Stem Cells Promising for Crohn's-Related Fistulas

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Contributing Writer

Since the discovery 3 years ago that adipose tissue contains a rich amount of stem cells, researchers have been trying to coax those cells into potential therapeutics for a variety of conditions. So far, one such therapy has made it into early human trials, to help close fistulas in patients with Crohn's disease.

Damian Garcia-Olmo, M.D., of La Paz University Hospital, Madrid, shared results from a phase I study with researchers and reporters at a recent teleconference on potential uses for fat-derived stem cells.

In 2001, researchers from the University of California, Los Angeles, and the University of Pittsburgh first reported that stem cells could be isolated from fat removed during liposuction. That led to a rush to make use of the 150,000 gallons of fat that is discarded each year from some 300,000 liposuction procedures, said J. Peter Rubin, M.D., president of the International Fat Applied Technology Society and assistant professor of plastic and reconstructive surgery at the University of Pittsburgh.

Unlike stem cells derived from human embryos, there is no anticipated funding difficulty or dearth of sources with adipose tissue. "We have plenty of fat in this country," Dr. Rubin said.

So far, researchers have determined that there is a huge density of stem cells in fat tissue, and that those cells can grow into new fat tissue, bone, cartilage, nerve, muscle, and endothelial cells.

Dr. Garcia-Olmo, a colorectal surgeon, said that after the first reports in 2001, he and his colleagues wondered if it would be possible to use the fat-derived cells to help Crohn's patients. They designed a phase I study, and enrolled five patients with fistulas who had failed to respond to all previous medical treatments.

All had fat removed through a minimally invasive process akin to liposuction, and the cells were cultured for injection back into the patient. One patient was discontinued due to contamination of the cell culture, Dr. Garcia-Olmo said.

He and his colleagues injected the stem cell mixture into the internal openings of nine fistulas in the four remaining patients. Eight of those fistulas were followed weekly for 8 weeks. By that time, external openings of six were covered with epithelium and considered cured. There was incomplete closure in the two other fistulas. With at least 6 months of follow-up, there have been no adverse events, he said.

The researchers, with support from a Madrid-based company, Genetrix, began a phase II study in 50 patients in September. That trial should take 2 years to complete, Dr. Garcia-Olmo said.

Though the therapy would not be a true cure because fistulas tend to recur with Crohn's disease, it could eliminate the need for multiple surgeries, he said. ■

Genetic Variants In Crohn's Disease

ORLANDO, FLA. — *NOD2* gene variants in children with Crohn's disease appear to predict disease onset in the first decade of life, James Markowitz, M.D., reported at the annual meeting of the American College of Gastroenterology.

Of 102 children aged 16 years or younger with newly diagnosed Crohn's disease, 38 had one or more *NOD2* mutations. Similar frequencies of serologic markers for inflammatory bowel disease were found in those with and without *NOD2* mutations, but 50% of the subjects with *NOD2* mutations were aged 10 or younger at diagnosis, compared with 20% of those with wild-type alleles, said Dr. Markowitz, professor of pediatrics at New York University, New York.

At diagnosis there were no detectable differences in disease activity as measured by pediatric Crohn's Disease Activity Index, or in rates of growth failure, poor weight gain, extraintestinal disease manifestations, or infliximab and steroid use within 30 days after diagnosis in those with and without *NOD2* mutations.

There did, however, appear to be important racial differences in the presence of *NOD2* mutations: Whites comprised 86% of the study population, but they comprised 97% of the study population with *NOD2* mutations, he noted.

—Sharon Worcester