Short communication

Endovascular cooling in a patient with neuroleptic malignant syndrome

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Abstract

We report a case of severe neuroleptic malignant syndrome with hyperthermia, rhabdomyolysis and hepatic failure where we applied endovascular cooling in order to reverse hyperthermia. After rapid normalization of core temperature at 37.5 °C, the patient’s condition improved and CK levels dropped. However, upon withdrawal of endovascular temperature control there was a relapse. This is the first case where endovascular cooling was applied successfully in neuroleptic malignant syndrome.
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1. Introduction

Neuroleptic malignant syndrome (NMS) is a rare but potentially life-threatening condition. A crucial therapeutic issue is to control hyperthermia [1]. However, standard approaches including antipyretic medication such as paracetamol or metamizole or external cooling are frequently ineffective [2]. We report a case of NMS where endovascular cooling was successfully applied in order to control hyperthermia.

2. Case report

A 59 year old woman was admitted to an outside hospital after attempted suicide with 7.5 g of promethazine. Initially, she was confused but not febrile and there was no muscular rigidity. Intermittent choreatiform movements were observed. Except for detoxification with enteral carbon, no therapy was administered. Since the patient had a psychiatric history with a known severe depression she was transferred to a psychiatric hospital, where she received 20 mg of i.v. haloperidol because of a ‘delirious state’. Soon after receiving haloperidol, the patient started shivering and hyperventilating, became comatose and developed muscular rigidity. After injection of 10 mg of diazepam for suspected status epilepticus, she was transferred to our neurocritical care unit. Upon admission, her core temperature was 40.4 °C (bladder temperature), she was comatose and had to be rapidly intubated and mechanically ventilated because of acute respiratory insufficiency. A cerebral CT scan as well as analysis of cerebrospinal fluid was normal. EEG intermittently showed generalized slowing, but no epileptic activity. The diagnosis of neuroleptic malignant syndrome was based on preceding exposure to promethazine and haloperidol, hyperthermia and severe rhabdomyolysis with substantially elevated serum creatinine kinase (CK) levels (CK on admission 3515 U/l, CK max 17433 U/l) and myoglobinuria (on admission 17450 ug/l). Other laboratory findings on admission included elevated transaminases (glutamic–oxaloacetic transaminase (GOT) 731 U/l, glutamic–pyruvic transaminase; GPT, partial thromboplastin time; INR, international normalized ratio; AT III, antithrombin III; NSAID, non-steroidal anti-inflammatory drugs.

Abbreviations: NMS, neuroleptic malignant syndrome; CT, computed tomography; EEG, electroencephalogram; CK, creatinine kinase; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvic transaminase; PTT, partial thromboplastin time; INR, international normalized ratio; AT III, antithrombin III; NSAID, non-steroidal anti-inflammatory drugs.

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of an infectious focus, the chest X-ray was normal, liquor and blood cultures remained sterile.

Intravenous metamizole (1× 1000 mg) and physical external cooling with cooling blankets did not lower temperature. Paracetamol was not administered because of potential hepatotoxicity. Instead an endovascular heat-exchange catheter (CoolLine®) was placed into the right femoral vein and connected to the ALSIUS® CoolGard® system. Endovascular cooling was initialized 4.5 h after arrival at our hospital. The temperature was gradually lowered to 37.7 °C (bladder temperature) over 5.5 h and then held around the target temperature of 37.5 °C. Additionally, dantrolene (40 mg q 6 h) and amantadine (100 mg q 12 h) were administered. Further treatment included high-dose catecholamine infusion due to cardio-circulatory insufficiency, forced diuresis and antibiotic therapy with tazobactam and clindamycin for suspected aspiration during emergency intubation.

