

The Scientist: NewsBlog:

Stem cell therapy triggers tumor

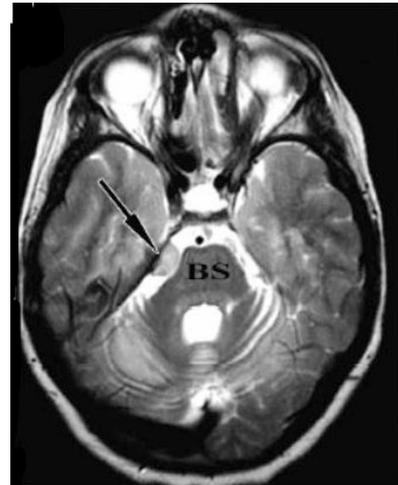
Posted by [Tia Ghose](#)

[Entry posted at 18th February 2009 01:24 AM GMT]

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A neural stem cell transplant from fetal cells performed in Russia led to a brain tumor in a teenage boy, researchers in this week's *PLoS Medicine* [report](#), raising concerns about the safety of neural stem cells treatments. The researchers confirmed that the cancer originated from the donor tissue, not the boy's own cells. This is the first report of cancer following fetal neural stem cell transplant.

However, outside experts raised concerns about the safety of the transplant procedure used in this case, suggesting that other stem cell transplants conducted with more oversight may not carry an increased risk.



MRI of brain lesion, courtesy of *PLoS Medicine*

The boy suffered from a recessive genetic disorder called ataxia telangiectasia (AT), an incurable, neurodegenerative disease that has left him wheelchair-bound. In 2002, when he was 9, his parents took him from Israel to Moscow to undergo experimental stem cell therapy. A team of researchers in Moscow injected multiple transplants of neural stem cells, which were derived and purified from the brains of aborted fetuses.

Four years later, the boy was diagnosed with a very slow growing form of cancer called glioneural neoplasm after coming to the Sheba Medical Center outside Tel Aviv, Israel, complaining of headaches.

A team led by [Gideon Rechavi](#), a pediatric hematologist and oncologist at Sheba Medical Center, performed a histological analysis on the tumor to determine its makeup. They found it contained a hodgepodge of different cell types -- this is unlike most brain tumors, which arise from a single cell type, he said. The different types suggest that the tumor "originated from a stem cell that can differentiate towards various directions," said Rechavi.

To rule out the possibility the tumor came from the boy's own cells, given that AT weakens the immune system and can predispose patients to cancer, the researchers tried to determine its source. The team found that the tumor could not have arisen from the boy, because he is homozygous for the mutation that causes AT, while the DNA from the tumor cells carried only the normal allele.

"This paper does a very good job of showing that the cells that constituted this tumor did not arise from the patient and [were] not genetically identical to either of the parents, and clearly came from the donor tissue," said [Arnold Kriegstein](#), a researcher at the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at the University of California, San Francisco.

The case study raises a number of questions. Because the patient's immune system was impaired, it's not yet clear whether the increased risk of cancer is specific to patients with suppressed immune systems, something particular to the procedure done in Moscow, or a danger with neural stem cell transplantation in general, said [Uri Tabori](#), a pediatric hematologist and oncologist at the Hospital for Sick Children in Toronto, Canada. "This is a case report," he said. "It has its role in saying it can happen, but we don't know if it's common, if it's uncommon," he said.

"It's a cautionary tale for studies currently being done in the US and elsewhere," said Kriegstein.

Since the patient developed the brain tumor four years after the initial injections, researchers may need to monitor patients for a long time after a treatment to evaluate safety, Kriegstein said.

However, it's premature to translate these findings to studies conducted in the US, said [Aileen Anderson](#), a neuroscientist who studies stem cells at the University of California, Irvine. The researchers who conducted the transplant followed the protocol of a group that has published only one other [paper](#) in an international, peer-reviewed journal, and the cells used are a mixture of glial cells, neurons, and progenitors -- "a sort of cell mush," she said. These are "completely uncharacterized populations, populations that would never be accepted in the US or any first-world country," she said.

Kriegstein agreed. "It's absolutely scary," that the group conducted the transplant, he said.

