Case Report

Exceptional Case of Hypothermia Induced Pancytopenia

Tariq Khurram1*, Farhangi Arezo2 and Rana Fauzia1
1Department of Internal Medicine, University of Florida, USA
2Department of Internal Medicine, Semnan University of Medical Sciences, Iran

Abstract

Therapeutic hypothermia is a commonly employed and a well-established treatment modality and has proven neuroprotective benefits in patients who have suffered from cardiac arrest following ventricular fibrillation. It can lead to various physiologic changes ranging from metabolic and electrolyte derangements to the ones seen on electrocardiogram. We report the case of a middle aged Caucasian male who was admitted to the Coronary Care Unit after suffering from a cardiac arrest from Ventricular Tachycardia while exercising at a local clubhouse. CPR was initiated by a bystander right away. Upon arrival to the hospital the hypothermia protocol was initiated and his body temperature was lowered to 33 degrees Celsius for a period of 24 hours. What makes our case unique is that there was a transient drop in all cell lines following the initiation of hypothermia, reaching the nadir point on day 5. A few days after the hypothermia protocol was lifted and the patient’s natural body temperature was restored, the pancytopenia began to improve and greatly resolved by the time he was discharged on day 8.

To our knowledge there have only been only a handful of cases describing the onset of pancytopenia from chronic exposure to hypothermia in the elderly, malnourished population or from thermoregulatory dysfunction after resection of craniopharyngioma. Our case is therefore a unique presentation that has not been previously reported in the literature. He was a middle aged male who acutely developed reversible pancytopenia from a short-term induction of therapeutic hypothermia. Unlike the other reported cases, our patient did not belong to the extremes of age, was neither malnourished nor had any history of surgeries for craniopharyngiomas, received therapeutic hypothermia for a very short duration of time and did not have any other etiological basis to explain the onset of transient hypothermia. This case emphasizes the need for keeping pancytopenia as a potential adverse effect of short term, mild therapeutic hypothermia.

INTRODUCTION

Therapeutic hypothermia refers to the lowering of body temperature to reduce the impact of ischemia induced tissue injury and has practical applications in modern medicine [1-3]. The use of therapeutic hypothermia is not new and successful use of medical hypothermia has been carried out since the 1950s for the treatment of patients with cardiac arrests [1-3]. Subsequent research conducted over the years on both animal and human subjects has established therapeutic hypothermia as the standard of care in cardiac arrest patients [4-9]. While therapeutic hypothermia has been associated with various adverse effects, pancytopenia is generally not seen as the consequence of this treatment modality. We present the unique and intriguing case of a middle age man who suffered an out-of-hospital cardiac arrest and developed reversible pancytopenia after being treated with therapeutic hypothermia (Figure 1-3).

CASE PRESENTATION

We present the case of a 63 year old male with past medical history of coronary artery disease, Hypertension, Diabetes Mellitus and Hyperlipidemia who was exercising at his local clubhouse when he collapsed. Cardiopulmonary resuscitation was initiated by a bystander without any delay and the EMS help was called. In the emergency department the patient was diagnosed to have suffered the cardiac arrest secondary to ventricular fibrillation and after the initial cardiac resuscitative efforts per the ACLS protocols, he had a return of spontaneous circulation. Patient was subsequently intubated and ventilated for appropriate cardiopulmonary support and was transferred...
to the Coronary Care Unit (CCU) and he was immediately placed under medically induced hypothermia at 33 degree Celsius for twenty four hours. Initial labs revealed elevated cardiac enzymes with ST elevation in the inferior leads on electrocardiogram. Patient’s Hemoglobin, white blood cell and platelet counts were 14.2, 15.4 and 211 respectively. Chest X-ray showed opacities which were empirically treatment for suspected pneumonia.

