Key Points

1. Identifying biomarkers for diseases is a very active area of research
2. Previous research has shown that neural trauma can be detected through changes in CSF metabolites
3. Indian group of researchers hypothesized that biomarkers for Tethered Cord Syndrome could be measured in CSF
4. Studied 12 young children with spinal dysraphism or retethering after surgery
5. Identified several metabolites that were significantly different between the patients and controls
6. Metabolites also returned to normal levels after surgery
7. If further refined an effective biomarker for TCS could be very useful

Definitions

biomarker - a biochemical characteristic that can be used to measure the presence and severity of a disease and the effectiveness of treatment

filum terminale - small thread of tissue at the bottom of the spinal cord; if abnormal can result in TCS

lipomyelomeningocele - birth defect where a lump of fatty tissue which protrudes from the spinal canal through the spinal column

lumbar - the lower back area

metabolism - the chemical and physiological processes by which the body produces energy and maintains itself

metabolite - any product of metabolism

MR proton spectroscopy - technology which can measure the molecular composition of a substance, such as CSF

myelomeningocele - spina bifida,

Possible Biomarkers Found For Tethered Cord

March 31, 2007 -- In a study published in the November, 2006 issue of the Journal of Neurosurgery: Pediatrics a group of researchers from India report that they may have found a set of biomarkers for Tethered Cord Syndrome. A biomarker is a biochemical characteristic than can be measured and correlated to the presence and severity of a disease and also used to assess the effectiveness of a treatment.

One of the best known, and widely used, biomarkers is the prostate specific antigen (PSA). The antigen is a substance produced by the prostate and elevated levels in the blood can be indicative of prostate cancer. Beyond prostate cancer, biomarkers are receiving an enormous amount of attention across the entire spectrum of medical research. Literally millions of dollars are spent each year by researchers and entrepreneurs trying to identify useful biomarkers for a wide variety of disease processes.

In the Indian study, the composition of the cerebrospinal fluid of infants and children with tethered cord was analyzed using a technique known as MR proton spectroscopy. Specifically, the researchers had two objectives for their work: first, to compare the pre and post-op levels of specific metabolites in the CSF of spinal dysraphism and in healthy controls; and second, to evaluate the use of MR proton spectroscopy as a means to assess surgical outcome in detethering surgery.

Recall that Tethered Cord Syndrome is when the tissue of the spinal cord is put under abnormal tension. One of the most common causes of tethered cord is spinal dysraphism, which refers to any of a number of birth defects involving the neural tube, including spina bifida and lipomyelomeningocele. Tethered cord can also be due to an abnormally tight filum terminale which essentially pulls down on the cord, or from scarring due to previous surgeries.

The researchers based their hypotheses on previous research (by both themselves and others) which has shown that trauma and damage to nerve cells results in local metabolic changes which are in turn reflected in altered levels of metabolites (metabolic by-products) in the CSF. In fact, Chiari & Syringomyelia News previously reported on a study which used CSF metabolites to show that lowered intracranial compliance can leave people more susceptible to head trauma (Chiari Patients May Be At Greater Risk With Head Trauma).

For this study, the researchers identified children treated between 2000-20002 for tethered cord at the All India Institute For Medical Sciences. They recruited six children with spinal dysraphism and another group of six children who showed signs of their cords retethering due to scar tissue from earlier surgeries. The scientists also created an age matched control group of healthy children who were evaluated for meningitis but found not have it. The children in the study were very young, in fact most were infants, and all the children with tethered cords underwent some type of detethering surgery.

CSF samples were taken from every child, both before and after surgery for the TCS patients, and analyzed using MR proton spectroscopy. When the researchers compared the CSF composition of the groups, they found a number of metabolites that were significantly different between them (see Table 1).

Specifically, both the children with spinal dysraphism and the children with retethering due to scar tissue had elevated levels of five metabolites as compared to the healthy controls. Also of note, these levels returned to normal after detethering surgery. The authors believe these metabolic changes are due to the mechanical stress put on the cord and the resultant alterations in blood flow. They also believe that the levels returning to normal after surgery indicates that the damage caused by TCS can be reversed if corrected early enough in the process.

While much more work is required to further refine these metabolites as a biomarker for TCS, such a test could prove to be very useful. A tethered cord due to spinal dysraphism in children can be obvious, but there are cases, especially in adults or if the situation is complicated by Chiari and syringomyelia, where the need for TCS surgery is not so clear.

In adults, it can be difficult to differentiate whether symptoms may be due to tethering form a tight filum or from a Chiari related syrinx, especially since some surgeons now believe that a tight filum can not always be detected by MRI. Also, for anyone who has had prior surgery which could lead to secondary tethering due to scar tissue, an objective measure of the presence of tethering could help determine if symptoms are residual or can be helped with more surgery.

As stated previously, biomarkers are a hot area of research, so one can only hope that more work is done to apply these techniques in ways beneficial to the Chiari community.

birth defect where the neural tube doesn't close properly and the spinal cord protrudes through the spine

spinal dysraphism - collective term for birth defects involving improper closure of the neural tube

TCS - Tethered Cord Syndrome; loose name for a spectrum of problems that all result in abnormal traction, or tension on the spinal cord

traction - a pulling force

cerebellar tonsils - portion of the cerebellum located at the bottom, so named because of their shape

cerebellum - part of the brain located at the bottom of the skull, near the opening to the spinal area; important for muscle control, movement, and balance

cerebrospinal fluid (CSF) - clear liquid in the brain and spinal cord, acts as a shock absorber

Chiari malformation I - condition where the cerebellar tonsils are displaced out of the skull area into the spinal area, causing compression of brain tissue and disruption of CSF flow

decompression surgery - general term used for any of several surgical techniques employed to create more space around a Chiari malformation and to relieve compression

Source

Source: Sharma U, Pal K, Pratap A, Gupta D, Jagannathan N. Potential of Proton MR Spectroscopy in the Evaluation of Patients with Tethered Cord Syndrome Following Surgery. J Neurosurg: Ped. Nov 06;105: 396-402.

Table 1
Possible CSF Metabolite Biomarkers For TCS

- Lac
- Ala
- Ace
- Cho
- GPC

Note: metabolites listed were all significantly different between spinal dysrapshism group and controls, and also pre and post surgically

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