nal cord infarction is often located in the anterior spinal artery territory with the grey matter of the anterior horns exhibiting the highest vulnerability to ischaemia.[4 5] This mechanism may lead to a typical "snake eye" configuration of medullary infarction.[3] Besides the supply via VA spinal branches, which is found in 19% only unilaterally,[4] there are branches originating from the ascendant cervical artery (thyreocervical trunk) and the costocervical trunk supplying the spinal cord.

DSA findings in the present case suggest that spinal branches originating from the right V2 segment were dominant feeders of the anterior spinal artery whereas there was no evidence of direct communication between vertebral and spinal arteries from the V4 segment. The dissection involved the V2 segment from which these spinal branches originate. A transient occlusion of these spinal branches is a likely consequence. This unusual type of arterial medullary supply may explain why VAD causes spinal cord infarction. Contrary to Pullicino,[5] who described upper limb atrophies due to cervical spinal cord infarction involving the anterior horns, the present case shows a unilateral involvement of commissural, spinothalamic, pyramidal, and vasoconstrictor tracts. To our knowledge sulcal spinal artery syndrome caused by bilateral spontaneous VAD has not yet been described. In conclusion, differential diagnosis of acute spinal symptoms in young adults should include spontaneous unilateral or bilateral VAD with cervical spinal cord ischaemia.

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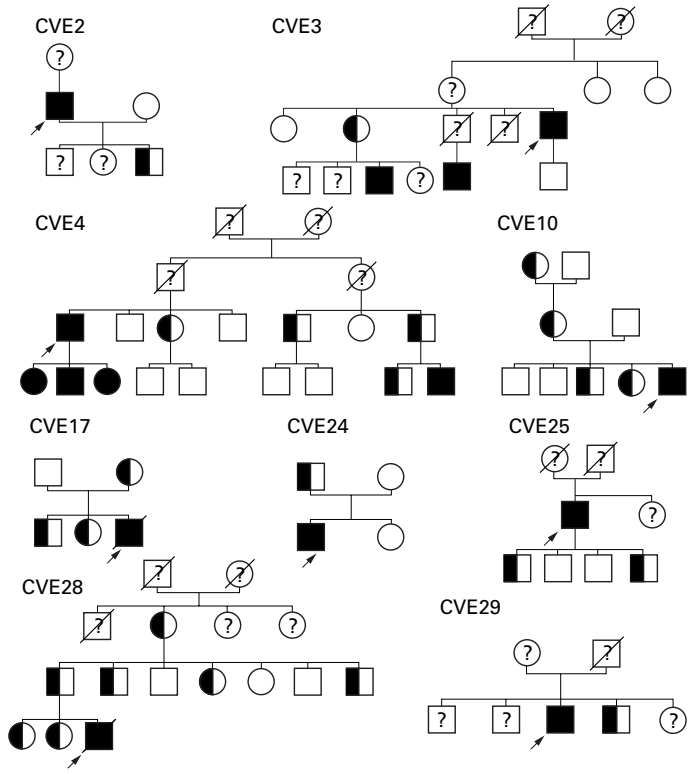
Spanish families with cavernous angiomas do not share the Hispano-American *CCM1* haplotype

Cerebral cavernous malformations are vascular malformations mostly located in the CNS. Their frequency is estimated close to 0.5% in the general population.[1] Cerebral cavernous malformations occur as a sporadic or hereditary condition. From the Hispano-American population, familial forms were reported with a high frequency.[2] *CCM1*, a hitherto unidentified gene mapping on chromosome 7 was shown to be involved in all families with cerebral cavernous malformations of Hispano-American descent with a strong founder effect.[2 3] Around 50% of non-Hispano-American families showed linkage to *CCM1* but no common haplotype was found.[4 5] A recent study showed linkage of cerebral cavernous malformations to two additional loci.[5] No Spanish family with cerebral cavernous malformations has been analysed so far.

