Immune response to spinal cord injury may worsen damage

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After spinal cord injury, certain immune cells collect in the spinal fluid and release high levels of antibodies. What, if anything, those antibodies do there is unknown.

A new study by neuroscientists at The Ohio State University Medical Center may have solved the mystery. It found that the antibodies may actually worsen and extend the spinal cord damage.

The antibodies first attach to nerve cells and other elements of the nervous system, then other components of the immune system attack the cells and substances marked by the antibodies as if they were infectious agents or foreign material.

"Our findings suggest that inhibiting or depleting B lymphocytes, the cells that produce antibodies, may promote healing and reduce the long-term effects of spinal cord injury," says study leader Phillip G. Popovich, professor of neuroscience and of molecular virology, immunology and medical genetics and director of the Center for Brain and Spinal Cord Repair.

"They may also help explain why the central nervous system does not repair itself efficiently and why other impairments often follow spinal cord injury."

The animal study was published online by the Journal of Clinical Investigation.

Earlier work by Popovich and his colleagues showed that B cells are activated as part of a general immune response following spinal cord injury, and that they accumulate around the spinal cord injury and begin producing antibodies.

For this study, Popovich, first author Daniel P. Ankeny, and research associate Zhen Guan, used mice that were anesthetized and given a moderately severe spinal injury that mimics a contusion-type spinal injury in humans.

One group of injured mice had a normal immune system, with antibody-producing B cells. A second group of mice was identical to the first except that they lacked B cells, and therefore produced no antibodies.

Nine weeks after spinal cord injury, the researchers compared the two groups.

They found that, on average, the area of spinal cord damage in mice without antibodies was 30 percent smaller than the damaged area in mice with antibodies.

They found that B cells and antibodies had accumulated around the spinal cord in the normal mice but not in the other group, and that antibodies had attached to damaged areas of the spinal cord.

They also found substantially higher levels of antibodies in the bloodstream of the normal group after spinal cord injury than were present before injury.

To learn whether these antibodies could on their own damage the spinal cord, the investigators purified them from the blood of injured mice and microinjected them into one side of the spinal cord of uninjured normal mice.

Within 48 hours, the hind leg on the side of the injection site became paralyzed, and remained partially so after one week. The animals also showed loss of neurons and other damage to the spinal cord.

"This was one of the more striking, remarkable aspects of the study, the fact that the antibodies alone from an injured animal can activate an immune response that damages tissue in an uninjured animal," says Ankeny, a research scientist in molecular virology, immunology and medical genetics.

"These experiments essentially prove that the antibodies have the potential by themselves to make spinal lesions worse."

The investigators speculate that because the antibodies are produced systemically, they also may damage other tissues. Popovich noted that, along with paralysis, individuals with spinal cord injury may also have systemic problems, such as chronic bladder problems.

These are usually attributed to chronic catheterization and loss of bladder control, he says. "But that doesn't explain changes that also occur in the kidneys. It may be that antibodies are targeting antigens within the kidney and causing kidney damage."

The same may be true in the sexual organs. "Male sterility is a major problem in men with spinal injuries," he says, "and there is no explanation for why this happens."

Source: Ohio State University Medical Center

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