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Informed Consent

Parkinson's Patient Sues for Negligence Over Catheter Misplacement During Study

A Parkinson's Disease patient, who contends misplacement of a catheter in his brain during clinical trial surgery caused permanent injury to his body and prevented him from ever receiving the treatment correctly, filed litigation Feb. 7 in federal district court (*Zeman v. Williams*, D. Mass., No. 1:11-cv-10204-MLW, *filed* 2/7/11).

Robert Zeman, a labor and employment attorney living in Santa Barbara, Calif., claims that as a result of the catheter misplacement, a double dose of an experimental gene therapy agent mistakenly was delivered to only one side of his brain, rather than a single dose to both sides as called for in the study protocol. He further says he was not informed by researchers about the mishap, and that they in fact made efforts to conceal the mistake from him.

According to the complaint filed in the U.S. District Court for the District of Massachusetts, Zeman was diagnosed with young onset Parkinson's disease in February 1996 at the age of 30. The disease is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the brain and resulting in tremors, shaking, slow movement, and muscle stiffness and rigidity.

By November 2008, the therapeutic effect of the medications Zeman had been taking to control the Parkinson's symptoms was wearing off faster and faster, and he was experiencing more ''off-time'' during which his symptoms were worse. He learned of a clinical ''gene transfer'' trial titled ''Safety and Efficacy Study Evaluating Glutamic Acid Decarboxylase Gene Transfer of Subthalmic Nuclei in Subjects with Advanced Parkinson's Disease.'' The design of the experiment was to deliver genes directly into both sides of the brain in the hope that they would produce an enzyme called glutamic acid decarboxylase, which in turn would result in an increased production of gamma-aminobutyric acid (GABA), a neurotransmitter in short supply in the brains of Parkinson's patients.

The principal investigator of the experiment was Dr. Emad Eskandar. The listed sponsor was Fort Lee, N.J., biotech company Neurologix Inc., and one of the largest investors was Minneapolis-based medical technology company Medtronic Inc., principally because it hoped to market the Acute Brain Infusion Delivery (ABID) system used in the experiment. The ABID System, which was not yet approved by the Food and Drug Administration, was to be used to deliver the genes directly into the brains of the human subjects.

The PI and sponsors chose Dr. Ziv Williams, a Harvard University neurosurgeon, to conduct the surgery using the ABID system. Together, Neurologix, Medtronic, the PI, the individual members of the institutional review board that approved the experiment, and Williams formed the ''Research Enterprise'' for the experiment.

Catheter Misplaced, Double Dose Given. When the study was first proposed to the Recombinant DNA Advisory Committee, the federal government body designated to oversee all gene therapy experiments, a member of the RAC warned that treatment in only one side of the brain was ''handicapping.''

Prior to enrolling in the experiment, Zeman was given an informed consent form to sign, and Eskandar discussed the contents of the form with him Nov. 17, 2008, for about five minutes.

The complaint states that Williams conducted the surgery at Massachusetts General Hospital Dec. 14, 2008, with representatives of Neurologix and Medtronic in the operating room. According to the complaint, rather than placing the catheters in the ABID system into each side of Zeman's brain, in accordance with the experiment's design and the warning of the RAC, the two catheters both were placed in the left side of Zeman's brain, delivering a double dose of the study agent only on the left side of the brain.

''After the surgery was completed, all the parties of the Research Enterprise had ethical, legal, and regulatory obligations to advise Plaintiff Zeman what went wrong; instead, they willfully chose to attempt to cover up what they knew to be a serious and catastrophic mistake,'' the complaint states.

According to the complaint, Zeman at first was told the surgery went well and two weeks later that he had received the study agent on only the left side because of a ''kink'' in the right catheter, although there was a small chance of the genes going into the right side subthalamic nucleus where they were supposed to go. ''This was not true,'' the complaint contends. ''The CT scan showed both catheters terminated 'within the left subthalamic region,' meaning that a double dose of the study agent was delivered on the left side of the brain.''

