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and

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Alcor A-1408 Case Report Contents:

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1. Overview

The cryopreservation of A-1408 is a prime example of the importance of having more than one response team, capable of covering multiple members simultaneously.

Two separate standbys were provided for member A-1408, who lived just north of the Tampa, FL area. Alcor team members initiated a standby at the hospital for three days during the time the individual was listed as critical and medical providers anticipated that he might stop breathing. The member stabilized and Alcor ended the standby while continuing to monitor the patient’s condition remotely. When his medical condition deteriorated again, Alcor was on the verge of initiating a standby for a different member and therefore decided to request Suspended Animation (SA) perform the second standby.

On the afternoon of the fourth day of the standby conducted by SA (May 26, 2011), the member was pronounced, stabilized and cooled on-site, followed by a field washout. The transport commenced the next morning by commercial airlines and the patient was brought to Alcor with the surgical team at the ready. After the neuro cryopreservation ensued, member A-1408 became Alcor’s 105th patient.

2. Personnel

Standby, stabilization and transport: Catherine Baldwin, Standby Team Leader, Suspended Animation, Inc; and trained response team members hired by Suspended Animation. Direction and oversight was provided by Max More, Ph.D., CEO; Steve Harris, M.D., Chief Medical Advisor; and Aaron Drake, NREMT-P, NAEMSE, Medical Response Director.

Surgery and cryoprotectant perfusion: Dr. Nancy McEachern, Surgeon: Aaron Drake, Surgical Assistant; Hugh Hixon, Cryoprotection Perfusionist; Steve Graber, Assistant Cryoprotection Perfusionist; Bonnie Magee, Scribe; Richard Cremeens, Refractometry; R. Michael Perry, Ph.D., Cooldown Coordinator; Jerry Searcy, surgical support; Catherine Baldwin and Max More, observers.

3. Background

On May 8th of 2011, Alcor received an emergency call regarding a 77 year old member in Florida who was in the intensive care unit of a hospital, suffering from respiratory distress. The individual spent three days on the ventilator before he was weaned off and placed on BiPap.
He had developed pneumonia and his blood pressure remained in the high 200’s, making him a very high risk for stroke.

Respiratory problems were fairly common for this individual, as Alcor had received occasional health updates over the past year, but on this occasion it had been much worse. Currently, the individual was admitted due to acute respiratory failure and severe hypertension coupled with an extensive medical history that included COPD, pneumonia, dementia, coronary artery bypass grafts and liver and kidney aneurysms.

Aaron Drake, Alcor’s Medical Response Director, spoke with the hospital’s medical providers regarding the patient’s post-mortem directives and queried if they would be willing to assist if he died while in their care. They agreed to administer the medications listed in Alcor’s abbreviated protocol, pack the patient on ice and call the morgue for immediate pickup. The patient’s Internist even wrote orders into the chart to help ensure this request would be taken seriously. The medical staff was very helpful in providing updates on the patient and for a while it appeared that he was improving.

The deployment committee continued to evaluate the situation for a few days in anticipation that a deployment might be necessary at some point. Although the patient was on BiPap for his respiratory problems, he began to struggle too much and the pulmonologist decided to intubate and place him back on the ventilator. Given this turn of events, and due to some intra-family dissention on supporting the cryonics directives, the deployment committee decided it would be better to have an Alcor representative on site to oversee the developments.

Alcor had begun to occasionally use SA for deployments, especially for members who were geographically closer to SA in Florida, as was the case for this individual. Unfortunately, SA was in the final preparations for a major conference they were hosting in Florida in a few days. Therefore, on May, 16th, Aaron and Richard Cremeens, flew from Arizona to Tampa with a response kit and drove to the hospital where the patient was admitted. Over the next three days, interaction and planning occurred among Alcor, the hospital, medical providers, the patient and his family members. It became evident that although the patient was improving enough to end the standby, he would eventually succumb to his respiratory problems and at-home hospice care was the best solution. The deployment committee had Aaron and Richard return to Scottsdale.

