Study identifies genetic mutations associated with tumor of adrenal gland

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Analysis has identified variations of a gene that are associated with a type of tumor that forms within the adrenal gland, according a study in the December 15 issue of *JAMA*. The age group in which these variations were found are frequently excluded from genetic screening models for this type of tumor.

Pheochromocytomas and paragangliomas are types of tumors. Pheochromocytomas form in the adrenal gland (gland located above the kidney) causing it to make too much adrenaline. Pheochromocytomas can cause high blood pressure, pounding headaches, heart palpitations, flushing of the face, nausea, and vomiting. Paragangliomas are rare, usually benign tumors that may develop at various body sites. Despite a broad spectrum of susceptibility genes for these tumors, the molecular basis for the majority of pheochromocytomas and paragangliomas, including most of the sporadic and rare familial cases, remains unknown, according to background information in the article. "These observations support the existence of additional pheochromocytoma susceptibility genes, which may account for some of the genetically undefined cases," the authors write.

Li Yao, Ph.D., of the University of Texas Health Science Center at San Antonio, and colleagues conducted a study to determine the prevalence in pheochromocytomas and paragangliomas of mutations in the gene FP/TMEM127, a recently identified pheochromocytoma susceptibility gene. The researchers sequenced the FP/TMEM127 gene in 990 individuals with pheochromocytomas and/or paragangliomas, including

898 previously unreported cases without mutations in other susceptibility genes from 8 independent worldwide referral centers between January 2009 and June 2010.

The researchers detected a total of 44 distinct FP/TMEM127 variants in 990 samples from pheochromocytoma or paraganglioma patients. "Of these, 19 mutations found in 20 patients were considered of potential pathogenic significance. Thirteen of these variants were novel changes, while the remainder had been previously reported," the authors write. Mutations were detected only in patients with tumors of adrenal localization (pheochromocytomas) but not with paragangliomas.

The average age at development of FP/TMEM127-mutated tumors was 42.8 years and the median (midpoint) age was 41.5 years, with this age at onset similar to the average age of non-mutated cases in this series, 43.2 years (median, 45 years) and to the reported average diagnostic age for sporadic pheochromocytomas (47 years). The most common presentation was that of a single benign adrenal tumor in patients older than 40 years. Malignancy was seen in 1 mutation carrier (5 percent).

"Germline mutations of FP/TMEM127 were associated with pheochromocytoma but not paraganglioma and occurred in an age group frequently excluded from genetic screening algorithms," the authors write. "Future studies should determine quantitative intracellular effects of individual variants."

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