



Angioma Alliance Newsletter

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Update of Latest Research Results

Molecular Genetics

The International Familial Cavernous Angioma Study (IFCAS) is comprised of researchers from Canada, Italy, Germany, Japan and Switzerland. In a recent study, IFCAS has begun to narrow down the location of CCM2 on chromosome 7. The study examined the differences in chromosome 7 among family members in 5 families who showed no mutation in the CCM1 gene. In these families, some individuals had cavernous angiomas, and some did not. By comparing the chromosomes of

those with the illness to those without, researchers can begin to isolate the location of CCM2 in relation to other known markers on the chromosome.¹

In molecular genetics, researchers continue to try to understand the role of the KRIT1 protein in the development of cavernous angioma cells. Researchers at Duke University have suggested modifications to the theory

that KRIT1 impairs cell structure through relationship with integrin proteins and their affect on cell microtubules. Duke researchers have postulated a number of possible mechanisms by which KRIT1 may impact cell function and formation through its relationship with integrin proteins. They suggest that loss of KRIT1 function may have an impact on the structure and adhesion ability of endothelial and/or neuronal cells, which may result in the impaired capillary formation that is seen in CCM1 lesions.²

Researchers at the University of Colorado are trying to determine how cavernous malformations differ from AVM's on a genetic level. They have identified nearly 200 genes which are differentially expressed between the two types of vascular malformation.

Future studies will attempt to determine which of these genes are related specifically to the development or function of vascular malformations.³

Researchers in Germany have examined the tissue of cavernous malformations in people who did not have a family history of the illness. They were attempting to determine whether the KRIT1 genetic mutation could be found in the tissue, and, therefore, be the cause of the sporadic development of some cavernous malformations. They did not find a KRIT1 mutation in any of the 72 samples they tested, and so determined that unsuspected germ line mutations in

KRIT1 are usually not the cause of sporadic cavernous malformations.⁴

Natural History

The Scottish Intracranial Vascular Malformation Study published its first paper detailing the incidence of intracranial vascular malformations (IVM's) they found in their work. IVM's include cavernous malformations, AVM's, and venous malformations. Their study is limited to residents of Scotland. The SIVMS group demonstrated a detection rate of 0.56%, or about 1 in 200 people, for cavernous malformations. This is comparable to large epidemiological studies in performed in the US. The SIVMS group hopes to continue their work in order to follow the long term course of individuals with IVM's. See International Ongoing Research Studies to learn more about participating in this study.⁵

Acknowledgments

Our thanks to Tracey Leedom, genetic counselor at Duke University, and to Dr. Issam Awad, head of our scientific advisory board, for their review of the information in this article.

Spinal Cavernous Angiomas

By Jack Hoch

Cavernous malformations are not limited solely to the brain. While not as common, spinal cavernous malformations do comprise a small, but important subset of those afflicted with the disease.

The composition of spinal cavernous malformations is the same as those found in the brain: thinly walled bubbled-shaped cavernous vessels which are underdeveloped and have little elasticity. There is very little, if any, intervening nerve tissue between the bubble-shaped caverns. Very small supplying arteries and draining veins

may connect to the cavernous malformation.

Other characteristics:

- The MRI appearance of spinal cavernous malformations is generally the same as its cerebral counterparts. These lesions are still not visible to angiography.
- They can be located in vertebral elements, nerve roots, or epidural tissues, but by far the largest number are located in the spinal cord substance itself (intramedullary).
- Spinal cavernous malformations account for 5 to 12% of spinal vascular malformations.¹
- They are slightly more common in women.
- Like their cerebral counterparts, spinal cavernous malformations tend to become symptomatic around the 3rd to 5th decade of life.
- An unspecified percentage of cavernous malformations remain asymptomatic.
- Symptomatic lesions may present with acute, episodic, or progressive deficits in functioning that correspond to the region of the spine affected by the cavernous malformation.
- In most cases, symptoms result from hemorrhage. Because the spinal cord is a small structure with many sensory and motor fibers crowded near a cavernous malformation, the

risks of hemorrhage from a spinal lesion are high, often leading to serious disability or total paralysis.

- Pain is normally overshadowed by motor symptoms and is also present in about one half of cases.²

- Surgery generally is recommended for symptomatic lesions.² Surgery is also considered for larger single lesions that are accessible to the surface of the spinal cord, or exophytic (bulging out from it).

- Radiosurgery offers no advantages versus having no treatment. This is analogous to brainstem cavernous malformations.²

- Surgery removing only part of the cavernous malformation frequently leads to a return of the cavernous malformation. There is up to a 66% potential re-bleeding rate.³

- Spinal operations are less problematic than brainstem ones.