Only a week had passed when Alcor received a call very early in the morning on May 23rd. The hospice nurse at the patient’s home expressed fear that his health had declined to the point where he could pass away that same day. She seemed so convinced of the possibility, and since we did not have the ability to see the patient in person, we had to take her word for it and deploy a team, despite the fact that the vitals she reported were not considered serious. Coincidentally, Alcor had just been notified the prior evening of a serious problem with another member in the Phoenix
area that required careful monitoring in anticipation of a standby. The deployment committee decided to send SA rather than an Alcor team, despite that SA had just wrapped up their conference the previous evening. This proved to be a fortuitous decision as Alcor was notified of a third potential standby in the Knoxville TN area later the same day.

4. Deployment & Standby

Alcor CEO, Max More, contacted Catherine Baldwin and requested a response. SA deployed seven team members within the next hour. Four members flew on the first available flight to Tampa with a full stabilization kit while a fifth drove the SA mobile operating vehicle from Boynton Beach, Florida to Tampa. A SA surgeon and perfusionist happened to be a short drive from Tampa and responded to the patient’s location by car. Two Alcor members in the Tampa/St. Petersburg area also responded to SA’s call for volunteers.

Upon arrival, SA found the patient stable and sleeping in a hospital bed that had been set up in his tiny living room where half a dozen family members and pets surrounded him.

In the event of sudden death, although not ideal, the family was amenable to having SA perform stabilization procedures in the living room since the nearest funeral home was 20-30 minutes away and the SA vehicle would not arrive until near midnight that night. Because of the limited space, however, the SA team members set up ice chests and equipment in a small corner of the garage of the home.

A local funeral home indicated that they would be able to assist with paperwork, a transit permit and shipping at a moment’s notice. Two SA team members remained on site in vehicles overnight while the rest went to the nearest motel, a short drive away.

On May 24, the patient was awake and alert periodically throughout the day. His family began feeding him yogurt and water while he watched television. His vitals were steady at BP 110/80, pulse 100, respiration 15, urine 250 ml in the morning and his O2 saturation numbers were in the low 90’s using a 100% O2 through a non-rebreather mask.

SA positioned its vehicle at the rear of the patient’s house and cleared a narrow path from the patient’s bed to the rear door of the home.

On May 25, the patient continued to wake occasionally and his vitals remained steady, averaging BP 105/82, pulse 99, respiration 14, 850 ml urine output over 24hrs.

By May 26, the patient did not wake and his vitals were BP 90/70, pulse 102, respiration 15 and urine output 575 ml over 24 hours. His respiration grew more shallow over the afternoon and O2
saturation fell to the high 80’s while still on 100% oxygen through the non-rebreather mask. The hospice nurse pronounced him legally dead at 3:39pm ET.

5. Field Stabilization, Washout & Cephalic Isolation

Immediately after pronouncement, team members moved the ice bath into the living room and transferred the patient from his bed before rolling him out of the house into the SA vehicle.

Team members started the AutoPulse, placed temperature probes and packed the patient in ice with ice water recirculation.

The Combitube was inserted and the patient placed on the automated ventilator. At the same time, other members of the team pushed Propofol (200mg), Streptokinase (250,000IU), and Heparin (100,000IU) through the patient’s existing IV line. Once the intraosseous line was set, streptokinase (250,000units), aspirin (300mg), an initial dose of vasopressin (100units) and epinephrine (1mg) and S-methylthiourea (400mg) were given, followed by niacinimide (500mg), L-kynurenine (1.5g), ketorolac (7.5mg), gentamicin (80mg), and hetastarch. Intermittent doses of epinephrine (1mg/3min) continued while and additional dose of vasopressin (100units), Vital-Oxy (70ml), THAM (100ml) and mannitol (100g) were administered.

