GENETIC ANALYSES OF FAMILIAL ISOLATED HYPERPARATHYROIDISM: IMPLICATIONS FOR CLINICAL ASSESSMENT AND SURGICAL MANAGEMENT

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Familial isolated primary hyperparathyroidism (FIPH) can result either from incomplete expression of a syndromic form of familial primary hyperparathyroidism [multiple endocrine neoplasia types 1 and 2A (MEN 1 and MEN 2A), hyperparathyroidism-jaw tumor syndrome (HPT-JT), or familial hypocalciuric hypercalcemia (FHH)] or still unrecognized causes.

We investigated the involvement of MEN1, HRPT2 and CASR genes by direct sequencing in seven well-characterized Italian kindreds with FIHP, with negative clinical features for MEN 1 and 2A, HPT-JT and FHH. The mean age at diagnosis was 45±17 yr (mean±DS; range 18-70 yr) in the probands and 42±18 yr (range 15-69 yr) in the other affected.

MEN1 mutations were detected in three kindreds. Multiglandular involvement was found in all but one affected subjects belonging to the three kindreds with MEN1 mutation. In these patients persistence/relapse of the disease was observed unless an extensive parathyroidectomy (excision of 3 ? glands) had been performed with the exception of one patient, who is currently normocalcemic 168 months after excision of two glands. No mutations of MEN1, HRPT2 and CASR genes were identified in the remaining four families.

MEN1 genotyping therefore appears worthwhile in FIHP families, since the finding of mutation(s) may predict multiglandular involvement and therefore have practical surgical implications, and prompt further investigation in the family, with the possibility of identifying new cases and beginning a program of periodic surveillance for emergence of tumours in all carriers.

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