Key Points

1. HDCT are a group of genetic disorders, such as EDS and Marfans, which affect the connective tissue
2. Doctors at TCI noticed a number of patients with indications of HDCT who were referred for failed Chiari surgery
3. Studied more than 2800 Chiari patients to identify those with HDCT
4. Found 357 with clinical indications of HDCT, such as joint hypermobility
5. These patients showed different signs and symptoms than other Chiari patients
6. In general showed symptoms involving the lower brainstem, suffered from cranial settling, and had specific morphometric features.
7. HDCT/Chiari group was predominantly women and showed symptoms at an earlier age
8. True prevalence of HDCT with Chiari can not be determined form this study due to sampling bias

Definitions

computed tomography (CT) - diagnostic test which uses computer controlled x-rays to create images of internal organs

connective tissue - material that holds body parts together

craniocervical - referring to where the skull and spine meet

dysphagia - trouble swallowing

EDS - Ehlers Danlos Syndrome, a group of connective tissue disorders

HDCT - Hereditary Disorders of Connective Tissue; in this study general term used to refer to any of a number of connective tissue

Connective Tissue Disorders Linked To Chiari In Some Patients

January 31, 2008 -- Dr. Milhorat at the Chiari Institute, along with Dr. McDonnell from the National Institute on Aging, have identified a subset of Chiari patients who also appear to have any of a number of connective tissue problems, which the doctors refer to as Hereditary Disorders of Connective Tissue (HDCT). Although this finding has been discussed on message boards, and even at conferences, for quite a while the details of the work were recently published in the December, 2007 issue of the Journal of Neurosurgery: Spine.

Connective tissue is what provides structure for the human body and its components. Disorders involving connective tissue, such as Ehlers-Danlos Syndrome, can lead to problems such as joint hypermobility, joint dislocations, fragile skin, poor wound healing, and vascular and heart problems. Although they are not always precisely defined and can be difficult to diagnose, many connective tissue disorders are genetic and hereditary in nature. People with disorders such as Marfan's Syndrome have distinct body and facial features.

The Chiari Institute began to focus on this issue after identifying a set of patients for whom decompression surgery had failed. Within this group, there were indications of craniocervical instability, possibly due to underlying joint hypermobility. To examine the phenomenon further, the researchers prospectively looked at 2813 Chiari patients who were evaluated between 2002 -2007.

Each patient underwent a variety of tests, including specifically designed questionairres, MR imaging, and complete physical and neurological exams. Some patients underwent additional tests such as 3D CT scans and upright MRIs. For the purposes of this study, the researchers used the traditional definition of Chiari as tonsillar descent of at least 5mm. HDCTs were identified using accepted criteria which take into account issues such as joint hypermobility, tissue fragility, poor wound healing, heart issues, and family history.

As an example, joint hypermobility was assessed using tests such as whether the little finger of either or both hands could bend past 90 degrees; whether one of both thumbs could touch the forearm, whether the elbows and/or knees could hyperextend past 10 degrees; and whether a person was able to, with legs straight, bend forward and place their palms flat on the ground.

Patients suspected of having craniocervical instability were evaluated using invasive surgical traction. Basically, for these patients traction was gradually applied to pull their head up in the operating room. The patients were awake for this and could provide feedback on whether there was symptom relief.

Utilizing this battery of tests, the researchers identified 357 people with both Chiari and at least one variation of an HDCT. Although this represents 12.7% of the overall group, the true prevalence of HDCT among Chiari patients could not be determined from this study. As word spread about the work being done at TCI, people with failed surgery and symptoms associated with HDCT naturally started seeking treatment there. This in turn resulted in significant bias in their sample of patients.

However, it was also clear that the subset of patients identified as also having HDCT were different in a number of ways. In general, patients in the HDCT group were younger, overwhelmingly women, and developed symptoms at an earlier age. In addition, these patients tended to exhibit more symptoms associated with lower brainstem function, such as dysphagia and facial pain (see Table 1). For example, 69% of the HDCT group suffered from dysphagia, compared to 26% of the Chiari only group. In total, the researchers found 9 symptoms which were significantly more common among the HDCT group. They also found 9 diagnostic signs, such as nystagmus, which were more common in the HDCT group.

Table 1
Selected Differences Between CM Patients With HDCT and CM Only

	w/ HDCT	w/out HDCT
Nausea	67%	14%
Dysphagia	69%	26%
Apnea	31%	11%
Facial Pain	25%	7%
Double Vision	26%	5%
Lhermitte Sign	69%	3%
Mitral Valve Prolapse	49%	3%
Retro odontoid	71%	12%

disorders

hypermobility - excessive flexibility and movement in a joint

Marfan Syndrome - an inherited connective tissue disorder

morphometric - refers to specific measurements of something; in this case of the skull area

nystagmus - rapid, involuntary movement of the eyes

odontoid - a toothlike bone that sticks up through the first vertebra and stabilizes the head/neck area

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

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

Source

Milhorat TH, Bolognese PA, Nishikawa M, McDonnell NB, Francomano CA. Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and chiari malformation type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine. 2007 Dec;7(6):601-9.

Scoliosis	49%	22%
TMJ	65%	17%

Note: *All differences shown are statistically significant; many are indicative of problems with the lower brainstem*

In addition, the team used imaging, both flat and upright, to identify structural differences between the two groups. The most striking finding was that more than 70% of the HDCT patients had an odontoid which was at an improper angle. The odontoid is a bone which sticks up through C1 and provides stability to the head-neck area. Only 11% of the patients in the Chiari only group had abnormal odontoids.

Similarly, using upright MRIs, the doctors found that patients in the HDCT group suffered from cranial settling. What this means is that when these people were lying down, there was not much crowding around the brainstem and cerebellum, but when they sat up, things moved down resulting in crowding and pressure.

Detailed family histories from 139 patients in the HDCT group showed the heritable nature of these disorders. Specifically, 32% had at least one first degree relative (parent, sibling, child) with physician diagnosed Chiari and 22% had a first degree relative with an HDCT.

Although the prevalence is likely much lower than 12%, this study clearly demonstrates there is a subset of Chiari patients with HDCT and details their anatomy and clinical signs and symptoms. It would be useful for the Chiari research community as a whole to begin to classify and characterize more such subgroups of Chiari patients, so that treatments specific to such groups can be developed.

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