While the AutoPulse continued running and medications continued to be administered, the surgeon prepped the patient’s right groin for surgery by swabbing with ChloroPrep and draping the area with sterile surgical towels. An 8cm incision was made and rough dissection was used to clear tissue to expose the femoral vessels. The entire area was filled with scar tissue and the vessels visible had been stented. The left femorals were similar.

The patient’s nasopharyngeal temperature was 23.2º C.

The surgeon then exposed the external iliac vessels on the patient’s right side and cannulated these.

The AutoPulse was turned off for insertion of the arterial and venous cannulae. Venous drainage was observed as soon as the venous cannula was inserted. Both cannulae were primed before being connected to the perfusion circuit. The perfusion pump was started slowly and venous drainage continued.

The patient’s nasopharyngeal temperature was approximately 17º C. Some blood-tinged foam was noted in the patient’s Combitube.
After 15 minutes on open circuit perfusion with MHP2, the patient’s nasopharyngeal temperature had dropped to 14.6º C and venous drainage was fairly clear. Perfusion pressures during open circuit averaged 187 mmHg. Flow rates averaged 1.2 lpm. The remaining Vital-Oxy (~70mls) was added to the circuit and closed circuit perfusion continued until the patient’s nasopharyngeal temperature reached 3.5º C, a little over an hour and a half later. Perfusion pressures on closed circuit averaged 174 mmHg. Flow rates were kept near 1.0 lpm. No edema was noted in the extremities or abdomen.

With the perfusion pump still running, the surgeon prepped and draped the patient’s neck and isolated and ligated the left and right common carotids. A query was made to Alcor about preferences for additional vessel ligations. No additional vessels were requested. The pump was shut off. The Combitube was removed. A support was placed under the patient’s neck to elevate it while lowering the head. A surgical saw was used to create the lateral incision to the vertebral column and a surgical mallet and osteotome applied to sever the vertebrae between C5 and C6. The cephalon was immediately inverted and double bagged. A metal eye hook was screwed into the exposed vertebrae before the bags were sealed around the nasopharyngeal probe and the entire package packed in ice.

6. i-STAT Data

The blood sample data below was taken by SA approximately 40 minutes post pronouncement.

16:16pm ET, 26th, June 2011
i-STAT CG4+

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
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</tr>
<tr>
<td>PCO2 mmHg</td>
<td>&gt;130.0</td>
</tr>
<tr>
<td>PO2 mmHg</td>
<td>21.0</td>
</tr>
<tr>
<td>BEecf mmol/L</td>
<td>&lt;&gt;</td>
</tr>
<tr>
<td>HCO3 mmol/L</td>
<td>&lt;&gt;</td>
</tr>
<tr>
<td>TCO2 mmol/L</td>
<td>&lt;&gt;</td>
</tr>
<tr>
<td>sO2%</td>
<td>&lt;&gt;</td>
</tr>
<tr>
<td>Lac mmol/L</td>
<td>&lt;&gt;</td>
</tr>
</tbody>
</table>

<> indicates a value outside analytical range
7. Transportation

While surgery and perfusion were taking place, an SA team member and two local Alcor members assisted the son in filling out the death certificate and running the paperwork to and from the local funeral home to obtain a transit permit and arrange air transport.

Using the SA vehicle, the patient’s trunk was transported to the funeral home for cremation and return to the family. As there were no remaining flights for the evening, the patient’s cephalon remained with SA team members overnight near the Tampa airport. Three hours before the first flight the next morning, the patient’s cephalon was repacked in fresh ice, secured in an insulated custom shipper and delivered to the airline’s human remains cargo center.

After the direct flight, Alcor’s mortuary received the body from the airline cargo division and transported to Alcor, arriving at 10:11am PT, May 27th, 2011.

8. Cryoprotective Surgery & Perfusion Summary

Upon arrival, the cephalon was removed from the shipping container and it was placed on the surgical table. Aaron Drake aseptically prepped the head prior to Dr. McEachern making an incision for burr holes. Using an air driven craniotome and Codman perforator, Aaron created bilateral burr holes which were then cleaned with a Kerrison rongeur. Crackphone elements were placed in each of the burr holes between the skull and dura and secured with surgical staples. A nasopharyngeal thermocouple was also placed.

