Etiological Observations in Seven Patients with Pancreatic Neuroendocrine Tumors (PNETs)

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Abstract. Background/Aim: Pancreatic neuroendocrine tumors (PNETs) are uncommon malignancies of largely unknown pathogenesis. Observations on patients and their families can provide clues on etiology. Patients and Methods: In a medical oncology practice cohort of 2,087 patients 5 females and 2 males with PNETs have been identified. Results: Observations of etiologic interest have been made in 2 patients with PNETs. One female patient belongs to a kidney cancer family with a balanced translocation t(3;11)(q13;q21). A second female patient with PNET had a de novo translocation (t3;5)(q27;q14), its braking point could contain a tumor suppressor gene. Conclusion: Chromosome studies in patients with PNETs point to an etiologic role of balanced translocations.

Alert clinicians have played a key role in recognizing environmental and genetic influences in cancer etiology (1, 2). Pancreatic neuroendocrine tumors (PNETs) are uncommon malignancies arising from endocrine cells of the pancreas (3). They can be part of hereditary syndromes like MEN-1, Hippel-Lindau disease (VHL), tuberous sclerosis complex and type 1 neurofibromatosis (4). The purpose of this article is to present oncogenetic data of 7 patients with PNETs and their families.

Patients and Methods

Patients. In 30 years of medical oncology practice (start on April 1, 1981), 7 out of 2,087 patients (0.34%) had PNETs: 5 female, 2 male; median age at diagnosis: 57 years, range= 24-74 years (Table I).

Results

Personal history. Patients’ characteristics are summarized in Table I. Three patients died after 1, 2 and 4 years. Two patients had a second malignancy (breast carcinoma, renal cell carcinoma). Two patients had a balanced chromosomal translocation.

Family history. Three of seven family histories (43%) are of special interest. Patient no.5 (female): she was from a second pregnancy. The first pregnancy of her mother resulted in an abortion at week 26. The fetus was a female with Turner syndrome. The mother has been exposed to ionizing radiation as a dentist assistant.

Patient no.6 (female): Her only sister shared the same balanced translocation. One of her three sons had brain cancer at age 6. The mother had kidney cancer at age 76. Six more relatives on the mother’s side had kidney cancer.

Patient no.7 (male): A sister had premenopausal unilateral, hormone receptor-positive breast cancer at age 39 and a carcinoid of the stomach at age 61. The mother had postmenopausal, bilateral, estrogen receptor positive breast cancer at age 66 and 70.

Discussion

In a small cohort of 7 patients with PNETs and their relatives we have made observations of special clinical etiological interest in 4 families (57%). One female patient belongs to a kidney cancer family with a balanced germline translocation involving the long arms of chromosomes 3 and 11. In addition to her PNET she has multilocular cystic renal cell carcinoma, a clear cell carcinoma subvariant. A second female patient had a de novo balanced translocation involving the long arms of chromosomes 3 and 5. The third patient was a male, whose sister had early-age unilateral hormone receptor-positive breast cancer, followed 22 years later by a NET of the stomach and whose mother had bilateral postmenopausal hormone receptor-positive breast cancer.
cancer. The fourth patient was a female with synchronous NET of the pancreas and unilateral triple negative breast cancer at age 49 with a negative family history.

A family history of cancer is a significant risk factor for NETs (5). Having a first-degree relative with any cancer in general, and NET in particular, was a risk factor for NETs. In our sample there was a familial association of PNET with gastric NET, renal and breast cancer.

Chromosomes should be studied in all PNETs families. Loss of heterozygosity (LOH) of chromosome 3 has been reported in 4 out of 8 (50%) sporadic PNETs with hepatic metastases, but in none of 8 sporadic PNETs without hepatic involvement (6). The smallest common-deleted region (SCDR) mapped to 3q27. This region lies in the braking point of the translocation found in patient no.5. It may contain a tumor suppressor gene that is important in the etiology of PNETs.

Conflicts of Interest

The Authors declare no conflicts of interest.

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