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## CLINICAL INFORMATION

### Atypical reaction to anesthesia in Duchenne/Becker muscular dystrophy



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#### KEYWORDS

Duchenne muscular dystrophy;  
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#### Abstract

**Background and objectives:** Duchenne/Becker muscular dystrophy affects skeletal muscles and leads to progressive muscle weakness and risk of atypical anesthetic reactions following exposure to succinylcholine or halogenated agents. The aim of this report is to describe the investigation and diagnosis of a patient with Becker muscular dystrophy and review the care required in anesthesia.

**Case report:** Male patient, 14 years old, referred for hyperCKemia (chronic increase of serum creatine kinase levels – CK), with CK values of 7,779–29,040 IU.L<sup>-1</sup> (normal 174 IU.L<sup>-1</sup>). He presented with a discrete delay in motor milestones acquisition (sitting at 9 months, walking at 18 months). He had a history of liver transplantation. In the neurological examination, the patient showed difficulty in walking on one's heels, myopathic sign (hands supported on the thighs to stand), high arched palate, calf hypertrophy, winged scapulae, global muscle hypotonia and areflexia. Spirometry showed mild restrictive respiratory insufficiency (forced vital capacity: 77% of predicted). The in vitro muscle contracture test in response to halothane and caffeine was normal. Muscular dystrophy analysis by Western blot showed reduced dystrophin (20% of normal) for both antibodies (C and N-terminal), allowing the diagnosis of Becker muscular dystrophy.

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**Conclusion:** On preanesthetic assessment, the history of delayed motor development, as well as clinical and/or laboratory signs of myopathy, should encourage neurological evaluation, aiming at diagnosing subclinical myopathies and planning the necessary care to prevent anesthetic complications. Duchenne/Becker muscular dystrophy, although it does not increase susceptibility to MH, may lead to atypical fatal reactions in anesthesia.

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## PALAVRAS-CHAVE

Distrofia muscular de Duchenne;  
Hipertermia maligna;  
Anestesia

## Reação atípica à anestesia em distrofia muscular de Duchenne/Becker

### Resumo

**Justificativa/objetivos:** Distrofia muscular de Duchenne/Becker afeta a musculatura esquelética e leva a fraqueza muscular progressiva e risco de reações atípicas anestésicas após exposição à succinilcolina ou halogenados. O objetivo do presente relato é descrever investigação e diagnóstico de paciente com distrofia muscular de Becker e revisar os cuidados necessários na anestesia.

**Relato de caso:** Paciente masculino, 14 anos, encaminhado por hiperCKemia (aumento crônico dos níveis séricos de creatinoquinase – CK), com valores de CK de 7.779–29.040 UI.L<sup>-1</sup> (normal 174 UI.L<sup>-1</sup>). Apresentou discreto atraso da aquisição de marcos motores (sentou aos nove meses, andou aos 18). Antecedente de transplante hepático. No exame neurológico apresentava dificuldade para andar nos calcanhares, levantar miopático (apoiava mãos nas coxas para ficar de pé), palato arqueado alto, hipertrofia de panturrilhas, escápulas aladas, hipotonia muscular global e arreflexia. Havia insuficiência respiratória restritiva leve na espirometria (capacidade vital forçada: 77% do previsto). O teste de contratatura muscular *in vitro* em resposta ao halotano e à cafeína foi normal. Estudo da distrofina muscular por técnica de Western blot mostrou redução da distrofina (20% do normal) para ambos os anticorpos (C e N-terminal), e permitiu o diagnóstico de distrofia muscular de Becker.

**Conclusão:** Na avaliação pré-anestésica, história de atraso do desenvolvimento motor, bem como sinais clínicos e/ou laboratoriais de miopatia, deve motivar avaliação neurológica, com o objetivo de diagnosticar miopatias subclínicas e planejar cuidados necessários para prevenir complicações anestésicas. Distrofia muscular de Duchenne/Becker, apesar de não conferir suscetibilidade aumentada à HM, pode levar a reações atípicas fatais na anestesia.

