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Genotype-phenotype analysis and long-term clinical outcome of MEN1-related pancreatic neuroendocrine tumor

Juwan KIM[1], Sung Hyun KIM[1], Hwang Ho KYONG[1], Woo Jung LEE[1], Nam Ki HONG[2], Yumie RHEE[2], Chang Moo KANG*[1]

[1]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Yonsei University, College of Medicine, Republic of Korea
[2]Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University, College of Medicine, Republic of Korea

Background : Multiple endocrine neoplasia type 1 (MEN1) is a rare autosomal dominant disease. Neuroendocrine tumor of the pancreas (PNET) is the leading cause of death in patients with MEN1. Considering that pancreatic tumors are found in the majority of patients with MEN1 during their lifetime, , predicting the progression of PNET is important.We analyze the clinical characteristics of MEN1 patients according to genotype and long-term oncologic outcome of MEN1-related PNET. In addition, relatively few studies had been carried out on the MEN1-related PNET in Asian countries, so we summarized and reported the the short-term and long-term outcome of MEN1 patients after surgery.

Methods : From January 2003 to December 2019, 68 patients diagnosed with MEN1 at Severance Hospital in Seoul, Korea, were retrospectively analyzed.

Results : Among 68 patients with MEN1, 43 patients (61.76%) were diagnosed with PNET and 19 patients (27.94%) underwent pancreatic resection. During the follow-up period, mean of long-term progression-free survival of the observation group was 6.4 years [95% confidence interval: 3.77~9.50]. Also mean of long-term recurrence free survival of the surgery group was 4.35 years [95% confidence interval: 3.27~5.43]. Mutations on exon 2 were 19 (21/65, 32.3%), which was the most common mutation site in the MEN1 gene.There was a significant difference in the penetration of PNET compared to the truncated mutation with others type of mutation (missense, splicing mutation, and no mutation detected) (65.1% vs 34.9%, p=0.003) patients with truncating mutation were diagnosed with PNET in an earlier age (p=0.026). Mutation on Exon2 also showed significant difference on the age-related penetrance of PNET. (p=0.036) Likewise, truncating mutation on Exon2 had significantly earlier diagnostic age. (p=0.022) In the surgery group, patients with a truncated mutation showed a significantly higher risk of recurrence. (54.5% vs 100%, Odd ratio; 1.833, 95% confidence interval 1.069~3.144).

Conclusions : The clinical manifestations of PNET may differ depending on the genetic mutation of MEN1 patients. A more individualized and detailed follow-up strategy may be required in young MEN1 patients with truncating mutations or mutation on exon2. Patients with a truncated mutation or may need more active surveillance after pancreas resection.

Corresponding Author : **Chang Moo KANG** (cmkang@yuhs.ac)