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Two Different Pituitary Adenomas in a Patient with Multiple Endocrine Neoplasia Type 1 Associated with Growth Hormone-Releasing Hormone-Producing Pancreatic Tumor: Clinical and Genetic Features

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Abstract. The clinical and genetic features of a 43-year-old male patient with multiple endocrine neoplasia type 1 were reported. He developed hyperparathyroidism, a GHRH-producing pancreatic tumor, and acromegaly between 1980 and 1983. Because his pituitary gland increased in size even after resecting the GHRH-producing pancreatic tumor, transsphenoidal hypophysectomy was performed six years later. The pituitary contained two histologically-different adenomas composed of somatotroph cells and null cells. Genetic analyses revealed loss of heterozygosity on chromosome 11 in common in the pituitary adenomas, the pancreatic endocrine tumors, and a parathyroid hyperplasia. On the other hand, mutations of *ras*, p53, Gsα, and Gi2α genes were not found in these tumors. The loss of the tumor suppressor gene on chromosome 11q12-13 was involved in the formation of two pituitary adenomas, two pancreatic endocrine functioning tumors, and a parathyroid hyperplasia in this patient, but the tumorigenic factors in the specific endocrine organs remain to be studied.

Key words: MEN 1, Pituitary adenoma, Ectopic GHRH-producing tumor, Loss of heterozygosity, Chromosome 11

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MULTIPLE endocrine neoplasia (MEN) is characterized by hyperplasia or neoplasia arising from multiple endocrine organs and classified into types 1, 2A, and 2B according to the combination of affected endocrine organs. Familial MEN 1 is inherited as an autosomal dominant trait and affects specific endocrine organs in the combination of the parathyroid, the pancreatic islet and the pituitary.

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The syndrome of MEN 1 is believed to be caused by a mutation or deletion in the *MEN1* gene on chromosome 11q12-13 [3]. The inactivation of the *MEN1* gene in MEN 1-associated tumors can be demonstrated by loss of heterozygosity (LOH) at the *MEN1* locus, which is localized between *PYGM* and *D11S146* on 11q12-13 [4]. Common LOH on chromosome 11 has been found in pancreatic and parathyroid tumors in MEN 1 patients [3–9], but few studies have been made on the LOH in MEN 1-associated pituitary tumors. Although LOH on chromosome 11 was not found in one MEN 1-associated pituitary adenoma by Byström *et al.* [4],