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## Introduction

The dystrophin protein stabilizes sarcolemma in the skeletal, cardiac and smooth muscle, and central nervous system; therefore its absence/decrease alters the sarcolemma structure, allows Ca<sup>2+</sup> influx, intracellular protease activation, and muscle fiber necrosis.<sup>1,2</sup> Duchenne muscular dystrophy is a myopathy that affects one in 3600 live births as a result of mutations in the dystrophin gene, which leads to its absence with a recessive inheritance linked to the X chromosome.<sup>1</sup> In Becker muscular dystrophy, mutations in the dystrophin gene allows expression of the protein, although abnormal.<sup>1</sup> Patients with Duchenne/Becker muscular dystrophy present with progressive necrosis of skeletal muscle that begins in childhood so the diagnosis may go unnoticed in the first years of life.<sup>1</sup>

In these patients, exposure to succinylcholine and halogenated agents may be followed by atypical reactions in anesthesia and even sudden cardiac arrest due to hyperkalemia resulting from massive rhabdomyolysis.<sup>1</sup>

## Objective

The aim of this report is to describe the investigation and diagnosis of a patient with Becker muscular dystrophy and review the anesthetic care needed.

## Case report

A 14-year-old male patient was referred to the malignant hyperthermia service for hyperCKemia (a chronic increase of serum creatine kinase levels – CK) investigation, with CK values in the three years prior to the consultation ranging from 7779 to 29,040 UI.L<sup>-1</sup> (normal value 174 IU.L<sup>-1</sup>).

After an uneventful gestation, the patient was delivered via cesarean section due to dystocia, with report of transient neonatal jaundice. He presented a mild delay in motor milestones (sitting at 9 months and walking at 18 months). At the age of three months, jaundice, dyslipidemia and coagulopathy were detected, what allowed

diagnosis of familial progressive intrahepatic cholestasis (Byler's syndrome) at six months of age. At the age of two years he was successfully submitted to liver transplantation and has since been maintained on immunosuppressive therapy – currently with tacrolimus and prednisone. Despite the effective immunosuppression to avoid transplant rejection the patient had hyperCKemia. Muscle biopsy at nine years of age showed condensed fibers (hyaline fibers) and necrotic fibers with perivascular lymphoplasmacytic infiltrate; at that time he was diagnosed with nonspecific chronic inflammatory myopathy. Investigation into other causes of hyperCKemia such as endocrinopathies showed no changes.

At the age of 14 years, a neurological examination revealed signs suggestive of myopathy: difficulty in walking on one's heels, myopathic standing up (Gowers' sign – hands supported on the thighs to stand), high arched palate (ogival), calf hypertrophy, winged scapulae, global muscle hypotonia, and generalized areflexia – with the exception of the Achilles tendon bilaterally. Electrocardiogram showed early ventricular repolarization and echocardiogram showed mild mitral and aortic insufficiency. There was mild restrictive respiratory insufficiency in spirometry (forced vital capacity 77% of predicted). Electroneuromyography revealed a myopathic pattern. Molecular test in peripheral blood was requested for Duchenne/Becker muscular dystrophy, which detected no gene deletions or duplications. Investigations for mutations in the exons most frequently affected in Brazilian patients with sarcoglycan-deficient limb-girdle muscular dystrophy of also showed no pathogenic alterations.

Thus, the patient underwent quadriceps muscle biopsy under peripheral nerve block (femoral and lateral femoral cutaneous), with prior preparation of the room and anesthetic machine for decontamination of halogenated compounds. The *in vitro* muscle contracture test in response to halothane and caffeine was normal, excluding the suspected susceptibility to malignant hyperthermia as the cause of hyperCKemia. The pathological study with histochemical and immunohistochemical analysis showed necrotic fibers, with conjunctival proliferation in the endomysium and perimysium; immunolabeling for dystrophin was negative for C-terminal antibody and positive but discontinuous for N-terminal antibody. Western blot analysis of muscular dystrophin showed reduced dystrophin (20% of normal) for both antibodies (C and N-terminal), and allowed the diagnosis of Becker muscular dystrophy.

