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CANCER

Pediatric *SDHB* pheochromocytoma: a link to metastasis

More than 70% of patients who develop a pheochromocytoma or paraganglioma in childhood or adolescence and metastatic disease later in life have been found to harbor a mutation in the *SDHB* gene.

King and colleagues compared the clinical presentation of 32 pediatric patients with pheochromocytoma or paraganglioma who developed metastatic disease with that of 17 pediatric patients who did not develop metastases, as well as with data from adult populations reported in the literature. "We did statistical analysis on the age at presentation (initial symptom onset, initial tumor diagnosis, metastatic diagnosis and metastatic interval), comparing those with an *SDHB* gene mutation and metastatic disease to those with *SDHD*-related or sporadic disease," explains senior investigator Karel Pacak (Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, USA).

The researchers found mutations in the *SDHB* gene in 23 of the 32 patients with metastatic disease whose primary tumor presented in childhood or adolescence, whereas only four of the 17 patients without metastases had mutations in *SDHB*. Furthermore, the study showed that "while *SDHB* gene mutations are associated with a high degree of metastatic development and a low age of initial tumor presentation, the age of initial tumor presentation alone does not predispose to metastatic disease development," explains Pacak.

If patients present with a primary abdominal tumor in childhood or adolescence, in the absence of other indicative signs or symptoms, the investigators suggest that they should first be tested for the presence of *SDHB* mutations. Genetic counseling of these patients should include discussion of the potential disease progression and the need for consistent follow-up. King and co-workers also suggest that all *SDHB* gene mutation carriers should undergo regular screening by measurement of plasma metanephrine and methoxytyramine levels.

This study highlights the need for a diligent follow-up and transition of pediatric patients into adult care. The time interval between initial tumor presentation and development of metastatic disease was 9 years on average, and with primary tumor diagnosis occurring at an average age of 13 years, metastatic diagnosis would occur after the patient has left the care of the pediatric oncologist. "We need to establish a very good screening program for children with *SDHB* gene mutations and put together the best biochemical and imaging approaches to detect this disease early enough," adds Pacak. "Delay in diagnosis means a delay in treatment, which can lead to a poorer prognosis."

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Original article King, K. S. *et al.* Metastatic pheochromocytoma/paraganglioma related to primary tumor development in childhood or adolescence: significant link to SDHB mutations. *J. Clin. Oncol.* doi:10.1200/JCO.2011.34.6353