

Title: Germline mutations in individuals with meningioma and breast cancer

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An association between meningioma and breast cancer in women has been described, indicating a moderately increased risk to develop one if already diagnosed with the other. However, the mechanism of this association is not fully elucidated. Given the potential impact of heritability within a family and the need for appropriate risk assessment and medical management, exploring the contribution of germline genetic mutations in these cases is important. All sequential cases submitted to our laboratory for hereditary cancer panels between March 2012 and December 2015 were retrospectively reviewed. Test request forms indicating meningioma were selected, and cases that did not undergo testing for *BRCA1* and *BRCA2* were excluded. Analysis of personal history of breast cancer and test results was conducted. Testing did not include *NF2*, *PTCH1*, *SMARCB1*, or *SMARCE1*, all established germline causes of meningioma. Of 115 cases with meningioma, 61 (53%) also had breast cancer; 33% had meningioma first, 23% had breast cancer first, 12% were concurrent, and the remainder were unable to be determined. In 10% (n=6), cases were found to harbor a germline genetic mutation in one of four genes: *BRCA2* (2), *CHEK2* (2), *BRCA1* (1), and *CDKN2A* (1). In the 54 cases of meningioma without breast cancer, germline mutations were identified in 15% (n=8): 2 in *BRCA2* and 1 each in *ATM*, *BAP1*, *CHEK2*, *PTEN*, *SDHB*, and *SDHD*. Our findings are consistent with previously reported associations between breast cancer and meningioma, however, germline mutations in known hereditary cancer genes such as *BRCA1/2* and *CHEK2* have not been described before. Additionally, the spectrum of genetic alternations seen in the larger meningioma cohort provides new information about the role that germline mutations may play in hereditary meningioma, which could have important implications for the provision of genetic counseling and test selection. Further studies are needed to clarify this association.