

Case Report

Prikaz slučaja

MALIGNANT HYPERTHERMIA-LIKE SYNDROME IN A CHILD WITH MULTIPLE EXOSTOSES...OR NOT?
(*Malignant hyperthermia – like syndrome*)**MALIGNA HIPERTERMIJA KAO SINDROM KOD DETETA SA MULTIPLIM EGZOSTOZAMA...ILI NE?**

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Summary. The authors describe a case of malignant hyperthermia - like syndrome in a child during general anesthesia provided for a rib exostosis removal. Patient experienced a hypermetabolic state after general anesthesia which was pretty similar to a malignant hyperthermia episode, but without muscle rigidity. Clinical and laboratory findings were consistent with a hypermetabolic condition but not quite definite. Reviewing the available literature did not reveal any similar case reported previously.

Key words: malignant hyperthermia, hypermetabolic state, multiple exostoses, general anesthesia, child

Sažetak. Autori opisuju slučaj sindroma nalik malignoj hipertermiji kod deteta u toku opšte anestezije prilikom odstranjenja rebarne egzostoze. Pacijent je imao hipermetaboličko stanje posle opšte anestezije koje je bilo veoma slično epizidi maligne hipertermije, ali bez rigiditeta muskulature. Klinički i laboratorijski nalazi su ukazivali na hipermetaboličko stanje, ali nisu mogli sa sigurnošću definisati dijagnozu. Uvidom u raspoloživu literaturu, nije nađen izveštaj sličnog slučaja.

Ključne reči: maligna hipertermija, hipermetaboličko stanje, multipla egzostoza, opšta anestezija, dete

Introduction

Clinical episodes and abnormal laboratory tests compatible with the diagnosis of malignant hyperthermia have been observed in patients with a diversity of syndromes, enzymopathies and coexisting disorders, thereby raising the likelihood of causal associations and heightened perioperative risk in others carrying a shared diagnosis¹.

The authors present a case of malignant hyperthermia – like syndrome in a child with multiple exostoses during general anesthesia.

Case description

A 20-months-old girl was scheduled for removal of an exostosis on the eighth left rib. Her medical history included a diagnosis of atopic dermatitis. Following the preoperative evaluation she was assigned an ASA II physical status classification. She was examined by an allergologist and had skin scarification tests for possible allergy to anesthetics. They all came back negative. Family history was unremarkable, except for a post anesthetic complication with the girl's aunt after a cesarean section.

Parents could not specify this complication and medical documentation was not available. This child had uneventful anesthesia previously for a CT scan and no known family history of malignant hyperthermia. Her preoperative laboratory work revealed mild leukocytosis and increased ASAT and alkaline phosphatase. Physical examination did not reveal any abnormalities. The girl's parents consented to general endotracheal anesthesia, the insertion of peripheral intravenous lines, urethral catheter and if required intraoperative blood transfusion.

The patient was taken to the operating room and following the placement of standard monitors, a 22G peripheral intravenous line was inserted, followed by the administration of propofol 2.5 mg/kg. Mask ventilation was easily established and rocuronium 1 mg/kg was given. A tracheal intubation was performed successfully on the first attempt and was verified with positive end-tidal CO₂ and equal bilateral breath sounds. A gas mixture of equal parts of oxygen and nitrous oxide and isoflurane were initiated for maintaining the anesthetic state. After three minutes of volume controlled mechanical ventilation with a tidal volume of 8 ml/kg, respiratory rate of 20 breaths per minute, and peak pressure of 20 mmHg, end-tidal CO₂ level was 56 mmHg. A direct laryngoscopy was performed to revise the position of the tube. The cuff was visible above the vocal cords. The endotracheal tube was replaced with a smaller internal diameter cuffed one. Fifteen minutes later end-tidal CO₂ level remained markedly high – up to 63 mmHg, and did

not decrease after changes of ventilation regimen. Then, a suspicion of malignant hyperthermia arose. Isoflurane was immediately withdrawn and the ventilation circuit replaced with a new one. An intravenous bolus of midazolam was administered followed by an infusion at the rate of 0.2 mg/kg/h. Intermittent boluses of fentanyl and rocuronium were injected during surgery. Prior to surgical incision oral temperature was taken – 37.4 °C.