The exposed carotid arteries were cannulated with Robinson catheters that were primed with B1 base solution. These were secured in place with a basket-weave suture using 2-0 surgical silk. After flow was initiated, the vertebral arteries were identified and the flow was stopped with DeBakey Bulldog Clamps.

Cryoprotection went smoothly, and ended when the [CPA] of the venous effluent from both jugulars had exceeded the desired target concentration for over 30 minutes (equilibrium endpoint).

The skin was uniformly darkened at the endpoint; the eyeballs had retracted as well as the brain, which had retracted by 12 mm on the left hemisphere, and 15 mm on the right hemisphere. Brain retraction indicated that the blood-brain barrier was intact over the course of the perfusion, which had begun ~22 hours post-arrest. The pharyngeal temperature responded very slowly to perfusate temperature change.

SA's DuaLogR and "bullet" thermocouple had become disconnected somewhere en route, so we
were unable to analyze transport temperatures. The shipping container put together by SA was impressive and there was very little melted water in the ice bags.

Perfusion time near the terminal concentration was extended (3.25 hours) compared to normal procedure (2.25 hours), due to adjusting the new ramp to support Field Neuro Cryoprotection. This was ultimately found to be the result of a mixing error in making up the step ramp; the bags were filled by weight, but the values in the volume column were used instead of the values in the weight column, so the terminal concentration was below what it should have been. To counter this error, additional M22x1.25 concentrate was added to the mixing reservoir.

Step ramp procedure: A geometric step ramp of eight steps was calculated ([M22] 0 % --> 110% CNV) and 2-liter bags were filled with varying mixtures of B1 and M22x1.25. For each step, the pump was stopped and the next bag spiked. At bag #10, the circuit was closed and the mixing reservoir filled. Since, as noted above, the terminal concentration was made too low, additional M22x1.25 was added to the mixing reservoir to achieve the terminal concentration conditions of over 50.35 Brix from both jugulars for over 30 minutes.

Given the pump speed of about 100 ml/min for a perfusion pressure of about 100 mmHg, the system reached equilibrium in 3-4 bags of terminal concentration, for a total of 12 bags. Since Field Neuro Cryoprotection was originally estimated (with a generous margin) to require 16 2-liter bags, it looks like either the margin may be retained, or the number of bags reduced (for a total exposure time of ~2.5 hours), or the ramp extended with extra steps.

No cracking events were noted over the entire cool down. This was unexpected, and was investigated electronically without any conclusion, and then again by CT scan. Tests were attempted to see if the in situ crackphone elements had failed, but were unsuccessful, as the testing devices could not distinguish between the piezoelement and the capacitance of the twisted-pair wire leads. A capacitance meter, an external oscillator and a crystal oscillator incorporating the element were all used. Testing of all the available crackphone elements, including ones made at the same time as the in situ elements was done. All the elements passed the standard impact test for function, so the possibility that two specific elements had failed together was very unlikely.

Arrangements were made to have CT scans of the head done locally, in LN2. On 30 July, A1408 was taken to the CT facility, where the neuro container placed in a foam box was filled with LN2 and run through the imaging machine. The resulting DICOM image files were run through a freeware 3D rendering program (Ginkgo) by Steve Graber and the brain and the crackphone elements visualized. Images revealed that the left crackphone element was dangling in the considerable space between the skull and the cryoprotection-shrunken brain. The right crackphone element was in contact with the brain. How well it was coupled is unknown.
9. Timelines

Stabilization:

