CryoPreservation Case Report: Patient A-2020

by Tanya Jones

Showing up on our doorstep with no notice, our latest patient came to Scottsdale on October 23, 2003. As a person who joined less than a year ago already afflicted with colon cancer, A-2020 read all of the available literature about how best to set up a transport situation. When the cancer metastasized to his liver, he made the move to Scottsdale. He set himself in an apartment close to the lab, arranged to have it furnished, and actually arrived in the area before calling us.

A family member joined him during his first weekend, and together they set about making certain the appropriate treatment—both medical and cryonic—was in a state of readiness. On extremely short notice, they arranged for an indwelling catheter (dual port, 18 gauge) to be surgically implanted into his left side with firm instructions to leave it in place for our team; and hospice personnel were hired to monitor and maintain the patency of the line, to administer medications and supervision, and to otherwise ensure medical treatment as needed.

He was convinced every single day was to be his last and wanted it to be; but we knew and tried to explain that this would not to be the case. Our patient had been an athlete, and he was well enough to travel on his own; but his belief exacerbated an initial state of high anxiety. Reassurance was not an easy thing to convey, and both hospice personnel and we had our moments of failure. Managing this case was problematic in the beginning, as the advocate, a woman who stayed for only a short time, disrupted the training class at Creekside for Dr. Lemler and myself with phone call after phone call. They made the hospice downright nervous, and served to emphasize the need for redundancy in our own organization. We were compelled to explain several times that the only legal course for hastening an otherwise unavoidable death was to undergo a medically supervised dehydration.

Our patient continued sporadic intake of both food and fluids, which we knew would prolong his decline. As both a precaution against the sudden death risk that particular cancer patients have and to ease his anxiety, we placed transport equipment and supplies into his apartment and replenished ice daily.

Weeks passed, and A-2020 became increasingly disoriented and combative, and we developed concerns that the cancer had spread to his brain. This resulted in his admittance for in-patient hospice care, under 24-hour supervision, though no additional tests were performed. While in the hospice, his care was challenging for their staff, but they managed him well and still had time to be sensitive to Alcor's needs. By this time, our patient had new representation—another relative—one holding legal authority via power of attorney. Getting to know this advocate was a pleasure for us, as he was a kind person, sensitive to the patient's dignity and willing to discuss Alcor's particular requirements. This advocate's involvement also allowed us to clear up the financial complications caused by a non-standard standby agreement. We'll be conducting a paperwork review that will search for similarly approved agreements, to ensure that no one else has a comparable arrangement.

During all this time, we maintained contact with the nurses, trusting their experience, knowing they would inform us immediately if our patient's condition changed. They assured us they'd call when they estimated a 24 to 48 hour agonal course. This call came early on November 30.

Standby and Transport

The patient was sleeping upon the arrival of the standby team. We'd brought the vehicle that will eventually become our new ambulance, the mobile advanced rescue cart (MARC), medications, and ice. When he later awoke, we found A-2020 still able to speak, but often responding inappropriately. Oxygen saturation levels were still high (92% on first reading), and his pulse was steady. Blood pressure readings were also respectable (120/80), but he had developed a large swelling on the left side of his neck. His level of consciousness had fallen sufficiently and suddenly enough to warrant the hospice contacting us. We settled in a team of two to monitor the situation.

After the first 24 hours, the patient's condition had declined markedly. Saturation levels were consistently below 80%. His pulse was irregular and his apnea worsened, and the swelling on his neck had grown. We added a third member to the standby.

By the next day, his sats had fallen to 65%, tachycardia set in, and he was running a slight temperature. We found the situation curious, as we have rarely seen an agonal patient with peripheral saturation readings so low. Usually the monitor fails as circulation to the extremities shuts down and blood flow is redi-

rected toward vital organs, and our readings were consistently strong. Those suspicions were confirmed when the patient was repositioned in his bed and immediately began sleeping more easily. We discovered the growth on his neck had been contributing to the observed decline. Oxygen saturation levels soon returned to 80% and his pulse steadied. But though his comfort improved for a time, we were now 24 hours from pronouncement. When pronouncement came (December 3, 11:40 am), we had the requisite four team members on-site to launch the transport.

Pronouncement was prompt, and we quickly implemented the transport protocol. Putting the patient into the ice bath, the cooling helmet in place, and activating the MARC's water circulation system all occurred within the next four minutes. (Circulating ice water over a surface cools slightly faster than ice alone.) Manual cardiopulmonary support was initiated using an Ambu Cardiopump, and the patient was intubated to facilitate direct oxygenation. We began injecting transport medications to stabilize the cells against ischemic insult. His initial nasopharyngeal temperature was 33.6°C.

