Atypical reaction to anesthesia in Duchenne/Becker 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 suxamethonium 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−1 (normal 174 IU.L−1). 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 arreflexia. 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.
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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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 creatinquinase – CK), com valores de CK de 7.779–29.040 UI.L.¹⁻¹ (normal 174 UI.L.¹⁻¹). 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 (apoia mãos nas coxas para ficar de pé), palato arqueado alto, hipertrofia de panturrilhas, escábulas aladas, hipotonía muscular global e arreflexia. Havia insuficiência respiratória restritiva leve na espirometria (capacidade vital forçada: 77% do previsto). O teste de contratura 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 susceptibilidade 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 Ca²⁺ influx, intracellular protease activation, and muscle fiber necrosis. 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. In Becker muscular dystrophy, mutations in the dystrophin gene allows expression of the protein, although abnormal. 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.

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.
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 arreflexia – 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 endomyosum 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 hypventilation, atelectasis, difficult extubation, dysphagia, arrhythmias, and congestive heart failure as well as dysautonomia and gastroparesis/paralytic ileus. Typically, MH is the most common cause of death in patients with myopathies undergoing anesthesia. The development of MH has been associated with anesthetic agents, such as succinylcholine and nonsuccinylcholine drugs. The use of succinylcholine in patients with myopathies may result in severe and rapid hyperthermia and can lead to cardiac arrest and death. The use of alternative anesthetic agents, such as rocuronium or vecuronium, has been recommended in patients with myopathies to prevent the development of MH. The use of intraoperative monitoring, such as pulse oximetry and transcutaneous oxygen saturation, can also help to detect the early signs of MH and to prevent its development.

In conclusion, the management of patients with myopathies undergoing anesthesia requires a multidisciplinary approach that includes anesthetic providers, critical care specialists, and rehabilitation experts. The use of alternative anesthetic agents, the implementation of intraoperative monitoring, and the early recognition of the signs and symptoms of MH are essential to prevent its development and to ensure the safe delivery of care to patients with myopathies.
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.

References