EDITORIAL

Familial Intracranial Aneurysm

The notion that intracranial aneurysms have genetic causes and follow racial and familial distributions has been in the neurosurgeon's mind for decades. However, genes that are associated with intracranial aneurysms have yet to be identified. Approximately 35 years ago, aneurysms were considered to be a disease of the Far East and did not exist in Arab countries or the Middle East. The paper published by Ammar *et al.* in 1992 to determine the existence of aneurysms in Saudi Arabia was received with great skepticism![1] Over the years, the development in neurosurgical practices in Saudi Arabia has proven that the incidence and prevalence of aneurysmal subarachnoid hemorrhage (SAH) are comparable to Western countries. It is important to determine the prevalence of familial aneurysms in Saudi Arabia for the following reasons:

1. There is strong evidence from literature that the first-degree relatives of patients with a history of intracranial aneurysms and SAHs have a higher risk of developing this disease[2-5]
2. Patients whose first-degree relatives suffered from an intracranial aneurysmal SAH have an even greater risk of developing an aneurysm every few years with SAH as demonstrated by the study published by Bor *et al.* in Lancet Neurology 2015[2]
3. These findings necessitate the development of a new follow-up screening and management strategy of these patients and their relatives who are at risk of this disease
4. Familial intracranial aneurysms show several characteristics including:
    a. Occurrence at a younger age
    b. Risk of frequent, multiple aneurysms in the same patient
    c. Female relatives of these patients are thought to have a higher risk of aneurysmal SAH than males; however, this risk was recently challenged.[2-4,6]

The phenomena of familial intracranial aneurysms have been studied by several scholars around the world. Wills *et al.* analyzed the data of 346 Finnish families diagnosed with familial aneurysm.[3] This study included 186 females (53%) and 160 males (46.2%) and revealed 937 aneurysms (2.7 per family). A genetic analysis of the 569 (60%) patients who had survived at the time of the study revealed autosomal recessiveness in 198 (57.2%), autosomal dominance in 126 (36.4%), and autosomal dominance with incomplete penetrance in 19 (5.5%) of these families.

A similar study on a Japanese population demonstrated the high-risk of SAH associated with positive family history of aneurysmal SAH with no difference between males and females.[5] Another Japanese genetic study on intracranial aneurysms revealed that ADAMTS15 is a candidate gene for intracranial aneurysms.[6] The study focused on 10 variants of 9 genes from 72 candidate variants.[6] These genes were GPR63, ADAMST15, MLL2, IL10RA, PAFAH2, THBD, 1L11RA, FILIP1L, and ZNF22.[6]

Other studies focused on determining the causes of intracranial aneurysms and their rupture. Until now, the genetic cause has not been identified; however, many genes have been identified that may or may not impact the development of aneurysms. Some researchers studied the renin-angiotensin system (RAS) and its possible impact on the development and rupture of intracranial aneurysms.[6,7] Recently, an association has been made between the development of intracranial aneurysms and brain RAS.[7] Researchers also believe that there is an association between polymorphisms in RAS-related genes and ruptured intracranial aneurysms. In this issue, Dr. Hossam Al-Jehani *et al.* will review the familial intracranial aneurysm among Saudi Arabian patients.

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