Familial nontraumatic, nonaneurysmal subarachnoid hemorrhage: a report on three first-degree siblings

Case report

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Family history is a recognized risk factor in aneurysmal subarachnoid hemorrhage (SAH). The genetic and environmental contributions are actively researched. The authors of this report present a case series of 3 first-degree siblings affected by nontraumatic, angiographically negative SAH. Data in this study suggest that familial predisposition may also apply to spontaneous, nonaneurysmal SAH and that family history should be actively investigated in all such patients. The identification of families with multiple affected members could lead to an improved understanding of the genetic and environmental factors associated with this condition. (DOI: 10.3171/2011.5.JNS1119)

Key Words • subarachnoid hemorrhage • cerebral angiography • familial aneurysm • familial subarachnoid hemorrhage • perimesencephalic subarachnoid hemorrhage • vascular disorder

Case Reports

Case 1

History and Examination. This 57-year-old woman woke up with a severe headache and nausea. There was no history of recent trauma. On presentation to our emergency department, she underwent an unremarkable neurological physical examination and her Hunt and Hess grade was 2. A noncontrast head CT showed SAH within the basal cisterns, tracking within the foramen magnum and along the tentorium (Fig. 1). Her medical history was significant for thyroid cancer following thyroidectomy as well as hysterectomy and hyperlipidemia. She had been a cigarette smoker but quit 25 years earlier; she did not drink alcohol, and she had no history of hypertension.

Treatment. In the subsequent hours and after transfer to the neurosciences intensive care unit, she became lethargic and an external ventricular drain was placed via a right frontal bur hole, with improvement in her level of consciousness. Digital subtraction angiography was then performed, showing no vascular aneurysms or other vascular etiology to explain the SAH.

Posttreatment Course. A repeat DS angiography study was performed 8 days after her admission and again revealed no vascular abnormalities. Her clinical course remained uneventful, the external ventricular drain was removed, and she was eventually discharged home 2 weeks after admission with no neurological deficits. She remains well and at full capacity 6 months after the SAH.

On further questioning, she informed us of 2 first-degree siblings (a brother and a sister) with similar clinical presentations. She also has 7 more first-degree siblings who are currently unaffected by any neurological condition. She is not aware of any relevant history in previous generations within the family. The cases of the affected brother and sister are briefly outlined below.

Case 2

This 48-year-old man presented with the new onset...
of a severe, bilateral frontal headache. He had a nonfocal neurological examination and a Hunt and Hess grade of 2. Computed tomography scanning revealed thick SAH in the basal cisterns, extending to the right sylvian fissure (Fig. 2), and was followed by an unremarkable DS angiography study. Magnetic resonance imaging and MR angiography studies of the head were also performed but were unrevealing. Cerebral angiography was repeated on hospital Day 10 without new findings to explain the initial SAH. The patient’s risk factors included tobacco use, heavy alcohol use, and hypertension. He remained clinically intact and was sent home 2 weeks after his admission. On outpatient follow-up he reported the development of chronic daily headaches as well as migraine headaches with and without auras, which have been well controlled with valproic acid. Three years after the SAH, he continues to have no neurological deficits.

Case 3. This 49-year-old woman presented with sudden severe headache followed by nausea and vomiting. She had a nonfocal examination and a Hunt and Hess grade of 2. Magnetic resonance imaging of the brain showed blood in the occipital horns of the lateral ventricles and a small amount of SAH in a prepontine distribution (Fig. 3). Her medical history was significant for anxiety and endometriosis. She had smoked cigarettes but quit 20 years earlier; she did not drink alcohol, and she had no history of hypertension. Two DS angiograms, obtained 7 days apart, revealed no underlying vascular abnormality. During her hospitalization she remained neurologically intact and was discharged home on hospital Day 10. Five years after the SAH, she has no neurological deficits or symptoms.

Discussion

The basis of the familial association between intracranial aneurysms and SAH has not been fully understood. Recommendations on optimal screening for family members with a history of aneurysms were recently published. The contribution of and interaction between environmental and genetic factors is being actively researched. A recent large, twin-cohort Scandinavian study of SAH documented a heritability estimate of 41%, suggesting only a moderate genetic contribution. Authors of this study recommended performing large genome-wide association studies and focusing genetic studies on families with multiple affected members. Another population-based case-control study on familial SAH found only 10 (0.19%) of 5282 patients to have 2 or more first-degree relatives with SAH. These studies did not differentiate between aneurysmal SAH and the angiographically negative variants.

Among patients with nontraumatic SAH, there are 10%–15% of events in which no source of bleeding can be found despite extensive diagnostic workup including multiple DS angiograms. van Gijn et al. were the first to describe a particular pattern of DS angiography–negative, nontraumatic SAH with a characteristic pattern of distribution in perimesencephalic, pretruncal areas and a benign clinical course. More recently, conflicting reports have suggested variations in venous drainage and, more specifically, the basal vein of Rosenthal as possible sources of pretruncal SAH.

The only report on familial angionegative SAH, by Tieleman et al., described 2 first-degree relatives with pretruncal SAH and abnormal venous drainage. Our re-

![Fig. 1. Case 1. Axial noncontrast head CTs revealing subarachnoid blood in a perimesencephalic, pretruncal location, at the midbrain level (left) and at the pons (right).](image1)

![Fig. 2. Case 2. Axial noncontrast head CTs revealing a thick subarachnoid clot in the basal cisterns and right sylvian fissure, at the midbrain (left) and at the pons (right).](image2)

![Fig. 3. Case 3. Axial FLAIR MR images revealing occipital cortical subarachnoid blood, blood in the occipital horns of the lateral ventricles, and prepontine clot, at the midbrain level (left) and at the pons (right).](image3)
Familial angiographically negative subarachnoid hemorrhage

port consists of 3 first-degree siblings with angiographically negative SAH. They all underwent repeated cerebral angiography with neither arterial nor venous abnormalities that could be appreciated. As a limitation, we note that the 2 siblings of the patient we treated did not undergo 3D rotational angiography as part of their DS angiography study, which has been reported to increase the yield. It would also have been of interest to obtain high-quality MR venography studies to further evaluate for venous sources of bleeding. Although we cannot rule out that SAH in these siblings did not occur by chance, we do believe that having 3 first-degree relatives with no history of trauma and similar imaging and clinical courses could suggest a familial genetic and/or environmental predisposition.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Lazaridis. Acquisition of data: Bodle. Analysis and interpretation of data: Lazaridis, Chaudry. Drafting the article: Lazaridis, Bodle. Critically revising the article: Lazaridis, Hays, Chalala. Reviewedsubmitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lazaridis.

Acknowledgment

The authors thank Emma Vought, M.S., for her assistance with figure editing.

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Manuscript submitted January 6, 2011. Accepted May 2, 2011. Please include this information when citing this paper: published online June 3, 2011; DOI:10.3171/2011.5.JNS11119.

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