After a total of twenty four hours the patient was slowly re-warmed back to room temperature. Frequent complete blood count panels (CBC) were drawn throughout his admission and soon it became evident that patient’s multiple blood lines were in a state of continuous decline compared to their values on admission. His hemoglobin, hematocrit, white blood cell and platelet counts continued to decrease and reached their nadir at 7.9, 5.9 and 96 respectively on the fifth day. CBC panels after this point showed an impressive upward trend in all blood lines and the patient showed remarkable recovery on the day of discharge after eight days. On the day of his transfer to the rehabilitation facility, patient’s hemoglobin, white blood cell and platelet counts...
were noted to be 10.2, 8.4 and 247 respectively. Hematology and oncology service was consulted during this entire episode and after an extensive workup, it was concluded that the decrease in multiple blood cell lines was secondary to the medically induced hypothermia.

During his stay, a patient sputum culture was positive for Klebsiella pneumonia and Staph aureus and was treated accordingly with antibiotics. He did not receive any medications that would explain the transient drop in his cell lines. He was still on all the same medications, including antibiotics, when his cell counts began to improve. All other labs were unremarkable and it was concluded that the pneumonia alone would not have explained his transient drop in cell lines. While in the hospital, the patient underwent angiography which showed complete occlusion of the circumflex branch of the left coronary artery (OM4), not amenable to surgery and received an implantable cardioverter defibrillator (ICD) to prevent any future episodes of ventricular fibrillation (V-Fib) arrests (table 1).

**DISCUSSION**

Therapeutic hypothermia refers to the lowering of body temperature to reduce the impact of ischemia induced tissue injury and has practical applications in modern medicine. The first successful use of medical hypothermia after cardiac arrests was conducted in 1950s [1-3]. Over the years the use of therapeutic hypothermia in cardiac arrests has further been validated not only in animal models, including dogs, [4-7] but also in two ground breaking human studies published in the New England Journal of Medicine. The first of these studies, Return of spontaneous circulation (ROSC) showed favorable results in over 55% of patients resuscitated after a cardiac arrest who were then cooled to a body temperature of between 32-34 degree Celsius over a 24 hour window [8]. A second study from Australia also looked into the use of hypothermia in comatose patients in out-of-hospital survivors of cardiac arrests and showed favorable outcomes in about half the patients compared with only 26% of the patient’s who did not receive management with medically induced hypothermia [9].

Several mechanisms have been proposed to explain the beneficial effects of hypothermia. Traditional understanding postulates the decrease in metabolism causing a protective affect on the ischemic tissue [10] with studies confirming a decrease in cellular metabolism by as much as 7% with a one degree Celsius drop in body temperature [11]. Traditionally, only the moderate to severe drop in temperature was assumed to cause the beneficial effects mentioned above and it was thought that the beneficial effects of the hypothermia protocol directly correlated with the level of this temperature drop [12]. However, this notion has been challenged by more recently published data which has shown that even mild hypothermia can lead to a significant improvement in morbidity [8-9]. Researchers now believe that hypothermia also improves cellular membrane stability, reduces apoptosis and markedly decreases the oxidative stress following reperfusion [13].

Several cooling mechanisms have been used over the years. These include the use of non-invasive techniques such as cooling blankets, vests and even helmets. These methods are fairly simple but are slow in reducing the body temperature which may hamper rapid implementation of the hypothermia protocols [14]. Invasive methods include the use of cooled normal saline into the femoral vein which has proven to be more efficient, rapid and precise compared to the less invasive methods mentioned earlier [15-19]. Data collected from studies has also shown favorable results with crystalloid solution chilled at 4 degree Celsius and infused at 30ml/kg over 30 minutes [20]. Besides hypothermia induction through the femoral vein, peritoneal and pleural lavage can also be performed but is rarely done in the clinical setting [21].