Despite adequate analgesia, level of unconsciousness and muscle relaxation, the patient remained tachycardic (up to 185 bpm) and end-tidal CO₂ level was slowly increasing (up to 68 mmHg). At the end of surgery oral temperature was 39.3°C. Tachycardia and hypercapnea were persistent. Blood and urine samples were withdrawn for free myoglobin testing. Urine output was adequate and normally colored. Physical and pharmacological cooling was initiated but the temperature remained high. Two doses of dantrolene (1 mg/kg and 1.5 mg/kg) were administered. Fifteen minutes later a decrease in oral temperature was registered. The laboratory work showed no free myoglobin either in blood or in urine. Results showed metabolic acidosis, high CK, high LDH but no hypercapnea or hyperkalemia (tab.1).

The girl was extubated and transported to the PICU for further monitoring and treatment. During the first 24 postoperative hours three intravenous boluses of dantrolene 1 mg/kg were administered. The child remained subfebrile (37.3 – 37.5 °C axillary) throughout her stay in the PICU.

Table 1.

Test	Preoperatively	During MH episode	6 hours later	12 hours later	24 hours later
pH	7.42	7.23	7.24	7.40	7.46
pCO ₂	35.1	41.8	67.0	47.3	37.2
pO ₂	61.6	203.3	166.2	160.1	47.1
BE	-1.6	-9.8	-1.1	3.7	2.4
K ⁺	4.60	4.40	NA	NA	4.25
Ca ⁺⁺	NA	2.19	NA	NA	2.24
CK	NA	374	1542	NA	950
LDH	NA	565	834	NA	721
Myoglobin	NA	neg	NA	NA	NA

Discussion

Malignant hyperthermia, first reported in humans in 1960 by Denborough and Lovell², is a rare, potentially lethal pharmacogenetic myopathy that usually manifests in response to anesthetic triggering agents as a fulminate malignant hyperthermia crisis in genetically predisposed individuals. Occasionally, malignant hyperthermia – like events also occur in patients with other myopathies or other conditions.^{1, 3, 4, 5}

In their editorial Davis P. and Brandom B.³, summarize most of the previously thought to be associated to malignant hyperthermia conditions. It appears that only three medical conditions are proven to be malignant hyperthermia susceptible – King Denborough syndrome, central core myopathy and multi-minicore disease with RYR1 mutation. Conditions like Noonan syndrome, osteogenesis imperfecta, arthrogryposis, Brody disease, idiopathic hyperCKemia and others, are shown to have weak evidence for malignant hyperthermia susceptibility. The risk of such a complication in these patients is not greater than it is in general population.¹

We performed a thorough search in literature using Pub Med search engine in order to find any published materials that show evidence of malignant hyperthermia susceptibility in children with multiple exostoses. No articles on the matter were found. Claiming that there is a relation between these two conditions should be supported by specific genetic tests. The patient had experienced uneventful anesthesia previously but it was of a short duration and malignant hyperthermia triggers were not used. But even if triggers were used, it would not be insurance for uneventful anesthesia in the future. Phadke A. et al.⁶ report a lethal malignant hyperthermia episode in an infant after his ninth general anesthesia using inhalational anesthetic.

The hypermetabolic state of our patient did not lead to muscle rigidity or muscle breakdown, which are the most specific early signs of a malignant hyperthermia crisis.⁷ All the possible reasons for increased end-tidal CO₂ were excluded. The susceptibility for malignant hyperthermia crisis was evaluated using the clinical grading scale for malignant hyperthermia⁸ and the result – “somewhat greater than likely”, was the breaking point of starting our clinic’s protocol for managing malignant hyperthermia.

The risk of recrudescence of malignant hyperthermia increases as time from induction to the initial malignant hyperthermia reaction increases, perhaps as a result of greater muscle exposure.⁹ Although the patient was exposed to isoflurane only for about 15 minutes, a decision of prolonged administration of dantrolene was made.

Conclusion

We have enough reasons to think that this patient experienced a hypermetabolic state after general anesthesia which was pretty similar to a malignant hyperthermia episode without muscle rigidity. Further genetic and laboratory tests would be necessary to conclude this episode is completely unrelated to the child’s main condition – multiple exostoses.

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