Currently, a company called Stem Cells, Inc., is conducting a Phase I clinical trial to evaluate the safety of fetal neural stem cell transplants for treatment of Batten Disease, an invariably fatal neurodegenerative disorder that affects young children.

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comment:

Primum non nocere

by anonymous poster

[Comment posted 2009-02-20 08:42:56]

Perhaps the most crucial point is what effect is all that, predominantly negative, publicity going to have on stem cell research. The news of the first-ever FDA approved stem cell clinical trial are still fresh and already stem cells are getting all this bad rap because a few half-wits decided to go ahead and play around with injecting mashed-up fetal brains into a sick kid's spinal cord. The non-scientific crowd is not going to dig into the difference between adult, fetal, and embryonic, stem cells. They will not care if the tumor was

benign or cancerous. They will just hear "stem cells give tumor to a child?" and that will be enough for them to form a skeptical opinion of stem cell research as a whole. On one hand, this may mean diminished funding for stem cell-based therapies, and loss of public and political support for CIRM-like initiatives. But maybe it will not turn out to be such a bad thing after all. Stem cells have been all the rage for about a decade now, and it is time we started to ask ourselves questions about whether the billions of dollars poured into this field was money well spent. Maybe it is also time we focused more on the safety of these highly invasive methods and the benefit/risk ratio. Overall, I am optimistic that in the long run this unfortunate experiment will serve as a warning sign for those who want to move too fast to bring untested therapies to the bedside to the detriment of the patients. Remember this, it will say: Primum non nocere!

I invite you to my [blog post](#) on the subject for more discussion. Feel free to leave your comment there as well.

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comment:

More test More information

by Erica W

[Comment posted 2009-02-19 19:33:57]

It is a shame that women aborting fetus' are not told the future of the aborted fetus. This study may warrant informing those women about what will be done so that they may give information about their family history of such diseases like cancer, epilepsy, sickle cell.

The secrecy of what is done to the aborted fetus may stem from monetary requests that the women getting the abortions may make. Since many women make the choice to have an abortion because of financial stress. Would it be unconscionable for an abortion center to pay its client to have an abortion if that fetus was going to be used to harvest stem cells? Will the cost of screening women for diseases change the entire abortion dynamic as we know it?

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comment:

This is why people rail against science.

by Sergio Vasquez

[Comment posted 2009-02-19 10:56:18]

Pouring uncharacterized and aborted fetal brain slurry into a diseased child's brain sounds like the stuff of nightmares to me and not an elegant fix.

Why not pre-clinical trials on pre-clinical models? One source reference on which to base a major experimental operation?

The US just pushed through a multi-billion dollar initiative for the NIH. Let's go about this the less wrong way...

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comment:

the treatment did not improve the boy's condition

by Tia Ghose

[Comment posted 2009-02-19 09:12:57]

A number of commenters wondered whether the treatment was helpful. In fact, it was not. What's more, the doctors at Sheba Medical Center advised the family against the procedure, and the other researchers I spoke to said it wasn't even clear why the Moscow team thought a neural stem cell transplant of this type *would* work for the boy's condition.

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comment:

ISSCR guidelines and patient handbook very appropriate

by JENS ZIMMER

[Comment posted 2009-02-19 03:30:02]

Besides of fully backing the comment by Evan Y Snyder, I find it very important, that researchers, clinicians, patients and policy makers in all countries make themselves familiar with the Guidelines for the Clinical Translation of Stem Cell Research and the Patient Handbook on Stem Cell Therapies, recently issued by the International Society for Stem Cell Research (www.isscr.org). With full respect for patient hope and demands,

and realizing that several clinics worldwide are willing to act prematurely, the guidelines and handbook provide a realistic picture of what is possible and what should be and should not be done in terms of "clinical therapy" at this time.

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comment:

Stem cell research and abortion

by Mike Brennan

[Comment posted 2009-02-18 22:55:56]

There are several different sources of stem cells; aborted fetuses being only one. It may or may not be the case that everything that can be done with stem cells from this source can be done with stem cells from other sources. However, we do not know that at this time, and will never know it without further research. I suspect it will turn out like my field of expertise, the use of radiation. You can make radiation with isotopes, and you can make radiation with machines. One is best for some jobs and the other is best for other jobs, and which is best has sometimes changed as technology changed.