Twenty-five minutes later, we'd done all we could in the patient's room. Only one problem had manifested: one of the new medications in the protocol was too viscous to administer through the small-gauge IV ports. We set those aside, connected the larger-volume medications, and secured the patient for transport. Once in the vehicle, the automated LUCAS device replaced the Ambu Cardiopump as the means to applying chest compressions. One team member replaced the oxygen saturation meter, and discovered that oxygen levels reached at least 83% during transport.

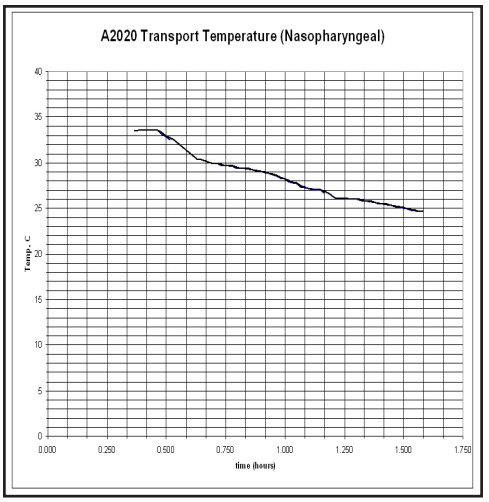
Also of note with the LUCAS is that it did not require a separate respirator. At the base of the plunger is a suction cup, and as the saturation levels attested, this was effective as a means for getting air into the lungs. Now that this device is approved for use in the United States, we will be looking to deploy it as standard transport equipment.

Shortly after his arrival at the facility, the viscous transport medication had warmed sufficiently to be administered. Chest compressions continued until 12:43 pm. None of the large volume medications were delivered in full as the preparations moved forward too quickly. External water circulation was shut off moments after the chest compressions, and the patient was moved to the operating table.

Cryopreservation

Our surgeon arrived quickly, and the patient was prepped. Burr holes were completed first. Use of a new cranial perforator accelerated this part of the procedure, and both holes were complete by 13:04. By this time, the patient's nasopharyngeal temperature had dropped nearly ten degrees to 25.1°C.

After repositioning and prepping the patient for the next incisions, the ventricular cutdown began on the right at 13:17. Transport temperature monitoring was discontinued at the start of the cutdown, with the patient's nasopharyngeal temperature



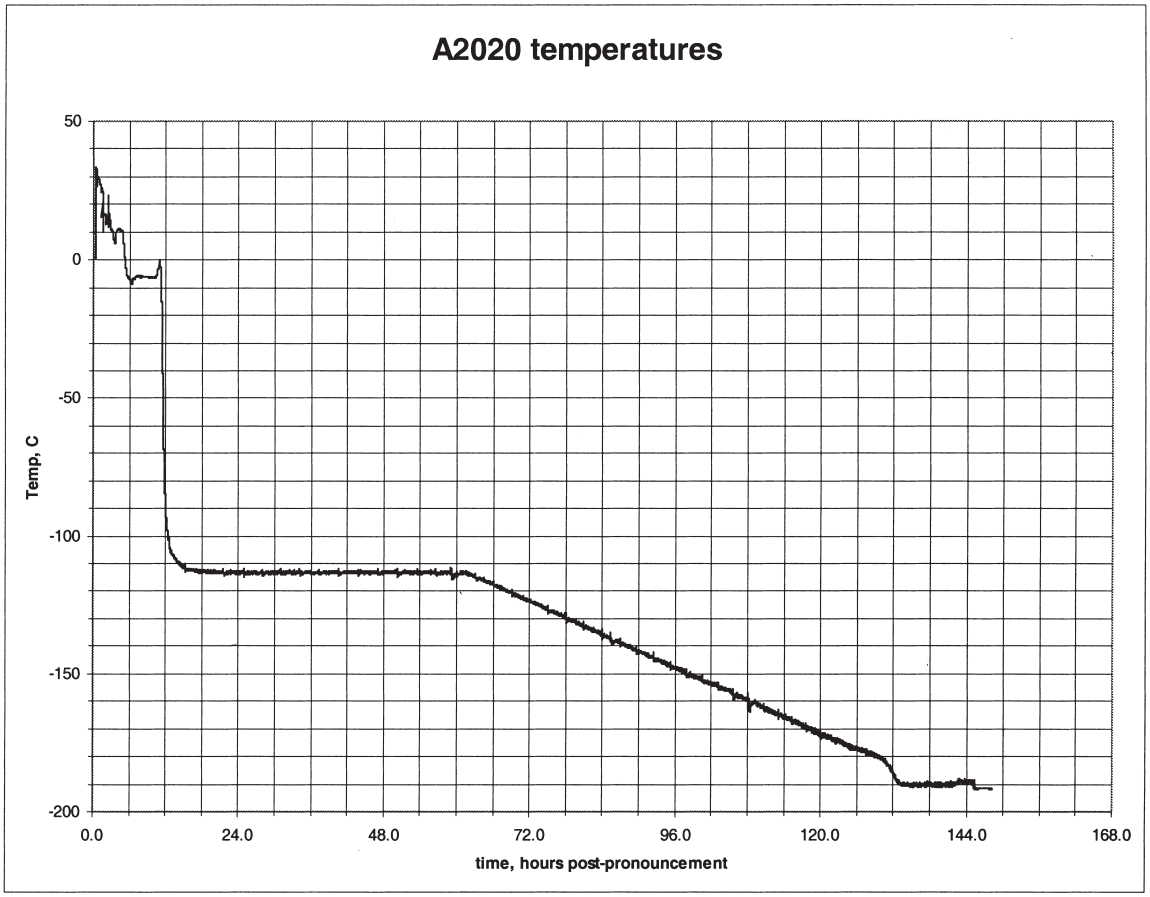
having reached 21°C. Isolation of the right carotid artery and jugular vein was completed in 12 minutes. The left jugular proved more elusive, and the attempt to isolate it continued until 13:49 at which point the decision was made to bypass that step since jugular cannulation was not essential to successful cryopreservation; we also assumed its location would become apparent once the washout started and we could trace the effluent.