<table>
<thead>
<tr>
<th>Time (EST)</th>
<th>Military</th>
<th>Pre-Announcement Time</th>
<th>A-1408 Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:50 PM</td>
<td>15:50</td>
<td>0:00</td>
<td>Patient pronounced</td>
</tr>
<tr>
<td>10:00 PM</td>
<td>15:59</td>
<td>0:05</td>
<td>Patient moved to stanchion</td>
</tr>
<tr>
<td>10:10 PM</td>
<td>15:59</td>
<td>0:10</td>
<td>Patient moved to ceiling</td>
</tr>
<tr>
<td>10:13 PM</td>
<td>15:59</td>
<td>0:15</td>
<td>Head of bed raised to 45 degrees</td>
</tr>
<tr>
<td>10:20 PM</td>
<td>15:59</td>
<td>0:20</td>
<td>First pulse in and breathing, AnesPulse and ventilator on</td>
</tr>
<tr>
<td>10:30 PM</td>
<td>15:59</td>
<td>0:30</td>
<td>First pulse in and breathing, AnesPulse and ventilator on</td>
</tr>
<tr>
<td>10:40 PM</td>
<td>15:59</td>
<td>0:40</td>
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</tr>
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<td>10:50 PM</td>
<td>15:59</td>
<td>0:50</td>
<td>First pulse in and breathing, AnesPulse and ventilator on</td>
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<tr>
<td>11:00 PM</td>
<td>15:59</td>
<td>1:00</td>
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</tr>
</tbody>
</table>

(Timeline provided by Suspended Animation, Inc)

Surgical:

10:11 Patient arrived at Alcor
10:25 Removed cephalon from box and placed on operating table
10:29 Covered with ice bags
10:30 Removed SA's nasopharyngeal tube
10:31 Steve shaved head
10:33 Aaron prepped head for burr holes
10:37 Dr. McEachern made incisions for burr holes
10:40 Aaron began drilling burr holes
10:44 Aaron began drilling second burr hole
10:46 Dr. McEachern cleaned up holes
10:50 Brain was more retracted on left than right; 2-3 mm
10:52 Crackphone elements inserted into burr holes/ Right: blue plug, blue wire. Left: white plug, green wire
10:59 Cephalon moved from operating table to neuro box
11:02 Inserted nasopharyngeal and burr hole probes to read temperatures

11:04 Brain surface, 2.9°C, pharyngeal 1.3°C
11:11 Placed left carotid artery catheter
11:12 Cannulated left carotid artery and secured it
11:19 Flushed the line
11:20 Cannulated right carotid artery and secured it
11:26 Visualized flow of fluid out of right vertebral artery. Left is small artery, tried to open up more
11:28 Clamped off right vertebral artery
11:28 Confirmed flow of left vertebral and clamped it off
11:30 Cannulated left jugular vein
11:34 Left jugular vein secured
11:37 Cannulated right jugular vein
11:40 Carotid and vertebral arteries not symmetrical, left side being smaller
11:42 Started refractometry readings
11:48 Started bag #3
11:55 No sign of [brain] retraction yet, per visual inspection by Hugh
11:55 L:4.5°C. R:4.6°C. Brain [surface] 5.5°C. Pharyngeal 4.4°C
11:58 Started bag #4 (14%)
12:08 Started bag #5 (23.3%) 98 mmHg, speed 24
12:18 Started bag #6 (38.9%) 103 mmHg, speed 26
12:22 Pressure jump at speed 26 to 112 mmHg. System pressure 4 psi
12:26 Started bag #7, pressure 117 mmHg at speed 26. Reduced speed. Switched to effluent to drip pan
12:33 Pressure 100 mmHg speed 18
12:37 Chiller temp -4.5°C
12:38 Started Bag #8 Target CNV
12:40 Skin browning
12:42 Brain retraction Left ~6 mm, Right ~12 mm. Pressure 105 mmHg at speed 18
12:44 Pressure bump L & R jugulars at -0.2°C
12:46 Pressure 126 mmHg reduced speed to 12 (~97 ml/min). Pharyngeal temp holding at 3.9 °C not getting much circulation into core
12:49 Pressure 108 mmHg reduced speed to speed 10 (~81 ml/min). System pressure up to 6 psi
12:52 RJ -1°C LI -0.3°C pressure 101 mmHg
12:57 Both eyes retracted
13:03 Brain retraction L 12mm, R 13 13mm
13:20 Started recirculation
13:29 Pressure 109 mmHg @ speed 12 (~97 ml/min)
13:40 Started Bag #10 - not making endpoint
13:48 System pressure 10 psi
13:55 Brain retraction L 13mm, R 15mm
13:57 Started recirculation mode again
14:25 System pressure 27 psi. Hugh opens filter #2
14:33 Drained mixing reservoir, continue with 108% CPA (bag 10)
14:49 Added 300 ml M22x1.25 to 800 ml reservoir effluent
15:05 Removed 600 ml effluent from mixing reservoir, added 500 ml M22x1.25 to 500 ml ~085 effluent
15:12 Started removing effluent from system
15:19 Added 600 ml M22x1.25 to 500 ml effluent
15:32 Reduced down to 500 ml, add 200 ml
15:36 130 mmHg, at speed 14 (~113 ml/min)
15:47 Shut down

