postoperative days of intensive care treatment. Propofol infusion was started at 1.5 mg/kg/h and reached a peak infusion of 4 mg/kg/h during the first postoperative day till adequate sedation was achieved; the second postoperative day the infusion dosage was gradually lowered and the drug was withdrawn 36 h after surgery.

With ambulation the patient noted pain in both legs (8/10 on a visual analogue scale). Examination of the tibial areas bilaterally showed no evidence of bruising or skin changes.

He was haemodynamically stable and was transferred on the third postoperative day to ward care. Walking was difficult and painful. Vague purple discoloration was noted over the pretibial areas; otherwise both pretibial regions were hardened and extremely painful upon touch or pressure (figure 1).

INVESTIGATIONS

Initial serum creatine kinase (CK; normal up to 240 UI/l) drawn when the patient began complaining of pain with ambulation was 5668 UI/l; the values of other significant enzymes or inflammation markers are summarised in table 1.

An MRI of the pretibial regions was performed the third day after the operation. Impressive

Figure 1 Right pretibial region, painful upon pressure and with discrete skin colour changes (third postoperative day).

To cite: Vyshka G, Morcka K, Andreou A. *BMJ Case Reports* Published online: 10 December 2012 doi:10.1136/bcr-2012-007288

Table 1 Values of enzymes and other biochemical markers collected during the follow-up.

Values collected	First postoperative day	Fourth postoperative day	1 week after surgery	2 weeks after surgery	1 month after surgery	2 months after surgery
CK (normal range 30–240 U/l)	5668	4780	3360	2890	780	388
ALT (normal range 15–55 U/l)	280	260	180	85	50	45
C reactive protein (normal range <10 mg/l)	220	165	127	40	8	2
Erythrocytation rate (normal values 3–15 mm/first hour)	45	35	20	25	25	15

The values of ALT, C reactive protein and erythrocytation rate returned to normality by 2 months after surgery; only CK value remained slightly above the upper normal range, with a clear and constant falling trend.

ALT, alanine transaminase; CK, creatine kinase.

changes in both anterior tibial muscles were noted; however, gastrocnemii muscles were surprisingly normal, clinically and in the imaging studies. The images of anterior tibial muscles, thus contrasting with an unaltered gastrocnemius structure and function, are reproduced in figures 2–4. Large oedematous changes in both anterior tibial muscles suggested myolysis, fluid extravasation and interstitial infiltration. The main characteristic of the entire case was the deep contrast between the rhabdomyolytic images of both pretibial regions (figure 2), with sparing of posterior compartments (figures 3 and 4).

DIFFERENTIAL DIAGNOSIS

The list of offending drugs and chemicals associated with non-traumatic rhabdomyolysis continues to expand. Authors distinguish a drug-induced and primary rhabdomyolysis and a secondary phenomenon, whereby a drug generates circumstances (such as hypokalaemia, hyperthermia, etc) predisposing to this complication.^{9–10} Table 2 summarises some of medications and drugs of abuse that are implicated with rhabdomyolysis.^{9–10–12}

TREATMENT

The patient was treated with intravenous fluids and alkalinisation of urine; non-steroidal anti-inflammatory drugs were administered till a substantial relief of pain was achieved (ketoprofen injections). The second week, a physiotherapeutic-rehabilitative

programme was put in place. The dorsal flexion of both legs returned completely at the initiation of the second postoperative month; however, pain upon pressure on the pretibial compartments disappeared 3 weeks after surgery. A nerve conduction study suggested mild axonal changes (decrease in the amplitude of the motor-evoked potential) nearly identical in both common peroneal nerves; a follow-up electroneurography was not completed due to the consistent improvement in the clinical image and the return of the dorsal flexion of both feet.

DISCUSSION

Rhabdomyolysis represents a serious challenge to the physician, especially in the postoperative setting. The diagnosis of rhabdomyolysis is defined as an injury to or necrosis of the striated muscle, and its presence and severity is proportionally related with an even more notorious complication, that is, the renal failure. Postoperative rhabdomyolysis has been associated with three factors, as some authors emphasise, that is, non-supine position during surgery (which might cause direct pressure damage to the muscle); tourniquet use and administration of certain medications, like suxamethonium, etc.¹³ However, propofol has been at the centre of several investigations, and a propofol-related infusion syndrome (PRIS) is described.^{14–15} Such a syndrome is potentially fatal not only due to the possible

Figure 2 Longitudinal MRI (STIR sequences) of both pretibial compartments, with anterior tibial muscles rhabdomyolytic changes, oedema, extravasation and interstitial infiltration. STIR, short T1 inversion recovery.

