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CLINICAL INFORMATION

Acute postoperative sepsis mimicking symptomology suspicious for malignant hyperthermia: case report

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Sepsis;
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Transrectal ultrasound

Abstract
Background: Sepsis is a life-threatening organ dysfunction with non-specific clinical features that can mimic other clinical conditions with hyper metabolic state such as malignant hyperthermia. Perioperatively anesthesia providers come across such scenarios, which are extremely challenging with the need for urgent intervention.
Objective: To illustrate the need for early intervention and consultation for added assistance to approach and rule out malignant hyperthermia and other possible causes during such a scenario.
Case report: A 63-year-old male underwent an uneventful elective flexible cystoscopy and transrectal ultrasound-guided prostate biopsy. Postoperatively he developed symptoms raising suspicion for malignant hyperthermia. Immediately malignant hyperthermia protocol was initiated that included administration of dantrolene and consultation of malignant hyperthermia association hotline along with other diagnostic and interventional management aimed at patient optimization. While early administration of dantrolene helped in hemodynamically stabilizing the patient, the consultation with other providers and malignant hyperthermia association hotline along with repeated examinations and lab works helped in ruling out malignant hyperthermia as the possible diagnosis. The patient later recovered in the intensive care unit where he was treated for the bacteremia that grew in his blood cultures.
Conclusions: Sepsis shares clinical symptoms that mimic malignant hyperthermia. While sepsis rapidly progresses to secondary injuries, malignant hyperthermia is life threatening. Providing ideal care requires good clinical judgment and a high level of suspicion where timely and appropriate care such as early administration of dantrolene and consultation of malignant hyperthermia association hotline for added assistance can influence positive outcomes.

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PALAVRAS-CHAVE
Sepse;
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Linha direta da associação de hipertermia maligna;
Ultrassonografia transretal

Sepse aguda pós-operatória simulando sintomatologia suspeita para hipertermia maligna: relato de caso

Resumo
Justificativa: A sepse é uma disfunção orgânica fatal com características clínicas inespecíficas que podem imitar outras condições clínicas com quadro hipermetabólico, como a hipertermia maligna. Esses cenários são extremamente desafiadores para a anestesia perioperatória e requerem intervenção urgente.
Objetivo: Ilustrar a necessidade de intervenção e consulta precoces para uma assistência adicional na abordagem e exclusão de hipertermia maligna e outras possíveis causas durante tal cenário.
Relato de caso: Paciente do sexo masculino, 63 anos, submetido à cistoscopia eletiva com cistoscópio flexível e biópsia transretal da próstata guiada por ultrassom sem intercorrências. No pós-operatório, o paciente desenvolveu sintomas que levantaram a suspeita de hipertermia maligna. O protocolo de hipertermia maligna foi imediatamente iniciado, inclusive a administração de dantrolene e uma consulta pela linha direta da associação de hipertermia maligna, juntamente com outros diagnósticos e manejos intervencionistas com vistas ao aprimoramento do paciente. Enquanto a administração precoce de dantrolene ajudou na estabilização hemodinâmica do paciente, a consulta com outros anestesistas e com a Associação de Hipertermia Maligna, juntamente com repetidos exames físicos e laboratoriais, ajudou a excluir a hipertermia maligna como o possível diagnóstico. O paciente recuperou-se mais tarde na unidade de terapia intensiva, onde recebeu tratamento para a bacteremia detectada em suas hemoculturas.
Conclusões: A sepse compartilha sintomas clínicos que mimetizam a hipertermia maligna. Enquanto a sepse progride rapidamente para lesões secundárias, a hipertermia maligna é uma ameaça à vida. Proporcionar o tratamento ideal requer um bom julgamento clínico e um alto nível de suspeita quanto aos cuidados oportunos e apropriados, como a administração precoce de dantrolene e a consulta pela linha direta da Associação de Hipertermia Maligna para assistência adicional, que podem resultar em desfechos positivos.