I believe there are ethical issues connected with aborting fetuses specifically to harvest stem cells (in fact, I think it's wrong). I believe there are legitimate ethical issues connected with abortion (though I do not believe they are as simple as people at either extreme try to make them out to be). However, given that the fetuses have been aborted, and that the appropriate permissions have been obtained, I do not believe there is any more of an ethical issue in using the cells for research and treatment than there would be in using the body of someone who had died in a crime for research or transplant components.

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comment:

Stem cell therapy

by Philippe Laveaux

[Comment posted 2009-02-18 19:57:16]

Like those that previously commented on this topic I too would like to know if the donated "stem cells" helped the kid neuro disease.

I do find it disturbing they would use an aborted fetus brain in this procedure. I think to commit a wrong to do another wrong is probably why this all ended up like this. Obviously more research needs to be conducted so another child won't have to face this similar circumstance.

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comment:

Do you suppose it was the presence of aggregates?

by anonymous poster

[Comment posted 2009-02-18 17:33:10]

It strikes me that this treatment might potentially have allowed some clusters of multiple cell types to form and/or remain intact, despite multiple trituration and culturing steps. One or more true stem cells in the blood that enter a target tissue might be able to adapt to fit a place in that tissue based on the local signalling environment. But a group of two or more cells of different cell types should already have some notion of a morphological structure in mind - in other words, they should already be sending signalling molecules to one another indicating their respective roles. Once nucleated from some tiny structure, these cells might not abandon it however much they grow.

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comment:

Is it abortion or stem cell therapy that's distasteful?

by Jill Cooper

[Comment posted 2009-02-18 15:24:14]

The practice of taking stem cells from aborted foetuses is no more or less desirable than the act of aborting foetuses in the first place. I suppose the extra distaste comes from creating a market for aborted foetuses but whether this would ever affect the actual number of abortions being carried out is debatable.

There is an argument (an old argument I admit, and used for all sorts of questionable research) that, if the research is not done in countries operating under world's best practice methodologies (due to current legislation, then it will be done in less optimal environments and in countries with fewer scruples. And there is a plentiful supply of customers from the west willing to fund it. The end result is poor research and more suffering to the families who choose to try such therapies.

How many people have actually received this type of therapy? I know personally of two people who have received it (it was totally ineffective and, in fact, detrimental), so perhaps there are lots, but of course it isn't documented.

I suppose that most recipients of this type of therapy never survive long enough to actually develop a brain tumor as a result of it.

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comment:

Ditto: did it work?

by anonymous poster

[Comment posted 2009-02-18 15:19:09]

I also would like to know if the transplant had helped the ataxia condition. Not to mention this outcome of the therapy was an editorial oversight in the story.

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comment:

maybe

by Berry Muhl

[Comment posted 2009-02-18 13:14:03]

Perhaps their approach didn't use legitimate "neural stem cell" lines...and perhaps it did, and apologists are simply saying what apologists say.

Whatever the case, some review is definitely in question.

Given that the past couple of years have produced advances in the practice of re-generating "stem" cells from fully-differentiated somatic cells, it should be noted that the need for embryonic stem cells is (or very shortly will be) less than proponents claim.

Regardless of one's feelings on the legitimacy of stem cell research (and I do believe it's a legitimate, useful line of research), the practice of taking stem cells from aborted human embryos is not something that is needed or politically desirable.

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comment:

Did it work?

by anonymous poster

[Comment posted 2009-02-18 12:28:16]

Was the boys condition ameliorated by the therapy?

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comment:

these were not neural stem cells being used

by EVAN Y SNYDER

[Comment posted 2009-02-18 12:21:08]

I am familiar with the protocols used by the Russian team and many of this group of patients "treated" by them; in fact I think I am familiar with this particular case. Although the Russians claim to be using "neural stem cells", they are not. They essentially take whole fetal brain, put in a cuisinart, and inject it uncharacterized as a graft slurry. This case has no bearing whatsoever on the legitimate biology and uses of stem cells, particularly neural stem cells. I am actually disappointed that the Israeli scientists who analyzed this material did not do a more careful characterization of the actual donor-derived tissue and cells. Had they done so, they would have known, as well, that what they saw could not have come from a rigorously defined neural stem cell.

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