- Most frequent complications from surgery ("acute surgical deterioration") are due to "posterior column manipulation" (25% of patients) normally resulting in transient deficits. The posterior column is the section of the spinal cord that is closest to the skin. A portion of the posterior column runs the entire length of the spinal cord. The posterior column contains sensory fibers that conduct the position sense (of where

joints are). Surgeons often must operate near this section of the spinal cord to reach a cavernous malformation.

- Approximately 5% of operations result in permanent deficits. (1988 thru 1997 studies: 47 patients of which 33 showed improvement, 12 had transient deficits, 2 with permanent deficits, 10 had subtotal resections, no deaths).³

- One study purports that intramedullary spinal cavernous malformations (IMSC- those lesions found within the spinal cord itself) may be suggestive of multiple cavernous malformations elsewhere in the "neuraxis" (spine and brain). Nearly 50% of patients in this particular study were found to harbor multiple cavernous malformations after initial IMSC diagnosis and additional MRI of the neuraxis.⁴

Spotlight: Johns Hopkins Medical Cavernous Angioma Research Lab

As a new feature, in each issue of this newsletter, we will give you information about a particular research lab. This month's featured lab is that of Dr. Daniele Rigamonte at Johns Hopkins University School of Medicine.

The Center for Inherited Neurovascular Diseases (CIND), headed by Dr. Daniele Rigamonti, is located at the Johns Hopkins University School of Medicine in Baltimore, Maryland. A

multi-disciplinary team of physicians and biomedical researchers are dedicating their efforts to the study and treatment of the inherited cerebrovascular diseases. The priority of the Center is to determine which genes are responsible for selected forms of neurovascular disease, and to use this information to improve the diagnosis and treatment of affected individuals. Our current studies include investigation of intracranial cerebral aneurysms and cerebral cavernous malformations.

Cerebral cavernous malformations (CCM) are collections of abnormal blood vessels found within the central nervous system. Some are clinically silent, whereas others can cause headache, seizures, focal neurological deficit, or intracranial hemorrhage (which can subsequently lead to stroke). Identification of these lesions is important because surgical removal of many is relatively easy. Magnetic Resonance Imaging (MRI) is a common diagnostic modality for identifying surgically correctable lesions. However, MRI testing is expensive and must be repeated throughout the lifetime of the individual at risk, because the malformations can develop later in life. One of the aims of our study is the development of a blood test for detecting CCM, providing a rapid screening method for early detection (and hence, treatment) that is both cheaper and more accessible to individuals. Overall, the information we aspire to uncover shall help elucidate the causative mechanisms responsible for the disease, as well as further the development of better diagnostic and therapeutic strategies for management of CCM.

The purpose of our ongoing study is to identify the gene(s) responsible for familial cerebral cavernous malformations, understand the underlying biochemical changes that

occur in this disorder, and investigate the molecular mechanisms contributing to the etiology of the disease. We are examining not only the known CCM1 locus (which contains the KRIT1 gene), but we are also working at identifying novel genes in the CCM2 and CCM3 regions. The information yielded may prove useful in developing a blood test to determine which members of the family are at risk for developing cerebral cavernous malformations. In addition, this information will be a useful first step in allowing researchers to determine why CCM develops in the first place. Such information may allow the development of better treatments for this disorder. People with CCM or their family members, including children, may join this study. We are comparing the DNA patterns and biochemical differences among those affected and unaffected to help us identify the gene(s) responsible for CCM. We are obtaining blood samples from individuals, no different than those obtained in a routine blood test. Blood specimens from the affected and unaffected members of the family are equally important to this study. All test procedures done as part of this study are at no cost to the participants.

[If you have questions pertaining to or are interested in being part of our study, please contact Ms. Sharmila Basu at (410) 614-0729, or via email at sbasu4@jhmi.edu].

Disability Information
Disability Resources

International Disability Resources

[International Center for Disabilities Resources](#)

The International Center for Disability Resources on the Internet (ICDRI) has a wealth of resources for everything from technology to travel to students with disabilities financial aid. ICDRI's mission is to collect a global knowledge base of quality disability resources and best practices and to provide education, outreach and training based on these core resources.

United States Disability Resources

Government Disability Information for Adults

[Social Security Administration Disability Benefits Guide](#)

If you want to know more about the various kinds of disability benefits available from Social Security, this booklet will tell you who may get benefits, how to apply and what you need to know once benefits start.

