Succinate Dehydrogenase Subunit B (SDHB) Immunohistochemistry Should Not Replace Clinical Genetic Testing for SDHx Mutations in Patients with Pheochromocytoma and Paraganglioma

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Mutations in ten known susceptibility genes predispose to the development of pheochromocytomas and paragangliomas (PCC/PGL). Five of those genes are part of the succinate dehydrogenase complex (SDHA, SDHB, SDHC, SDHD) or a complex cofactor (SDHAF2), all involved in the Kreb’s cycle and mitochondrial respiratory chain. Knowledge of a germline mutation in a susceptibility gene is important for surveillance of the patient for recurrence, metastatic disease or additional primary tumors and for screening of affected family members. Expression of SDHB protein by immunohistochemistry (IHC) has been proposed as a surrogate marker for SDHx mutation status, with absent or significantly decreased expression of SDHB by IHC suggesting the presence of a germline SDHB mutation or disruption of the SDH protein complex by mutation in another subunit. We aimed to evaluate the effectiveness of using SDHB IHC to predict SDHx germline mutation status in patients with PCC/PGL. We performed a retrospective review of the pathology reports between March 2011-April 2013 which included SDHB IHC on PCC/PGLs from patients who had clinical genetic testing and either tested positive for a SDHx germline mutation or had no identified mutation. Nineteen patients (with 20 tumors) were identified for analysis (ten with no known heritable mutation, three with mutations in SDHB, one SDHC, four SDHD and one SDHD VUS, likely pathogenic based on in silico analysis, tumor multiplicity and positive family history). SDHB staining was evaluated by light microscopy and signal was determined to be negative (no staining), weak cytoplasmic positivity, and moderate to strong cytoplasmic positivity. SDHB IHC results were concordant with the presence or absence of a SDHx mutation in only 11 of the 20 cases. Therefore, we conclude that there is not a strong correlation between known SDHx mutation and SDHB IHC results. In our experience, SDHB IHC does not predict the presence of SDHx mutations and should not replace clinical genetic testing.