We report herein a genetic linkage analysis conducted on nine Spanish families with cerebral cavernous malformations. All procedures were approved by an ethics comittee. The families were unrelated and originated from different regions of Spain (south west (CVE2, 3, 4, 10, 17, 25), central (CVE24), south east (CVE28), and north east (CVE29). Seventy seven subjects including 55 potentially informative meioses and 12 spouses gave their informed consent. They were examined by a board certified neurologist, underwent cerebral MRI, and blood samples were taken. Magnetic resonance imaging was used to establish status for linkage analysis. Thirty four members had MRI diagnosis of cavernomas and were considered as affected. Among them, 14 experienced neurological symptoms (cerebral haemorrhage n=6, seizures n=8). Nineteen members with normal cerebral MRI were considered as healthy. Twelve members without MRI investigation had an unknown status. Analysis of pedigrees was consistent with an

A



B

Marker	Hispanic-American	CVE2	CVE3	CVE4	CVE10	CVE24	CVE25	CVE28	CVE17		CVE29	
D7S2410	279	273	265	269	265	265	267	263	265	263	263	269
D7S2409	ND	221	219	215	221	219	219	223	219	223	223	219
D7S1813	137	123	127	127	127	125	127	131	125	127	127	127
D7S1789	137	139	133	133	129	131	133	129	129	133	129	133
MS65B	ND	135	133	131	133	135	133	129	ND	ND	137	133
D7S646	185	185	185	187	197	183	185	181	187	197	201	197	185
D7S558	107	107	107	103	107	103	103	103	103	103	103	103
D7S689	129	127	125	129	127	127	139	127	125	127	129	127

(A) Pedigrees of the nine families with cerebral cavernous malformations. Black symbols=symptomatic patients with cavernous angiomas on MRI; half filled symbols=asymptomatic members with cavernous angiomas on MRI; empty symbols=asymptomatic members with normal MRI; question mark=members with unknown status. (B) Comparison of the Hispano-American CCM1 haplotype and the haplotypes segregating with the disease phenotype within Spanish families. Polymorphic markers are shown on the left. Numbers indicate the sizes in base pairs. Primers used to amplify D7S2409 were different from those in the Hispano-American families resulting in a different size of the amplified fragment. M65B was not studied in the Hispano-American families. Family CVE24 was not informative for D7S646. For families CVE17 and CVE29, the two haplotypes of the affected siblings are indicated. ND=not determined.

autosomal dominant pattern of inheritance (figure A).

Eight polymorphic microsatellite markers spanning the *CCM1* interval were selected for linkage analysis. Four were chosen from the Généthon linkage map (D7S2410, D7S2409, D7S646, D7S689), and three from the Cooperative Human Linkage Center (D7S1813, D7S1789, D7S558). The last one (M65B) was identified by SL based on sequencing data of a bacterial artificial chromosome (Genbank HSAC000065; BAC RG085C05). The length of the genetic interval flanked by markers D7S2410 and D7S689 is 4 centimorgans (cM). Marker distances between D7S2410/D7S2409, D7S1813/D7S1789/D7S646/D7S558, and D7S689 have been estimated to be 2.2 cM, and 1.8 cM, respectively.[3] Oligonucleotide sequences are available through the Genome Data Bank (John Hopkins University, Baltimore). Genotyping and linkage analysis (LINKAGE package version 5.1) were performed as previously described.[5]

Lod scores were calculated in the five families having a sufficient number of potentially informative meioses—that is, CVE3 (eight), CVE4 (16), CVE10 (seven), CVE25 (five), and CVE28 (seven). Lod scores higher than 1 were obtained for three families (CVE3, 4, and 28) for at least one marker. Due to incomplete informativity of three markers within family CVE4, lod scores did not reach the level of 3. In family CVE10, lod scores were close to 1 for four markers (D7S2410, D7S1789, D7S558, D7S689). Family CVE25 showed a lod score close to 0 for all markers. In this family, two affected and one asymptomatic sibling with normal standard MRI inherited the same haplotype from their affected father. When the data of all examined families were pooled, a maximum combined lod score of 5.92 was obtained for marker D7S2410 at θ=0.

In seven families (CVE2, 3, 4, 10, 24, 25, and 28), all affected members inherited an haplotype that was not shared by their healthy relatives (figure B). In family CVE17, both affected siblings inherited a distinct haplotype from their affected mother. Although the limited size of this family does not allow to formally conclude, this suggests genetic heterogeneity. In family CVE29, the two affected siblings inherited the same haplotypes from their mother and father whose status was unknown.