[State Vocational Rehabilitation Agencies](#)

State Vocational Rehabilitation agencies furnish a wide variety of services to help people with disabilities return to work. These services are designed to provide the client with the training or other services that are needed to return to work, to enter a new line of work or to enter the workforce for the first time.

[U.S. Labor Department Job Accommodation Network](#)

The Job Accommodation Network (JAN) is a free consulting service that provides information about job accommodations, the Americans with Disabilities Act (ADA), and the employability of people with disabilities.

[DisabilityInfo.gov](#)

This is the White House comprehensive guide to federal disability-related government resources. Topics include employment, education, housing, transportation, community life, health, income support, technology, and civil rights. For example, the community life section covers such topics as homeland security and the disabled, national park accessibility standards, and provides a link to the government TTY directory.

[National Council on Disability](#)

National Council on Disability provides resources for everything from disabilities legislation to service agencies. Their [resources](#) page provides a comprehensive listing of sites and publications related to adults and children with disabilities.

[Resources for Families and Children Social Security Benefits for Children](#)

Is your child eligible for Social Security disability benefits? This booklet provides information for parents and caregivers of children with disabilities and of adults who were disabled as children.

[US Dept of Education - Helping My Child with Special Needs](#)

This site offers a wealth of information for parents of special needs children. The Department of Education publication [Including Your Child](#) provides an overview of the many issues and services listed below:

[A Guide to the Individualized Education Program](#)
[Disability Discrimination](#)
[Equal Opportunity](#)
[Family & Advocates Partnership for Education](#)
[National Information Center for Children & Youth with Disabilities](#)
[National Information Clearinghouse on Children Who are Deaf-Blind](#)
[National Technical Assistance Consortium for Children & Young Adults who are Deaf-Blind](#)

[Office of Special Education Program Sponsored Web Sites](#)
[Office of Special Education Programs](#)
[Parent Training and Information Centers](#) – State-by-state listing
[Rights & Responsibilities of Parents of Children With Disabilities](#)
[The HEATH Resource Center of the American Council on Education](#)

[Office of Special Education and Rehabilitation Resources Services](#)

The U.S. Dept. of Education, The Office of Special Education and Rehabilitative Services (OSERS) is committed to improving results and outcomes for people with disabilities of all ages. OSERS provides a wide array of supports to parents and individuals, school districts and states. It offers explanations of the No Child Left Behind agenda and New Freedom Initiatives as they relate to special needs children.

[Dragonfly Special Needs Store](#)

This is a commercial site which offers toys and technology for children with special needs in the US and Canada.

[Community and Non-governmental Resources](#)

[Disability Resources](#)

Disability Resources is an extremely comprehensive listing of governmental and non-governmental resources for the disabled and others. It provides a listing of support organizations by diagnosis, information about assistive technology and home modifications, sections for children and women with disabilities, etc. A "wonderfully well-organized site ... for cutting through the morass of disability-related material on the Web" -- *Encyclopedia Britannica Internet Guide*

[I Can!](#)

I Can! is the leading on-line disability community site. It offers message boards, product reviews and more.

[Assistive Technology Organizations and Vendors](#)

[ABLEDATA](#)

[EnableMart](#)

[ADA Technical Assistance Centers](#)

[Dragonfly Special Needs Store](#)

[Toll Free Hotline for Disabled Air Travelers](#)

The U.S. Department of Transportation has asked for help in promoting public education about its Toll Free Hotline for air travelers with disabilities. The Toll Free Hotline for disabled air travelers has been in operation since August 2002 and is available for callers from 7 a.m. to 11 p.m. Eastern Time, seven days a week. It is currently not being fully utilized. The Hotline serves two main purposes: (1) education and (2) assistance in resolving disability-related air travel problems.

Call the Toll Free Hotline 7 a.m. to 11 p.m. EST

1-800-778-4838 (Voice)

1-800-455-9880 (TTY)

Many disabled air travelers are not aware of their rights and the Hotline, in part, exists as an educational service to inform air travelers with disabilities about their rights under the Air Carrier Access Act and the Department's implementing regulations 14 CFR Part 382 (Part 382). Hotline operators are well versed in the ACAA and Part 382 and can provide callers with on the spot general information about the rights of air travelers with disabilities. The Hotline operators also respond to requests for printed consumer information about air travel rights of the disabled.

