Endovascular cooling for neuroleptic malignant syndrome; a case report

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Abstract - We report the case of a patient admitted to our hospital with neuroleptic malignant syndrome with hyperthermia, rhabdomyolysis, loss of consciousness and muscle rigidity after treatment with haloperidol. Dantrolene was immediately administered intravenously. Following sedation and mechanical ventilation, endovascular cooling was applied to normalize body temperature rapidly. The condition of the patient improved after normalization of body temperature. This is the first case in the Netherlands for which the use of endovascular cooling in a patient with neuroleptic malignant syndrome is described.

Keywords - endovascular cooling, neuroleptic malignant syndrome, hyperthermia, Coolgard

Introduction

Neuroleptic malignant syndrome (NMS) is an uncommon, but severe complication that can occur during the administration of neuroleptics, antidepressants and medications for the treatment of Parkinson’s disease. The diagnostic criteria are the sudden appearance of hyperthermia, muscle rigidity, autonomic dysfunction, altered consciousness and increases in liver enzymes, leucocytes and creatinine kinase [1]. The incidence of this condition in people treated with neuroleptics is estimated to be 0.9% [2].

An important therapeutic goal in the management of NMS is to control the hyperthermia, since the duration and peak of hyperthermia may be related to morbidity and even mortality [3].

We report a case where endovascular cooling was applied successfully in order to rapidly control hyperthermia in a patient who presented with NMS after haloperidol had been administered to treat a gamma hydroxy butyrate-withdrawal induced psychosis.

Case report

A 27 year-old man with a history of chronic gamma hydroxy butyrate (GHB) abuse (45 gram/day) had reduced his usage by 2.5g/week to 30g/day voluntarily in an attempt to reduce his dependency on this drug.

Five days before admission, he acutely refrained from taking GHB and became agitated and anxious with psychotic symptoms thereafter. His general practitioner, prescribed haloperidol 5 mg twice a day. Unfortunately, his psychotic symptoms increased giving him extreme hallucinations, paranoia and progressive confusion. Because of the severity of his symptoms he was obliged to be admitted to a psychiatric hospital. Again he was treated with haloperidol 5 mg which was combined with diazepam 10 mg and administered intramuscularly. Later, on the same night, another dose of diazepam was administered because of a relapse of anxiety. In the early morning, he was found in a restless state with altered consciousness, was sweating profusely and unable to communicate, for which he was referred to our hospital.

At presentation in our emergency department, he was restless, with a Glasgow Coma Scale (GCS) of 9 (E3M5V1), and hyperventilation. Physical examination revealed hyperthermia with a body temperature of 40.4 °C, a heart rate of 160 beats per minute, a respiratory rate of 32 per minute and a blood pressure of 125/75 mmHg. He showed severe rigidity of all extremities, without hyperreflexia.

There were no signs of meningism, no tongue bite or urine incontinence. The electrocardiogram showed a sinusoidal tachycardia with a QTc duration of 400 ms. Chest X-ray was normal. Laboratory investigations showed normal electrolyte values, creatine kinase 7285 IU/l , ASAT 81 IU/l, LDH 1186 IU/l, creatinine 384 µmol/l , blood urea nitrogen 23.7 mmol/l , C-reactive protein 5 mg/dl and a leukocyte count of 37*10⁹/l. The toxicology screen in blood and urine for alcohol, cocaine, opiates, ecstasy and amphetamines was negative. There were no signs of infection on admission and all blood cultures remained sterile.

Although a neurologist was consulted, because of the altered level of consciousness, no lumbar puncture or EEG was performed or thought necessary.

The diagnosis of neuroleptic malignant syndrome was presumed and based both on the clinical picture that concurred with the predefined diagnostic criteria and the certainty of the patient’s prior exposure to haloperidol. The patient was treated with intravenous fluids and 60 mg of dantrolene. After the administration of dantrolene, muscle rigidity resolved for about half an hour and his temperature dropped to 39.4 °C. Hereafter, muscle rigidity returned and was accompanied by an increase in body temperature to 40.4 °C, despite the use of a cooling mattress.

To improve the treatment, the decision was made to sedate and intubate the patient in order to facilitate endovascular cooling and to preserve the airway. Acetaminophen was not administered.
In the literature the use of dantrolene, bromocriptine and central thermoregulation. The peripheral effect within the skeletal action. The central dopaminergic effect is derived from the fact syndrome include both central and peripheral mechanisms of Theories of the pathophysiology of neuroleptic malignant syndrome are associated with the use of antipsychotic drugs, antidepressants and medications for the treatment of Parkinson’s disease. As our patient presented with all the necessary diagnostic criteria for this syndrome, the diagnosis of NMS seemed most likely. GHB-withdrawal syndrome was considered as well, because an identical constellation of symptoms has been reported in association with acute cessation of GHB after prolonged use.

Although GHB withdrawal is typically characterized by anxiety, insomnia and tremors, in some cases it may indeed be associated with extra ocular motor impairment, profound disorientation, increasing paranoia with hallucinations, tachycardia, seizures and elevated blood pressure. However, profound hyperthermia as seen in our patient was not reported in these cases [4]. Furthermore, rhabdomyolysis is described in only 7% of cases [5].