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Zeman was asked by Williams to have an MRI done in December 2008 and to return to Boston in March 2009 for a follow-up. He then was told that Eskandar had replaced Williams and that Eskandar had been replaced as PI by Dr. Alice Flaherty. He was asked to sign a second consent form because of the change of PI. The form was the same as the one he had signed prior to surgery except for the change of PI and the insertion under the heading of ''risks'' of this sentence: ''There is also a risk that the catheter (the tube used to inject your brain) used in surgery might be misplaced or incorrectly placed.''

The complaint argues, ''Since Zeman had already had the Gene Transfer, the only conceivable reason said plaintiff was given this form to sign was so the members of the Research Enterprise could claim they had warned him of the risk of precisely what happened to him during the surgery when, of course, they had not.''

Negligence, Battery, Other Claims. Zeman's condition worsened. Zeman first learned what had happened during the surgery when the doctor he had been told to call to get an interpretation of PET scan results said to him, ''So you're the guy who got the double dose of the gene on one side.''

At first, the Research Enterprise recommended that Zeman undergo a second surgery to insert the gene on his right side and ''balance out his body,'' but he was advised in January 2010 that he had developed a ''slight'' buildup of antibodies as a result of the first surgery and there was a risk that if he had the second surgery he might have an immune reaction that could cause inflammation in the brain, encephalitis, and/or death.

''As a result of the infusion of a double dose of the study agent on only one side of the brain, Plaintiff Zeman has suffered and will continue to suffer severe and debilitating 'handicapping' injuries. [He] has forever lost the possibility of having an infusion on the right side of his brain or of ever correcting the dose imbalance,'' the complaint contends.

Zeman and his wife assert the following counts in their complaint:

- negligence, lack of informed consent, battery, intentional infliction of emotional distress, and deceit/intentional misrepresentation/fraud in the inducement/breach of fiduciary duty against Williams, with damages to be adjudged by a jury plus interest and cost;
- lack of informed consent, negligence, intentional infliction of emotional distress, and deceit/intentional misrepresentation/fraud in the inducement/breach of fiduciary duty against Eskandar, with damages to be adjudged by a jury plus interest and cost;
- negligence against the individual members of the IRB, with damages to be adjudged by a jury plus interest and cost;
- negligence against Neurologix, with a demand for damages of $15 million plus interest and costs;
- negligence (product liability) against Medtronic and Neurologix, with a demand for damages of $15 million plus interest and costs;
- breach of warranty (product liability) against Medtronic and Neurologix, with a demand for damages of $15 million plus interest and costs; and
- loss of consortium against all defendants, with a demand for damages based on their liability as set forth in counts one through 10 in a sum to be adjudged by a jury plus interest and costs from Williams, Eskandar, and individual IRB members, and damages of $3 million plus interest and costs from Medtronic and Neurologix.

Zeman Attorney, Neurologix Respond. The complaint was filed by Scott E. Charnas of the Charnas Law Firm, New York, with Alan C. Milstein of Sherman Silverstein Kohl Rose & Podolsky, Moorestown, N.J., of counsel.

Milstein told BNA Feb. 15, ''Like other cases I have brought [see 1 MRLR 10, 3/20/02; 1 MRLR 227, 7/3/02; and 2 MRLR 514, 7/16/03], this is really an action to protect the rights of human subjects to be fully informed before participating in clinical trials and to be fully advised of the results of any such experiments.''

Neurologix issued a statement Feb. 11: ''The company does not believe that Robert Zeman's claimed injuries are related to the drug used in the trial or to the protocol of the trial. The company believes that the claims against the company set forth in the complaint are without merit, and the company intends to vigorously defend against such claims once properly served with the complaint.''

BY JOHN T. AQUINO

The complaint can be found at http://op.bna.com/hl.nsf/r?Open=jaqo-8e4lcr.

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