None of the families shared a common haplotype (figure B). In addition, the extended Hispano-American haplotype was not segregating with the disease phenotype in any of the nine families including the four families with suggested linkage to *CCM1*. However, two out of nine families (CVE2 and 3), the D7S646 (185bp) and D7S558 (107bp) alleles segregating with the disease phenotype were identical to the ones observed in the Hispano-American haplotype. Consequently, we analysed the frequency of this combination of alleles within a panel of 80 haplotypes of 40 healthy white subjects. Frequency was 17% compared with 22% in our Spanish sample. Therefore, this finding might be attributed to a random distribution of these alleles.

In conclusion, linkage analysis of Spanish families with cerebral cavernous malformations did not show any evidence for Hispano-American haplotype sharing or a founder effect. Although our sample was limited in size and does therefore not formally exclude the presence of the Hispano-American haplotype in additional Spanish families with cerebral cavernous malformations, this haplotype is most likely not predominant in Spain, and the strong founder effect seen in all published Hispano-American families with cerebral cavernous malformations might be specific for this population.

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Hydrocephalus caused by metastatic brain lesions: treatment by third ventriculostomy

Metastasis to the brain occurs in 20%–40% of cancer patients.[1] About 20% of these metastases are located in the posterior fossa, cerebellum, and brainstem. Metastatic disease to periventricular brain tissue can obstruct the flow of cerebrospinal fluid (CSF) produced in the ventricles to the subarachnoid space where it is normally absorbed by arachnoid granulations. This typically causes an obstructive or non-communication hydrocephalus. A shunt has been customarily placed to drain CSF from a lateral ventricle through a pressure regulating valve and into the atrium or peritoneal or pleural cavity. Even though this technique has been successful in relieving the hydrocephalus, it has about a 50% chance of infection or failure from blockage.[2]

Another option for the treatment of obstructive hydrocephalus is third ventriculostomy, a minimal invasive endoscopic neurosurgical procedure. In performing third ventriculostomy, a hole is created in the floor of the third ventricle, allowing CSF inside the ventricle to drain out to the CSF space surrounding the brain. Although third ventriculostomy has a low operative morbidity and a high probability of success in secondary hydrocephalus, it is only commonly used on patients with aqueductal stenosis and the pediatric population. To avoid placing shunts in patients with inoperable metastatic brain tumours who typically have only a few months to live, we have offered the patients third ventriculostomy as a palliative procedure.

We performed third ventriculostomy on seven patients with hydrocephalus due to metastatic tumours of the posterior fossa or thalamus. They typically presented with symptoms of acute hydrocephalus in addition to any local mass effect of the tumour. Postoperatively, five patients were relieved of hydrocephalic symptoms and follow up brain imaging studies disclosed decreased ventricular size. These five patients had a median hospital time of 6.5 days and median survival of 9.5 weeks after the operation (table). Their hospital stay was prolonged by care of their primary disease. However, most of our patients who underwent this operation for hydrocephalus caused by other diseases were discharged from the hospital between 24 and 48 hours from the procedure. There were no operative complications. All five patients had no evidence of redevelopment of hydrocephalus up to the last clinic visit.

Two patients had unsuccessful results from their third ventriculostomy. One patient (case 4) showed no change from his initial neurological exam after the procedure, but his mental status deteriorated on post operative day 6. Brain CT showed no change in the size of his ventricles compared with the scan obtained on the day of admission. The patient's family requested comfort care only and the patient died 2 days later. In the second case (case 6) the patient had improvement in his neurological examination and ventricle size by CT scan immediately after the operation, but had recurrent symptoms of hydrocephalus 11 days later. After placement of a ventriculoperitoneal shunt, his examination returned to baseline.

Every patient except the person described in pase 4 received brain radiation therapy after the palliative procedure. One patient (case 3) underwent a course of radiation treatment prior to the operation. Another (case 5) had radiation to her orbit in the distant past after enucleation for retinoblastoma. Even though previous radiotherapy may be considered a contraindication for third ventriculostomy by some authors, it did not seem to affect the success of third ventriculostomy in our patients. Carcinomatous meningitis which could have caused a concomitant communicating hydrocephalus was not grossly evident on examination, on any of the brain imagings, or during endoscopy. However, tumours in contact with CSF space can also cause a communicating hydrocephalus by raising CSF protein which can obstruct distal CSF space and arachnoid granulations.

Our success rate of about 70% (five of seven) for third ventriculostomy in periventricular metastatic disease is consistent with the results obtained with third ventriculostomy for adult patients with secondary hydrocephalus.[3] This is comparable with the alternative shunting with an implanted catheter which has a first year revision rate as high