Cephalic isolation was carried out and the head transferred to the cooling chamber by 14:00. Arterial and venous cannulation commenced, and the blood washout began at 14:08. No clots were observed exiting the patient's circulatory system, and the color of the effluent lightened appropriately. The vessels exposed by the burr holes provided visual evidence that our solutions were passing through the circulatory system. Temperature probes and crackphone elements were then secured, and the first perfusate samples were taken at 14:39. Washout proceeded quickly and without incident. The circuit was closed and cryoprotection started at 14:54.

Current protocols require a graduated introduction of higher levels of cryoprotectant, and it takes significantly longer than past protocols. As cryoprotectant is introduced, it is allowed to circulate and given time to equilibrate at 50% before maximum concentrations are introduced. The first samples were analyzed for cryoprotectant uptake at 15:25, and yielded readings of 23.0 and 24.7 brix (3.45 M and 3.70 M respectively). An hour later, those concentrations had climbed to 30.3 and 30.8 brix (4.55 M and 4.62 M). Cryoprotection continued until 22:19, at which point final samples were taken and perfusion discontinued.

Equilibration typically takes about 30 minutes, and this one took longer. We had concerns about lateralization, since we'd been unable to locate the left jugular vein. We also observed the right hemisphere receding faster than the left. As a result the pause stage in the middle of the cryoprotection was given more time, just to ensure that we'd given the tissues in both hemispheres time to take up the chemicals.

Correcting an error in *Alcor News*, the complete cryoprotection took 10.65 hours post-pronouncement (not the



5.5 previously reported). The error in data documentation that led to release of false information has been corrected.

Temperature Descent

Cooling the patient proceeded largely according to protocol. Cooling to –110 °C was prompt. The next stages took somewhat longer than typical as the result of too many staff members being incapacitated with the flu, but at those temperatures, the damage was minimal.

Five cracking events were recorded. The first occurred at a temperature significantly lower than we'd seen before (–134 °C), and may be a reflection of the quality of the transport and cryoprotection. The total number of cracking events was also much reduced (normal range: 20–30 incidents).

Conclusion

We've already discussed the medication viscosity issue and are revising the protocol to reflect necessary modifications. Operating room organization will be improved, since there were several things not in place when the patient arrived. Training protocols need to expand to include prep, though this is more a refinement of existing procedures than implementation of new ones. Overall, this case went fairly well, and it certainly went more smoothly after pronouncement than we could have hoped when the situation first escalated.

Preliminary data seems to indicate this cryopreservation itself went particularly well. We're awaiting the results from additional sample testing, but the patient appears to have achieved the necessary cryoprotectant concentrations to vitrify. We still need to carry out additional research into the specifics of our procedures to improve our understanding of the dynamics, but that will take time. In the meantime, a new format is being developed for data representation, one that we expect will prove useful in comparing individual cases and our various protocols directly. We'll keep you posted.