Despite massively elevated serum CK levels as high as 17344 U/l and myoglobinuria of 17,450 μg/l our patient did not develop acute renal failure (highest creatinine level 0.61 mg/dl). Instead, elevated transaminases indicated hepatic failure (GOT max 13675 U/l, GPT max 3655 U/l). Furthermore, thrombocytes fell to 53/nl and had to be substituted. PTT and INR spontaneously rose and ATIII fell to 36% either as sign of hepatic failure or disseminated intravascular coagulation. Hepatic ultrasound showed diffuse parenchymal hyperechoic signals as seen in chronic alcohol abuse. Elevation of transaminases is a common finding in neuroleptic malignant syndrome, however differential diagnosis of severe hepatic failure in this case included toxic side effects of dantrolene superimposed on a previously ethyltoxic injured liver [3].

The CoolLine® catheter was removed 158 h after placement. Interestingly, in the days following removal of the CoolGard® system the patient’s body temperature climbed again up to maximum 39 °C which was accompanied by rising CK levels (see Fig. 1). During the entire episode of endovascular cooling our patient remained sedated and mechanically ventilated. Shivering, a frequent side effect of endovascular cooling, was not observed. The patient’s general condition stabilized over the next two weeks and liver function recovered. Due to prolonged weaning, she underwent tracheotomy. After 21 days she was transferred to a rehabilitation clinic. At that time, she was awake, followed simple verbal commands and showed no serious sensory-motor deficits.

Upon follow-up three months later, the patient had no remaining deficits.

3. Discussion

The most urgent therapeutic issue in neuroleptic malignant syndrome, after immediate withdrawal of neuroleptic medication, is reversal of hyperthermia [4]. Commonly accepted treatments include external physical cooling (e.g. cooling blankets or ice-packs) and intravenous application of non-steroidal anti-inflammatory drugs (NSAIDs). Some hospitals perform gastric lavage with cool fluids [5].

Additional general pharmaceutical approaches include dantrolene for muscle relaxation and dopaminergic drugs which are aimed at antagonizing the effect of neuroleptic drugs at dopaminerg receptors. Dopamine antagonism of neuroleptics is the suspected mechanism for induction of central thermodyregulation.

In our case, NSAIDs and physical cooling were not successful and both, paracetamol and dantrolene, were relatively contraindicated because of their potential hepatotoxic side effects [3]. Therefore we placed an endovascular heat-exchange catheter (CoolLine®) in the right femoral vein and started endovascular cooling with the ALSIUS CoolGard® system. The CoolLine® heat-exchange catheter has two balloons at the distal end which are connected to a closed loop system. Inside the loop system cooled saline is circulating from the external temperature control unit into the catheter and back to the control unit. Cooling rates can be chosen between maximum power and controlled rate (from 0.05 °C/h to 0.65 °C/h). Compared to standard methods,
Endovascular cooling is relatively invasive since it requires placement of a central line. However, most intensive care patients will need a central venous catheter and the CoolLine® catheter provides a triple lumen central line. In addition to being highly effective, the main advantages of the CoolGard® system compared to standard treatments are that cooling rates can easily be controlled and temperature can be held stable at the desired level for several days.

In our patient, the system proved to be highly effective in lowering and controlling body temperature (Fig. 1). Bladder temperature fell from 40.4 °C to 37.7 °C 5.5 h after initialization. Temperature was held stable around 37.5 °C until day 6. At that time we had to remove the cooling device since it was needed for another patient. Remarkably, therapeutically induced normothermia preceded partial remission of rhabdomyolysis parameters, and secondary worsening of rhabdomyolysis was observed when endovascular cooling was terminated prematurely (Fig. 1).

Until now endovascular cooling has been performed in patients undergoing therapeutic moderate hypothermia in acute stroke or after cardiopulmonary resuscitation [6–10]. There have also been single case reports of the successful application of endovascular cooling in patients suffering from heat stroke [11]. To our knowledge, controlled endovascular cooling has not been previously studied in NMS.

Our experience suggests that it is an effective option to lower body temperature and reduce rhabdomyolysis.

4. Conclusions

Severe hyperthermia in NMS is a life-threatening complication of neuroleptic medication. In our case, endovascular cooling was a comfortable, safe and effective option to cope with hyperthermia. This technique should be considered in severe cases of NMS when conventional treatment of hyperthermia fails. Further studies are warranted to evaluate efficacy and influence on prognosis of endovascular cooling in NMS.

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References