Introduction

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] It has been reported with postoperative incidence rates more than 1% and 4% following elective and non-elective surgeries respectively.[2] This concern follows any intrusive procedure and urologic instrumentation is no different. Sepsis shares non-specific clinical features that mimic other clinical conditions. Malignant hyperthermia, a life threatening hyper metabolic state is one such condition. Malignant hyperthermia is a pharmacogenetic disease, indeed one among the first group of such conditions reviewed in anesthesia literature. Abnormal skeletal muscle Ca^{2+} regulation triggered by several anesthetic drugs leads to sustained muscle contractions and a hyper metabolic state. Anesthesia providers encounter patients manifesting enhanced systemic responses that pose challenge for clinical diagnosis and treatment. We present a case report of sepsis after a cystoscopy and transrectal ultrasound-guided prostate biopsy resembling malignant hyperthermia symptoms requiring activation of malignant hyperthermia protocol and how such a presentation can be diagnostically challenging and subsequent interventions can be critical in the course of management.

Written consent for the publication of this case report was obtained from the patient.

Case report

A 63-year-old male with benign prostatic hyperplasia and urinary retention presented for elective flexible cystoscopy and transrectal ultrasound-guided guided prostate biopsy. Medical history included chronic obstructive pulmonary disease, hypertension, hyperlipidemia and osteoarthritis, and had undergone foot surgery in the past. Active medications included antihypertensives and nebulization. He declined any positive history of malignant hyperthermia or other problems with anesthesia in him or among any family members. Preoperative vital signs and labs were within normal limits except for an elevated baseline creatinine of 1.5 $mg.dL^{-1}$. General anesthesia was planned and the patient was induced with intravenous 100 mg of lidocaine, 200 mg of propofol and 50 mcg of fentanyl. A supraglottic laryngeal mask airway was then placed and general anesthesia was maintained with inhaled sevoflurane. Throughout the surgery the patient breathed spontaneously, and continuous end tidal CO_2 monitoring was stable between 45 and 50.

Table 1 Clinical data.

	Preoperative	Intraoperative	Postoperative
Muscular dysfunction	None	None	Rigidity
Temperature	36.9 °C	37.2 °C	38.6 °C
Blood pressure	Normotensive	Normotensive	220/110 mmHg
Heart rate	Normal	Normal	110
Respiratory rate	Normal	Normal	40
CO_2	N/A	45–50 (ET)	62 mmHg ($PaCO_2$)
White blood cell count	$5.6 \times 10^9.L^{-1}$	N/A	$11.2 \times 10^9 \cdot L^{-1}$
Creatine kinase	N/A	N/A	204 $U \cdot L^{-1}$

He continued to remain normothermic and hemodynamically stable. He received another 50 mcg of fentanyl for analgesia and 4 mg of ondansetron for antiemesis prophylaxis intraoperatively. The surgery underwent uneventfully and at the end he was extubated and transported to recovery unit. After arrival to the recovery unit he remained alert, awake, non-anxious and comfortable following adequate intraoperative narcotic administration. His vitals were stable including normothermia, normal oxygen saturation, normotension, normal heart and respiratory rates. Approximately 40 min later he suddenly started exhibiting muscle rigidity along with elevated temperature of 38.6 °C, elevated blood pressure of 220/110 mmHg and marked tachypnea of 40 and tachycardia of 110. Based on his clinical presentation, malignant hyperthermia was suspected. Malignant hyperthermia protocol was initiated and the malignant hyperthermia hotline was contacted. Patient was reintubated with 200 mg of intravenous propofol alone. Radial artery cannulation and emergent lab studies were performed. As per protocol, 2.5 $mg.kg^{-1}$ of intravenous dantrolene was administered. His initial labs and blood gas analysis were within normal limits except for an elevated CO_2 of 62 mmHg, elevated white blood cell count of $11.2 \times 10^9.L^{-1}$ and creatine kinase of 204 $U.L^{-1}$. Table 1 illustrates all the above clinical data. Repeat physical examination revealed no more muscle rigidity. While his elevated temperature remained, his blood pressure normalized probably secondary to dantrolene administration. His repeat labs showed normalized CO_2 and elevated but stable white blood cell count and creatine kinase. At this point the providers and hotline consultant deemed malignant hyperthermia to be unlikely. With sepsis being a probability, blood cultures were drawn. The patient continued to remain clinically and hemodynamically stable, and was subsequently extubated and transferred to intensive care unit for further management. In the unit as his elevated temperature, white blood cell count and creatine kinase improved, he was eventually managed for urosepsis with antibiotics sensitive for *Escherichia coli* that grew in his blood cultures. He improved and ultimately got discharged home without any significant sequelae.

