Mutation spectrum of the CFTR gene in Taiwanese patients with congenital bilateral absence of the vas deferens

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摘要

Abstract

BACKGROUND: Clinically affected cystic fibrosis (CF) patients present a spectrum of genital phenotypes ranging from normal fertility to moderately impaired spermatogenesis and congenital bilateral absence of vas deferens (CBAVD). Little is known about the CF incidence in the Taiwanese population. It has been shown that the CBAVD in men without clinical evidence of CF is associated with a high incidence of mutated CFTR (cystic fibrosis transmembrane conductance regulator) alleles. In order to understand the involvement of the CFTR gene in the aetiology of Asian/Taiwanese male infertility, we screened the entirety of the CFTR gene in 36 infertile males with CBAVD. METHODS: Temporal temperature gradient gel electrophoresis (TTGE) followed by direct DNA sequencing was used. RESULTS: Five mutations, p.V201M, p.N287K, c.-8G>C (125G>C), p.M469I and p.S895N, were found in five of the patients. p.N287K occurred in the first transmembrane-spanning domain, p.M469I in the first ATP-binding domain and p.S895N in the second transmembrane-spanning domain, were novel. In addition, seven homozygous and seven heterozygous 5T alleles in the intron 8 poly(T) tract were found. The overall frequency of CFTR mutant alleles in Taiwanese CBAVD males was 26 out of 72=36%. This finding was lower than the published frequency of CFTR mutations in other ethnic CBAVD patients (ranging from 50 to 74%). The frequency of p.M470V in Taiwanese CBAVD patients is not significantly different from that in the general population (P=0.12). CONCLUSIONS: The results of this study add to the short list of Taiwanese/Asian CFTR mutations. Unlike Caucasian patients, the CFTR mutations cannot account for the majority of Taiwanese CBAVD. This is consistent with the low incidence of CF in the Asian/Taiwanese population. Furthermore, the mutation spectrum of CFTR in CBAVD patients does not overlap with the Caucasian CFTR mutation spectrum