

Media Focus on 'Miracle Cure' for Cerebral Palsy Pits Science vs. Hype

The annals of medical history are littered with “miracle” treatments that defy scientific rationale or evidentiary standards, and the modern-day version often involves stem cells. But in today’s environment of 24-and-7 news and Web communications, it doesn’t take long for the hype about a new therapeutic approach to get ahead of the science. Sometimes way ahead.

Just ask Joanne Kurtzberg, a cord-blood researcher at Duke University. She has just finished an open-label feasibility and safety trial for children with cerebral palsy from various etiologies, in which the children’s own cord blood, banked at birth, is infused intravenously. Kurtzberg has not yet published or presented any scientific results, and has been cautious in the few public statements she has made about the study.

Nevertheless, numerous local and national news programs have reported on a few children enrolled in the study whose parents have attributed dramatic changes in their child to the cell therapy. Many reports have sensationalized the stories. A July 2008 Fox and Friends interview with the parents of one child was slug-lined “Miracle Cure?” and used the word “miracle” or “miraculous” five times. An accompanying article on FOX News.com was headlined “Cord Blood Stem Cells Reverse Girl’s Cerebral Palsy.”¹

NBC’s Today Show interviewed the parents of another child in the Duke study in a lengthy segment that also carried the title “Miracle Cure?”² In it, NBC’s chief medical editor Nancy Snyderman argued that such cases should not be overlooked just because they’re not part of a randomized, controlled study, opining that “medicine has not . . . made a big enough deal about anecdotes.”

These and dozens of similar stories, most focusing on the same few children, are recycled endlessly on YouTube, on Web blogs related to CP, and on the Web sites of the cord-blood banks that are referring parents to the Duke study. They are even being highlighted on some of the sponsored chat sites of many overseas “stem cell clinics” that are not involved in the

Duke research but appear to be using the reports to justify stem cell-based treatments for CP.

‘Hyped Up’ Media Reports

Kurtzberg said the press attention has made her “insane.” She said: “Some of the stuff that’s been in the press about children who have been treated has definitely been hyped up, [and] some of the things that were reported to have happened, didn’t.” For example, one child was reported to not be able to walk before the treatment and to walk afterward, but Kurtzberg said, “That child was walking at the time we treated him.”

She is convinced that private banks like Cord Blood Registry and Viacord, based in Cambridge, Mass., have been behind a lot of the publicity surrounding her study.

“CBR and Viacord are using this as marketing tools,” she said. “They have exploited our work and they have exploited parents. They are inappropriately promoting this procedure as successful, in the press and on their Web site.”

She said changes that parents may notice within a few days post-infusion are unlikely to be due to the transplant. “It is really not possible for the cells themselves to make differences that quickly,” she said. “These children are not static — sometimes things may have happened for real, but they should not have been attributed to the cells.”

In some cases, she thinks there is “a big placebo effect” and “lots of wishful thinking” behind parental reports. “We do have some descriptive evidence that some kids’ function is improving more than we would have predicted by certain neurodevelopment scales, but it’s soft [data]; it’s not hard.”

Kurtzberg said the research has shown, in about 100 children, that IV administration of the autologous cord blood is safe and feasible. While there are “some hints that there may be some benefits,” she emphasized that “it’s very, very difficult to successfully assess efficacy.”

Growing Demand

In the meantime, word of the Duke trial has spread fast in the CP patient/family community. Parents are

¹ <http://www.foxnews.com/story/0,2933,392061,00.html> (Accessed May 25, 2009)

² <http://www.msnbc.msn.com/id/23572206/> (Accessed May 25, 2009)

going to great lengths – and reportedly incurring costs up to \$15,000 – to get on the Duke protocol. (The costs are typically borne by the family, though in some cases Duke waives its professional fees and/or the referring cord blood bank provides financial assistance.)

“More patients are being treated because more families are hearing about this, some through the lay press and through these message boards and online [forums], and more doctors are hearing about it from patients who’ve gone [to Duke] and come back,” said David Harris, a professor of immunobiology at the University of Arizona, Tucson who is affiliated with Cord Blood Registry (CBR), the largest private cord-blood bank and the source of autologous blood for many of the patients in the Duke study.

The University of Arizona is among a handful of institutions now moving forward with their own clinical programs using cord-blood transplantation in children with CP; UA treated the first child in May. Harris estimated that having the procedure in Tucson would cost about \$4,000, which he said was about one-half to one-third the cost at Duke.

The Medical College of Georgia is also starting a trial using autologous cord-blood to treat children with CP, according to MCG neurology chairman David Hess. Hess said in an email that the trial will be led by neurology vice chair James Carroll, who has done pre-clinical work in a neonatal rat model of hypoxia-ischemia as well as a mouse model of adult ischemic stroke using multipotent adult progenitor cells (MAPC) derived from bone marrow. Carroll’s research is funded in part by Athersys, Inc., a Cleveland-based biopharmaceutical company that received FDA approval in December for a clinical trial in adult ischemic stroke, using bone marrow-derived MAPC.

