The role of immunochemistry in the SDHx mutations in pheochromocytomas and paragangliomas


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Introduction: Early detection of succinate dehydrogenase complex (SDH) mutations in patients with pheochromocytoma and paraganglioma (PPC/PGL) has important implications as when present the risk of malignancy is increased. The use of negative immunohistochemical (IHC) staining for SDH subunit B, D, A (SDHB/-D/-A) has been proposed as an indicator of SDHs mutation and as an effective substitute for the high-cost genetic screening of all of these genes.

Methods: We have performed SDHB/-D/-A and Ki-67% immunohistochemical staining in a series of 29 paraffin embedded PPCs/PGLs specimens. Screening for point mutations by direct Sanger sequencing was performed in germline DNA from patients with potential aggressive (PASS>6) PPC or metastatic PPCs at the initial diagnosis or in cases of PGLs.

Results: Twenty-six cases with PPCs and 3 with PGLs were enrolled (18 females). Three cases were metastatic at diagnosis whereas two developed metastases during follow up. Ten cases (40%) had a PASS >6. Mean Ki-67% was 2% for cases with mutation and 2.6% for cases without mutations (p=0.8). Genetic testing for germline analysis had previously been performed in 21 cases and positive results were found in 7 cases (1 case was found positive for SDHB mutation, 1 for familial SDHD, 2 for RET, 2 for NF1 and 1 for VHL mutation) Table 1. The patient with the SDHB germinal mutation exhibited negative SDHB and positive SDHD/-A staining pattern. The patient with the SDHD germinal mutation exhibited negative SDHB/-D and positive SDHA staining pattern. Cases with RET, NF1 and VHL germline mutation as well as those without any mutations exhibited positive SDHB/-A and negative SDHD immunostaining.

Discussion: Our results are in agreement with previous series which have shown that SDHB/-D/-A immunohistochemical analysis could be a low cost technique to predict the presence of SDHx mutations. SDHB immunochemistry when used as a guide to genetic testing could potentionaly reduce the effort, time and costs of testing among patients with PPC/PGLs.