Discussion

Transrectal ultrasound-guided biopsy, a gold standard technique used to diagnose prostate cancer, has an increased risk for developing bacteremia and sepsis.[3] Sepsis ultimately results from a complex interaction of pro-inflammatory, anti-inflammatory, activated complement system and coagulation mediators triggering a host systemic response. Malignant hyperthermia being one such condition that can trigger a systemic response, its early manifestations can be variable and can become indistinguishable from sepsis and many other disorders. Malignant hyperthermia is a diagnosis of exclusion. Determination of susceptibility to malignant hyperthermia requires muscle biopsy and in vitro contracture tests, however prompt initiation of therapy becomes crucial.[4] In the above reported case malignant hyperthermia was suspected firsthand because of the clinical presentation of hyperthermia, muscle rigidity, hypertension, tachypnea, and tachycardia after receiving volatile anesthetic. While muscle rigidity may be an early sign, marked increase in temperature along with increase in carbon monoxide production and oxygen consumption have been useful in early recognition. Other differential diagnoses such as muscular disorders, thyrotoxicosis, pheochromocytoma, withdrawal and overdose from drug abuse, serotonin and neuroleptic malignant syndrome were ruled out from unremarkable preoperative history and evaluation. Normothermia and normotension throughout the procedure and in the immediate postoperative period implied iatrogenic causes for elevated temperature and blood pressure were unlikely. Tachypnea and tachycardia from pain or anxiety was excluded. While sepsis rapidly progresses to secondary injuries, malignant hyperthermia progresses rapidly to become life threatening. Early suspicion and treatment initiation to normalize the metabolic state becomes imperative in such scenarios, which was the thought process behind initiation of malignant hyperthermia protocol.

The cornerstone for any effective critical management is soliciting help and rapid initiation of therapy as executed in this case. Dantrolene is a skeletal muscle relaxant that directly blocks intracellular calcium from being released in the sarcoplasmic reticulum. While dantrolene should be administered early in a malignant hyperthermia episode to be effective, it also has non-specific antipyretic activity that makes it useful during hyperthermia treatment without a definitive diagnosis. Malignant hyperthermia association hotline is a 24-h service to help guide diagnosis and treatment for difficult clinical scenarios where malignant hyperthermia is suspected. While a call to the malignant hyperthermia hotline is not an absolute requirement, it is advisable to do so early in the treatment process. Given its high lethal nature if not treated promptly, patients

can universally benefit from early recognition. As malignant hyperthermia is a rare condition, many anesthesia providers may experience hesitation and discomfort when confronted by it. These scenarios are further compounded when providers are without immediate assistance from colleagues. The malignant hyperthermia hotline tends to receive the most call volume in surgery centers or during off hours.[5] Since its inception, the hotline has proven itself to be a useful resource to aid clinicians during times requiring difficult clinical decisions.

It is clinically difficult to distinguish malignant hyperthermia and sepsis postoperatively. There is a paucity of evidence-based data to suggest appropriate management strategies. Providing ideal care requires good clinical judgment and a high level of suspicion where timely and appropriate care such as early administration of dantrolene and consultation of malignant hyperthermia association hotline for added assistance can influence positive outcomes. Although this case fortunately turned out not to be a malignant hyperthermia for the patient, the thought process helped to rule out one of the grave complications encountered in perioperative period secondary to anesthesia and streamline the management course appropriately.

Conflicts of interest

The authors declare no conflicts of interest.

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