Theories of the pathophysiology of neuroleptic malignant syndrome include both central and peripheral mechanisms of action. The central dopaminergic effect is derived from the fact that neuroleptics, through dopamine depletion or blockade, upset central thermoregulation. The peripheral effect within the skeletal muscles is cause of the rigidity and excessive heat production.

In the literature the use of dantrolene, bromocriptine and amantidine has been described to resolve muscle rigidity and heat production in cases of NMS. We chose the option of using dantrolene because it was directly available in our hospital and we had more experience with dantrolene compared to bromocriptine and amantidine in this setting.

Dantrolene is a peripheral muscle relaxant that inhibits intracellular calcium release from the sarcoplasmatic reticulum. Initially, it was used to treat malignant hyperthermia and subsequently also to treat NMS in the early 1980s [6]. Dantrolene is now specifically recommended for more severe cases with extreme body temperatures, rigidity and hypermetabolism [7,8].

In the case described here, the administration of dantrolene resulted in a temporary resolution of muscle rigidity and unfortunately a drop of only 1 °C in central core temperature.

The most urgent therapeutic issue in NMS is the immediate withdrawal of neuroleptic medication and rapid reversal of hyperthermia as the duration and peak of hyperthermia may be related to morbidity and mortality [3,9].

Different approaches to lowering body temperature, such as with ice packs and wet (alcohol) blankets were considered for this patient. However, these methods were not used in the end because they are known to be often ineffective [10]. This last argument also applied to antipyretic agents like acetaminophen and aspirin since the underlying mechanism of heat generation does not involve a change in the hypothalamic set-point [11].

We decided to try endovascular cooling because it has been shown to be effective, fast and easy for controlling and maintaining a set temperature [12]. For this purpose, we used the Coolgard heat-exchange catheter, which uses two intravascular balloons at the distal end filled with cold saline. These balloons are connected to a closed loop system. Cooled saline is circulating inside this loop system from an external temperature control unit into the catheter and back to the control unit. The patient is cooled as venous blood passes over each balloon, which enables the exchange of heat. The Coolgard does require an invasive procedure, but many intensive care patients need a central venous catheter anyway and the Coolgard catheter provides two side ports apart from the cooling side ports.

We cooled the patient by 1 °C /hr as this rate of decreasing temperature has been proven safe with little or no side effects [12]. This is in contrast to external cooling systems which decrease temperature only at a rate of 0.3-0.5 degree/°C /hr [13]. After 6 hours of treatment, the patient reached normal body temperature, with subsequently rapid decline of his blood CK levels. Endovascular cooling was discontinued after 24 hours. The increase in temperature after cessation of endovascular cooling was not accompanied by a new rise in CK or other manifestations of NMS. Moreover, the rise in CRP, accompanied by an evident new infarct in the right lower lobe on the chest radiogram, together with purulent sputum positive for S. Aureus, made the diagnosis of aspiration pneumonia or pneumonia more likely than rebound hyperthermia after cessation of cooling. The pneumonia was presumed to be caused by aspiration, as the patient had probably been comatose for several hours before admission to the hospital.

We maintained the target level for 24 hours. The safety and
efficacy of the Alsius Cooling system has been described over a period of 36 hours. However, we chose to maintain the target level for 24 hours only since the complication rate is very low when the catheter is left in place for a short period of time (≤24h) [12]. One small retrospective study showed circa 50% asymptomatic catheter thrombosis with an indwelling catheter time of 5 days [14]; however, this is similar to what has been observed in studies with ‘regular’ intravascular catheters [15].

Diedler et al. recently reported a patient with NMS in which endovascular cooling had been used after failure of conventional treatment to reach controlled normothermia [16]. In our case, we also did a short trial using a cooling mattress, but finally decided that endovascular cooling might be a more effective treatment method.

Controlled normothermia is closely related to controlled hypothermia. Maintaining normothermia is easier and associated with fewer side effects. Suppression of immune function does not occur; however, shivering may be more pronounced. This is thought to be caused by intact counter-regulatory mechanisms working at maximum efficiency in the normal temperature range [17]. Our patient showed signs of shivering, but was treated effectively with opioids.

Patients undergoing mild hypothermia are more susceptible to respiratory infections due to suppressed inflammatory response, however, this is more frequent in patients treated for longer than 24 hours [18,19]. Endovascular cooling was highly effective for controlling body temperature in this patient with neuroleptic malignant syndrome. Since the option of endovascular cooling is available in many hospitals nowadays, it should be considered without reservations when conventional methods have been applied unsuccessfully.

Conclusion
As far as we know, this is the first case in the Netherlands in which endovascular cooling has been applied successfully to reverse hyperthermia in a patient with neuroleptic malignant syndrome. This syndrome is a life-threatening complication of neuroleptic medication. As the duration and peak of hyperthermia may be related to morbidity and mortality, it is of the utmost importance to lower the body temperature fast and safely. Endovascular cooling is proven to be well tolerated, fast, effective, and safe in the management of hyperthermia. Nowadays, it is available in many hospitals and it should be considered in every patient when conventional measures fail or are contra-indicated. As the prevalence of neuroleptic malignant syndrome is very low, studies evaluating the efficacy of endovascular cooling and its influence on prognosis do not seem very feasible.

References

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