And at the University of Texas-Houston, pediatric surgeon Charles Cox and pediatric neurosurgeon James Baumgartner are seeking FDA approval for a study using autologous cord blood to treat acute brain-injured children, including children with CP due to hypoxic-ischemic injury. The researchers have been conducting a preliminary trial in TBI using bone marrow-derived stem cells since 2006 at Children’s Memorial Hermann Hospital in Houston, and have published results using this approach in an animal model of brain injury.

The Rationale for Cord-Blood Transplants

Duke’s transplant program has treated about 1,200 children with cancer or genetic diseases since the early 1990’s. Kurtzberg, the program’s director, said her hypothesis that autologous cord-blood transplants might be beneficial in children with CP is based on research using allogeneic cord-blood transplants for children with neurogenetic conditions. Her team published results in 2005 from 25 newborns with infantile Krabbe’s disease.

“In those children, we were able to show that donor cells could get into the brain, that remyelination could occur in demyelinating diseases, and that we could see improvement in neurologic disabilities, particularly when we transplanted early in the course of the disease,” she said.

Evan Snyder, a neuroscientist and pediatric neurologist who heads the stem cell and regenerative medicine program at the Burnham Institute for Medical Research in La Jolla, Calif., said he thinks that umbilical cord blood cells can be “surprisingly useful” in some cases, including early treatment of lysosomal storage diseases, particularly Krabbe’s disease. He said the work published by Kurtzberg and colleagues in the *New England Journal of Medicine* showed a “fairly impressive impact” in some children with these genetic diseases when cord-blood transplants were done very early, in the first couple weeks of life.

Snyder collaborated with Kurtzberg to conduct autopsies on some of the children who were transplanted. He said “very preliminary” unpublished data suggests that “the cells do make it through the blood-brain barrier, they will produce the missing enzyme, and they will become functioning microglia. . .but they do not become nerve cells.”

Kurtzberg pointed to an autopsy report from her own group, in which a child who was transplanted showed evidence of engrafted cells and remyelination in the brain, which led her to hypothesize that “we could grow oligodendrocytes from cord blood.”

Snyder said the idea that umbilical cord cells can make oligodendrocytes “is exceptionally controversial. Given how controversial it is, I don’t know whether one should predicate a clinical trial based on those data.”

Kurtzberg is forging ahead, preparing an IND for FDA approval to begin a trial in children with advanced leukodystrophies, in which cord blood-derived oligodendrocytes will be delivered intrathecally into the spinal cord. She said animal work suggests that intrathecal administration gets the largest number of cells to the brain, and appears to be safe even at up to 100 times the dose that would be used clinically.

‘Tremendous Potential’ for Harm

Stephen Back, a pediatric neurologist and research scientist at Oregon Health Sciences University who studies mechanisms of white matter disease, including models of neonatal hypoxia-ischemia, said it is still “very unclear” how these injuries evolve from one stage to another. He said many basic questions need to be answered “before you start marching in and giving therapy for kids with CP.”

“It frightens me to think of something like that without understanding what the pathogenesis of the

disorder is,” Back said. “There is tremendous hesitancy on the part of the world medical community to initiate a stem cell trial in a nonfatal, nonprogressive disorder like CP. There is always a tremendous potential to do harm.”

The first two FDA-approved stem cell trials in this country, which use neural stem cells, are being conducted in children with progressive, invariably fatal conditions: Batten disease and Pelizaeus-Merzbacher disease.

Steven Levison, a neuroscientist who directs the Laboratory of Regenerative Neurobiology at the University of Medicine & Dentistry of New Jersey in Newark, shares Back’s concerns about cord-blood treatment for CP: “I think there is a lot more that we need to know. There is not enough in the published literature in terms of preclinical models of people putting in umbilical cord blood cells.”

“I do think it is worth evaluating, because there have been lots of studies that suggest that stem cells can modify the brain after injury and promote behavioral recovery,” he said. “As far as I can tell, the use of umbilical cord cells is safe – they’ve been used in lots of other diseases – so there may be no harm done. But there needs to be some additional evidence and unbiased studies that are done to evaluate the efficacy of these cells.”

Kurtzberg is seeking stimulus funding for a randomized, placebo-controlled trial to “really see if the cells are benefiting these kids.”

“We really have to have nonbiased studies that are not influenced by any level of support by any private bank,” she said.

Brenda Patoine

LONG AGO in the Annals...

DEMENTIA IN PARKINSON DISEASE

LIEBERMAN A, DZIATOLOWSKI M, KIPERSMITH M, ET AL.

OCTOBER 1979

ABSTRACT

In 520 patients with parkinsonism seen over eight years, 168 (32%) had moderate to marked dementia. Although the demented patients were older than the nondemented patients (70.4 versus 65.5 years), the incidence of dementia in Parkinson’s disease (PD) was tenfold higher than among controls (similarly aged spouses of PD patients), and dementia is held to be related more to the disease than to age.

Demented patients, in addition to being older, developed PD later, were more severely involved in a shorter time, and responded less well to levodopa. It is suggested that PD with dementia may represent a different disorder from PD without dementia.