The use of invasive hypothermia techniques is more efficient and reliable however it involves the insertion of catheters bigger vessels and predisposes the patients to certain adverse affects including bleeding, formation of deep vein thrombosis and infections [22] which is especially true of the resuscitated patients who are particularly vulnerable to systemic infections and their complications [23]. Hypothermia also predisposes to cardiac arrhythmias, sepsis, coagulopathies, electrolyte and metabolic disturbances [24, 25]. Data pooled from various studies has shown that the risk of bleeding increases if coronary artery disease is present at the same time [26-29]. This may be due to the concomitant use of invasive catheters for induction of hypothermia protocol with dual antiplatelet therapy following the angiography in these patients. Coagulopathy is also caused by the dampening of the coagulation cascades by cardiac arrest which is further aided by hypothermia associated inhibition of direct and indirect coagulation pathways [30-32].

These adverse affects mentioned above are all relevant to our patient who suffered from an acute MI along with V-Fib arrest. His electrocardiogram showed prolonged QTc interval along with profound bradycardia and Osborn waves during the time he was cooled under the hypothermia protocol. Our patient presented with opacities on chest XR and was empirically treated with antibiotics. Sputum cultures later revealed the presence of Klebsiella pneumoniae and methacilline -sensitive Staphylococcus Aureus. Patient had been an avid smoker for years and the onset of productive cough over the week before the event suggested that the pneumonia predated cardiac arrest. This patient arrived with normal to elevated cell lines and it

| Table 1: Trends in cell lines following hypothermia protocol (HP) and the eventual recovery on discharge. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Hypothermia Protocol (HP)** | **Day3** | **Day4** | **Day 5 Nadir** | **Discharge Day 8** |
| **Platelets** | 217 | 159 | 120 | 114 | 96 | 247 |
| **Hemoglobin** | 13 | 11.8 | 9.4 | 8.3 | 7.9 | 8.4 |
| **Hematocrit** | 34.7 | 27 | 25 | 23.9 | 23.3 | 24.7 |
| **White Blood Cells** | 16.4 | 12.8 | 11.7 | 9.6 | 5.9 | 10.2 |
was only after his core temperature was lowered from the hypothermia protocol that his cell lines began to drop, reaching their nadir on day 5. Patient was treated with empiric antibiotics and one could assume that the onset of hypothermia could have been medication induced. While this argument is plausible, the improvement in cell lines occurred while the patient was still on the same regimen of hospital antibiotics and home medications. At no point during his admission was the patient septic. A review of his labs was also unremarkable for potential viral etiologies including mononucleosis, HIV etc. Serum analyses for other causes including the evaluation of peripheral blood smear, antibody testing for Heparin induced thrombocytopenia, hemolytic anemia panel, hepatitis panel, iron panel, Vitamin panel, was all investigated and were successfully ruled out as a possible explanation for the transient pancytopenia. A CT scan of the abdomen was pursued and showed no evidence of retroperitoneal bleed from femoral vein catheter used for the hypothermia protocol or from splenic sequestration. Stool samples were also unremarkable for occult bleed. As a diagnosis of exclusion, medical hypothermia was concluded to have lead to the transient onset of pancytopenia.

Not many cases of pancytopenia from hypothermia have been reported in the literature. To our knowledge there have only been only a handful of cases describing the onset of pancytopenia from chronic hypothermia in an eight year old girl from thermoregulatory dysfunction after resection of craniopharyngioma to two malnourished elderly patients who also had hypoglycemia and thyroid derangements which could explain the pancytopenia [33-34]. Our case is therefore a unique presentation that has not been previously reported to our knowledge. Patient was a middle aged male who acutely developed reversible pancytopenia from a short-term induction of therapeutic hypothermia. Unlike the other reported cases, our patient did not belong to the extremes of age, was neither malnourished nor had any history of craniopharyngiomas leading to surgeries, received therapeutic hypothermia for a very short duration of time and did not have any other etiologies to explain the onset of transient hypothermia.

CONCLUSION

Therapeutic hypothermia is a well established treatment modality and has proven neuroprotective benefits especially in patients who have suffered from cardiac arrest following ventricular fibrillation. It can lead to various complications as previously discussed. Our patient represents a very unique case modality and has proven neuroprotective benefits especially in patients who have suffered from cardiac arrest following ventricular fibrillation. It can lead to various complications as previously discussed. Our patient represents a very unique case.

REFERENCES