Figure 3 MRI (STIR sequences) of posterior leg regions, with an unaltered structure of mm. gastrocnemii. STIR, short T1 inversion recovery.

Figure 4 Axial MRI (T1-weighted, TSE sequences) of both legs; hyperintense signals in the pretibial compartments, contrasting with the unaltered image of the gastrocnemii and of the other posterior muscular territories, bilaterally. TSE, turbo spin echo.

appearance of the renal failure, but metabolic acidosis and cardiac failure are some other very serious features of PRIS.¹⁶

Apart from the challenge of finding the responsible drug, and possibly anticipating the complication, therefore implementing the necessary therapeutic measures, another issue has been the CK threshold used to classify a situation such as rhabdomyolysis. Different authors have used largely divergent values of CK to define the syndrome; historically, a cut-off of 500 UI/l was adopted to classify a situation as rhabdomyolysis, while most authors require a CK value to exceed 5000 UI/l, or approximately 25 times the upper limits of normal.^{17–19}

Our case had a surgical intervention in the supine position, thus large muscular regions like thighs were not endangered, as opposed to prone position and the use of the Jackson surgical frame.¹³ However, even in a supine surgical position and with the use of buttock support, rhabdomyolysis has been reported to involve severely gluteal regions, creating a compartment syndrome in that case.²⁰

As far as local pressure causes have been excluded, the clinical picture we described had to be related to one of the several active principles used during anaesthesia; since propofol was used in infusion and therefore in a more prolonged way, suspicions were mainly directed to the latter drug. As we summarised in table 1,

CK values reached a peak of approximately 5700 UI/l, and no compartment syndrome features were noted. In the case of a compartment syndrome, surgical intervention, such as monitoring of compartment pressures and fasciotomy, is often necessary.²¹ Much higher values of CK can be found in the literature, in other aetiological backgrounds, with CK of more than one million UI/l in the acute phase of the syndrome.²² The falling trend of CK during the course of the disease clearly predicts a good outcome, as in our case, which fairly illustrates the improvement of the clinical picture as the lab values returned towards normal, with the patient recovering completely within the second month from the event.

Bilateral anterior tibial compartment syndrome is a clinical rarity, and authors reporting isolated cases accept the fact that its aetiology might remain unidentified.^{23–24} The completely localised character of rhabdomyolysis, and its symmetrical nature, with involvement of only the tibial compartments with sparing of other areas, was a particularity of our case, and the MRI reproduced above demonstrate this phenomenon.

Table 2 Chemical agents implicated with non-traumatic rhabdomyolysis

Drugs of abuse	Medications
Ethanol	Lipid-lowering drugs
Cocaine	Azathioprine
Amphetamine	Zidovudine
Heroin	Propofol
Opiates	Colchicine
Barbiturates	Amphotericin B
Benzodiazepines	Sodium valproate
Ecstasy	Isoniazid
Lysergic acid diethylamide (LSD)	Antihistamines
Caffeine	Salicylates
	Suxamethonium

Learning points

- ▶ Postoperative rhabdomyolysis is a rare complication, which should be considered if unexplained pain and swelling is seen in body regions that are at particular risk, such as lower extremities or the gluteal muscles.
- ▶ The cause of rhabdomyolysis in the postoperative period may be multi factorial; several medications are implied, including anaesthetics.
- ▶ In the case we presented, a combination of the length of surgery, the lack of change in position during that time (the patient immobilised in the operating room with antithrombotic stocks across the extremities) and possible (relative) dehydration were likely contributory to the development of this complication.
- ▶ Perhaps propofol; some undiagnosed and unrecognised metabolic disorders and other factors (as mentioned above) all played a part here.
- ▶ When there is clinical suspicion, serial creatine kinase levels are helpful to diagnose and follow the course of this complication, which as a rule seems to have a good prognosis.

Competing interests None.

Patient consent Obtained.

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