Case Lessons

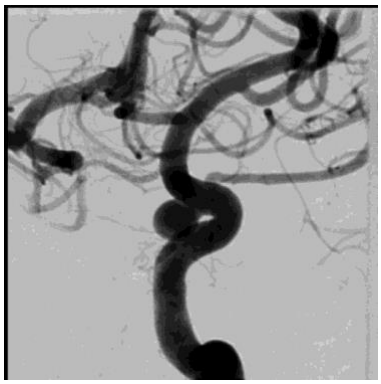
What we know about the genetic testing of DNA sequencing help in predicting the development of cerebral aneurysm

Vojsava Leka, Oneda Cibuku, Mirel Grada, Arben Rroji, Eugen Enesi, Mentor Petrela

Introduction: Although several acquired risk factors associated with cerebral aneurysms have been identified, genetic factors still remain understudied. Multiple familial aneurysms account for more than 1% of cases, often undiagnosed until the moment of rupture[3]. Less is known about the development of intracranial aneurysms in relation to autoimmune diseases[1,2].

Key words: Genetic studies, ruptured aneurysm, autoimmune disease

Case report: A 38-year-old woman presented to the emergency department of SAH Hunt Hess II clinic, with evidence of a 6 mm saccular aneurysm of the posterior communicating artery, for which endovascular with coiling treatment is performed.



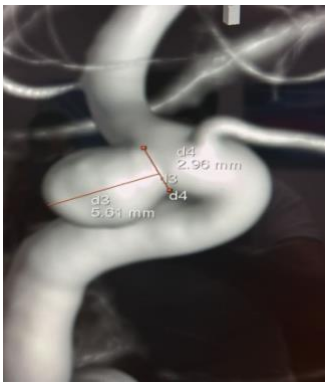


Figure1: DSA before the embolization: angiogram: Aspect 6mm left PCOA

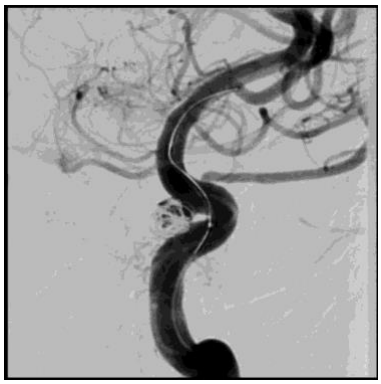


Figure 2: Left internal carotid post-embolization (coils)

Autoimmune comorbidities are evident in her medical history: Hereditary Angioedema, Hashimoto's Thyroiditis under treatment with 50 mcg Letrox, Celiac Disease, Familial Hypercholesterolemia, Polycystic Ovary Syndrome and Stillbirth at 22 weeks of pregnancy due

to placental thrombosis. While positive family history for hereditary angioedema and cardiovascular disease.

In February, of her own accord, she carried out complete genetic testing of DNA sequencing, where a high genetic predisposition (99th percentile) for the development of cerebral aneurysms was found. Next, she was scheduled for a genetic consultation, which she did not complete including MRA.