The Hotline can also assist air travelers with disabilities in resolving real time or upcoming issues with air carriers. The purpose of "real-time" assistance is to facilitate airline compliance with DOT's

rules by suggesting to the passenger and the airline involved alternative customer-service solutions to the problem. The airline remains responsible for deciding what action will be taken to resolve the issue in accordance with the ACAA and Part 382. Generally, if a caller has a real time problem or an upcoming issue with an air carrier, a Hotline Duty Officer will contact that air carrier and attempt to resolve the issue. For example, there have been a number of incidents in which Hotline Duty Officers have contacted air carriers and convinced them to accept service animals and electric wheelchairs on board flights, to stow folding wheelchairs in the cabin, and to provide requested wheelchair assistance.

Air travelers who want information about the rights of persons with disabilities in air travel or who experience disability-related air travel service problems may call the Hotline to obtain assistance.

Air travelers who want DOT to investigate a complaint about a disability-related issue still must submit their complaint in writing via e-mail at airconsumer@ost.dot.gov or postal mail to:

Aviation Consumer Protection Division
U.S. Department of Transportation
400 7th Street, S.W.
Washington, D.C. 20590

Tidbits

Our Patient Education Brochure

Through email and regular mail, Angioma Alliance has notified an additional 1200 neurosurgeons and 250 neurologists about our organization since our last newsletter in March. We are grateful for the positive response we

have received. To date, we have received physician orders from all over the world for more than 1200 copies of our brochure.

With the help of Norma Villa, an Angioma Alliance volunteer, we are in the process of translating our brochure and our website into Spanish. We hope to have Spanish brochures printed and available some time in late fall.

Dr. Michael Scott

Dr. Michael Scott has joined the Angioma Alliance Scientific Advisory Board. Dr. Scott is the Director of Pediatric Neurosurgery at The Children's Hospital, Boston, Massachusetts and a member of the faculty of Harvard Medical School. As well as being a pediatric neurosurgeon, Dr. Scott is a cerebrovascular specialist and has published a number of articles on pediatric cavernous angioma. He has offered to serve as a resource for our families with children. Please let us know if there are any particular issues you would like to see him address either in a future newsletter or on our website.

Volunteer Needs

We are in need of a few volunteers with specialized skills. We are looking for volunteers with public relations experience to assist us in working with the media to provide public education about this illness and our organization. We would like to find a volunteer with grant-writing experience to advise us as we begin to seek foundation funding for special projects. Finally, we are seeking a volunteer with a background in

English-French translation who could assist us in reviewing future French story submissions and Community Forum exchanges.

Our Bookstore

Our website now features a bookstore of cavernous angioma related titles. It can be found as a choice from the Resources menu. The bookstore features some initial books that we have

found useful. If you have any titles to suggest, please don't hesitate to send them to info@angiomaalliance.org. The bookstore is set up in conjunction with Barnes and Noble. As an added benefit, if you go to the Barnes and Noble site through our bookstore page, a percentage of any purchase you make will go to Angioma Alliance. This is a wonderful way to get good information and help Angioma Alliance at the same time.

Ebay Auction Results

Our Ebay Celebrity and Sports Auction netted a total of \$1000 for the work of Angioma Alliance. We are grateful to the many celebrity and sports donors who made this auction possible. We are also grateful to the bidders whose purchases will help us to continue and expand our work.

Stories

The Angioma Alliance website is adding a Stories section. As a permanent part of the site, we would like to publish the experiences that you have had with cavernous angioma. Our model is [Bill Maples' Aneurysm & AVM Support site](#) – many of you may be familiar with the powerful narratives found there. Sharing and reading stories can be a way to give or get support, to share information, and to express feelings.

If you have been affected by cavernous angioma personally or as a family member or friend, please consider submitting your experiences for our site. Your story may include whatever aspects of the illness experience you feel have been important to you. This is not limited to, but could include the story of your surgery experiences, symptoms and diagnosis, recovery and disability experiences, parenting or spouse experiences, workplace or community issues, or health care provider/patient relationships.

We will publish the stories as they are submitted, editing for spelling but not for grammar. We will contact you if we feel we need to edit for medical accuracy, and will not do so without your permission.

To submit your story, please email it with your name to stories@angiomaalliance.org. Your story will be published with your name. Please let us know whether you would like your email address to appear with your story. This would allow readers to make contact with you with questions or to share their experiences. You may include a digital picture of yourself, if you like. Also, please consider sending periodic updates to your story to stories@angiomaalliance.org. These will be added to your original story with the date of submission. You will be able to find your story on the Stories page under the Community main menu selection.

We encourage international submissions and can accept stories written in Spanish and German. If you are writing from outside of the US, it would be helpful for you to include your country somewhere in your narrative. Spanish and German stories will remain in their original language.

References

Latest Research Results

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Spinal Cavernous Malformations

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