10. Issues and Actions

STABILIZATION

Issue: AutoPulse battery malfunction during initial application; battery swapped but used up a spare unnecessarily.

Action: AutoPulse battery returned to manufacturer and replaced with new.

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Issue: Blood sample collection incomplete

Action: Initial sample post pronouncement and before meds administration will be assigned to whomever sets EZ-IO. Requesting/drawing and processing of blood samples 30 min and 60 min post pronouncement will be assigned to the perfusionist.

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Issue: No record of Maalox administration.

Action: Maalox administration should be called out and the used bottle saved just like all other meds.
SURGERY AND CANNULATION

Issue: Surgeon was not briefed specifically on patient surgical history and was unfamiliar with scarring patterns. Significant surgical time and effort wasted during dissection of areas likely unsuitable for cannulation.

Action: Team leader will provide as much patient history as possible in writing and in advance to assigned surgeon and perfusionist as well as verbally review patient medical and surgical history with surgeons and discuss surgical plan in advance.

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Issue: No record of cannulae sizes used.

Action: Cannulae size and successful insertion times should be called out, as with all other procedures. Standardized perfusion report should be used by all perfusionists and should include recording of cannulation sites and cannulae used.

11. CT Image Analysis

The two computed tomography (CT) visualizations below indicate that: 1) the brain volume was been reduced by ~50%; 2) blood washout was incomplete; and 3) the distribution of cryoprotectant was erratically uneven.

Prior to obtaining CT images of post-cryoprotected brains, we have been estimating the degree of brain shrinkage by observation through established burr holes. This CT scan shows that the previous method of visualization is clearly inadequate. The brain's volume had been reduced by ~50%, with the brain being anchored to the top of the skull by the dura and collapsing in laterally from the sides. This finding is similar to shrinkage pattern that was observed many years ago with X-rays images of cryoprotected canine brains. Further analysis of CT images of neuro patients may help us better understand the dehydration processes involved.
Positioning of the crackphone elements needs to be reconsidered in view of the shrinkage of the brain. There are two possibilities: using the wires of the crackphone elements as springs to hold the element against the brain surface; or placing the elements between the dura and the skull toward the centerline of the brain, where it remains attached by the dura – the method that we currently employ.
Additional observations include:

- The pilot shot for the CT scan (not shown) shows that the void in the skull left by shrinkage is nearly full of LN2, since we can see the liquid level. The composition of the gas in the space above the liquid is unknown, but very puzzling, since the liquid is under the normal atmospheric column.

- There were a number of ice patches observed around the skin of the lower jaw, indicating incomplete cryoprotection of the skin.
12. Graphs
A1408 cryoprotection pressure

A1408 cryoprotection temperatures
A1408 cooldown - plunge to -110°C

A1408 cooldown
A1408 cooldown - LN2

-End of report -