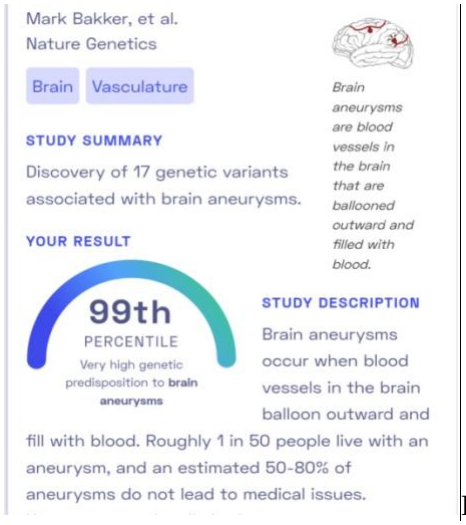


Figure 3:Genetic test result based on GWAS

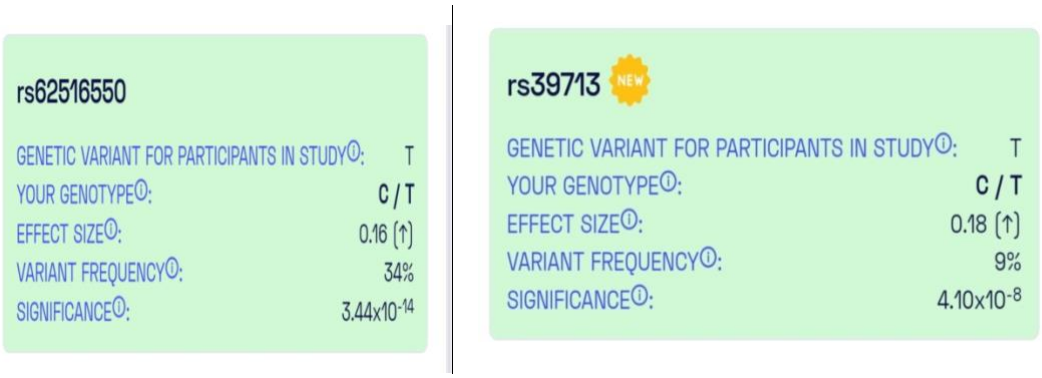


Figure 4: *The results of genetic variants with positive effect sizes and increase genetic predisposition to brain aneurism in our patient*

During hospitalization, she underwent a complete workup for autosomal dominant polycystic kidney disease and Ehlers Dawson, which were negative. The patient leaves the hospital in very good condition with the recommendation of Angio-MRI examination for her siblings.

Discussion: As presented in our case, genetic testing in the development of cerebral aneurysms has an essential role in prognosis. Contributing to their development are factors such as smoking, the use of medications such as estrogens, autoimmune pathologies[1,2]. In the study developed by Mark Bakker et al. where 370,000 patients were tested, 17 genetic mutations were found and based on individual percentiles, the risk of developing cerebral aneurysms was determined[4.] Although after the identification of genetic mutations, there are still no standardized international protocols for the follow-up of patients[3]. Currently, in the United Kingdom, follow-up with Angio-MRI is recommended every year in high-risk cases and genetic study of first-degree relatives in cases with relatives diagnosed with a ruptured aneurysm under the age of 35[2,5].

Conclusion: Genetic studies in cerebral aneurysms may help to understand their causes, biology and identify targets for therapeutic intervention[2]. The association between size and autoimmune disease requires detailed studies, as autoimmune disease may influence the trajectory of aneurysm development and the decision to treat[1.]

References:

1. Association between underlying autoimmune disease and small aneurysm size at rupture. Abhijith V. Matur, MD, Ali S. Yamani, BA, Michael W. Robinson, MD, PhD, Matthew S. Smith, MD, Peyman Shirani, MD, Aaron W. Grossman, MD, PhD, and Charles J. Prestigiacomo, MD *https://thejns.org/doi/abs/10.3171/2022.5.JNS22750*
2. Genetic and heritable considerations in patients or families with both intracranial and extracranial aneurysms Anna L. Huguenard MD Vivek P. Gupta MD, Alan C. Braverman RalphMD, G.

Dacey MD
https://thejns.org/view/journals/j-neurosurg/134/6/article-p1999.xml

3. Genetics of Intracranial Aneurysms Sirui Zhou, Patrick A. Dion and Guy A. Rouleau
https://www.ahajournals.org/doi/10.1161/STROKEAHA.117.018152
4. Genetics of Intracranial Aneurysms Mark K Bakker ,Ynte M Ruigrok
https://pubmed.ncbi.nlm.nih.gov/34399582/
5. Genetic factors involves in intracranial aneurysms D.Mohan, V.Munteanu, AV Cuirea
https://ncbi.mim.mih.gov