## Discussion

In myopathies, clinical decompensation has been reported during/after anesthetic procedures with resulting hypoventilation, atelectasis, difficult extubation, dysphagia, arrhythmias, and congestive heart failure as well as dysautonomia and gastroparesis/paralytic ileus.<sup>3,4</sup>

Moreover, particularly following the use of succinylcholine or anticholinesterase drugs, atypical anesthetic reactions resembling malignant hyperthermia (MH) (reactions similar to MH or malignant hyperthermia-like reactions) may occur. However, there is no hypermetabolism

typical of MH as there is no increase in oxygen consumption or carbon dioxide production.<sup>3</sup> In malignant hyperthermia-like reactions there may be, (isolated or associated), respiratory failure, muscle spasms, rhabdomyolysis, myoglobinuria leading to acute renal failure and, in most severe cases, sudden cardiac arrest due to hyperpotassemia.<sup>2</sup> The etiology of these reactions differs from that of MH as they result from up-regulation of acetylcholine receptors (AChR).<sup>3</sup> AChR up-regulation results from the emergence of immature and neuronal isoforms in an extrajunctional area, which are not desensitized, are hypersensitive to depolarization (excessive potassium output) and lead to muscle injury.<sup>3</sup> Treatment of atypical anesthetic reactions due to the up-regulation of AChR is directed to hyperpotassemia.<sup>1,5</sup>

Thus, in myopathies previously detected, preanesthetic evaluation should focus on the detection of restrictive ventilatory insufficiency and/or underlying cardiopathy, in addition to planning the patient's positioning due to osteoarticular retractions and spine and rib cage deformities.<sup>3</sup> The recommended basic monitoring with oximetry, cardioscopy, capnography, and blood pressure should always include temperature measurement.<sup>1</sup> Neuromuscular block monitoring detects changes in response to non-depolarizing neuromuscular blockers, which may occur in myopathies, as delayed onset of action and prolonged effect.<sup>3</sup> Succinylcholine should not be used in patients with myopathy due to the risk of atypical reaction.<sup>5</sup> Available intensive care unit is recommended, as well as the preference for performing procedures in a hospital setting.<sup>4</sup>

Often, as in the present case, despite the suggestive clinical symptoms and signs, the myopathy diagnosis had not yet been made prior to anesthesia.<sup>4</sup> In these situations, the anesthesiologist is required to have a high degree of suspicion at the preanesthetic assessment visit, which may require referring the patient for neurological evaluation and diagnostic clarification before the procedure.<sup>4</sup>

In Duchenne/Becker muscular dystrophy there is the aggravating fact that atypical reactions in anesthesia occur not only with succinylcholine, but also with halogenated inhalational anesthetics.<sup>1,5</sup> These drugs may damage the already compromised muscle fiber membrane, cause rhabdomyolysis and result in increased CK, acidosis, and hyperkalemia.<sup>3</sup> Therefore, it is also recommended to avoid halogenated agents in this dystrophy (with the anesthetic machine decontamination before the procedure) or, if necessary, the lowest possible dose/duration should be used.<sup>1-3,5</sup> Details on anesthesia workstation preparation for decontamination of halogenated agents are available on the website of the American Malignant Hyperthermia Group (<http://www.mhaus.org/healthcare-professionals/mhaus-recommendations/anesthesia-workstation-preparation>).

Our patient had already undergone previous anesthesia for liver transplantation without complications; apparently, even without the necessary precautions there was no atypical reaction, which emphasizes the fact that a prior history of anesthesia without complications does not rule out the possibility of future anesthesia problems.

## Conclusion

In preanesthetic evaluation, a history of motor development delay, as well as clinical and/or laboratory signs of myopathy should motivate neurological evaluation, in order to diagnose subclinical myopathies and plan the necessary care to prevent anesthetic complications. Patients with myopathies should be advised of the risk of atypical reactions during anesthesia, as well as the need to inform the anesthetic and surgical staff. Although Duchenne/Becker muscular dystrophy does not increase susceptibility to malignant hyperthermia, it may lead to fatal atypical reactions during anesthesia.

## Conflicts of interest

The authors declare no conflicts of interest.

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