A 63-year old male was referred for the evaluation of mass in the pancreas head after routine check-up with abdominal ultrasonography. Fifteen years ago, he underwent left nephrectomy due to renal stone. Nine years ago, he also underwent parathyroidectomy due to hyperparathyroidism. At that time, he was heard of pancreas head mass, but he neglected and not followed-up. He had past medical history of DM, HT, gout and spinal stenosis. His younger sister also underwent nephrectomy and pancreatic resection. The patient denied any systemic symptom except low back pain. Physical examination was unremarkable. The patient’s laboratory data showed Hb 8.5 g/dL, HbA1C 7.2%, potassium 7.2 (3.5–5.5 mmol/L), BUN/creatinine 52/2.4 mg/dL, neuron specific enolase 12.4 (4.7–14.7 ng/mL), chromogranin A 298 ng/mL (27–94), ionized calcium 9.2 (8.5–10.0 mg/dL).

**CASE DESCRIPTION**

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**Figure 1** Abdominal CT findings. (A) Abdominal CT of 9 years ago shows about 1 cm-sized round enhancing mass at pancreas uncinate process (arrow). (B) There is also about 2.4 cm-sized nodular mass at the left adrenal gland (arrow). (C) Abdominal CT at admission shows about 5 cm-sized enhancing mass at pancreas uncinate process. The mass invades superior mesenteric vein and abuts superior mesenteric artery. There is also about 3 cm-sized metastatic LN at peripancreatic space (arrows). (D) Size of the nodular mass at the left adrenal gland is not changed (arrow).
Calcium 1.41 (1.05-1.35 mmol/L), PTH (intact) 178.37 (10-65 pg/mL). Other pituitary, pancreas or adrenal hormone levels were all within normal range. Abdominal CT of 9 years ago showed about 1 cm-sized round enhancing mass at pancreas uncinate process (Fig. 1A). There was also about 2.4 cm-sized nodular mass at the left adrenal gland (Fig. 1B). Abdominal CT at admission showed about 5 cm-sized enhancing mass at pancreas uncinate process. The mass invaded superior mesenteric vein and abutted superior mesenteric artery. There was also about 3 cm-sized metastatic LN at peripancreatic space (Fig. 1C). Size of the nodular mass at the left adrenal gland was not changed (Fig. 1D). MRI Sella revealed no demonstrable abnormal focal lesion in the pituitary gland. Parathyroidectomy specimen of 15 years ago revealed parathyroid hyperplasia.

Pylorus preserving pancreaticoduodenectomy and left partial adrenalectomy was performed (Fig. 2). Adrenalectomy specimen revealed typical adrenal cortical adenoma. Although it was not immunoreactive with synaptophysin, it was strongly immunoreactive with neuron specific enolase, cytokeratin 19 and CD56. It was also focally immunoreactive with chromogranin A. Ki-67 was positive in 3% of nuclei and there was 3 mitosis per 10 high power fields (Fig. 3).

Diagnosis of pancreatic neuroendocrine tumor, grade 2 (WHO classification, 2010) with multiple endocrine neoplasia type I (MEN 1) was made. Peripancreatic tissue invasion and lymph node metastasis in two out of 26 lymph nodes were noted (AJCC 7th pathologic stage, pT3N1). His sister, son and daughter also have some features of MEN 1 (Fig. 4). At the gene analysis of MEN 1 on Chromosome 11q13 from the genomic DNA isolated from peripheral blood leukocytes of
The term "multiple endocrine neoplasia" was first used by Steiner in the late 1960s when he described three distinct endocrine disorders. The first disorder, multiple endocrine neoplasia type I (MEN 1) (also known as Wermer syndrome), described patients with familial pituitary, parathyroid, and pancreatic islet cell tumors. Today, the term "multiple endocrine neoplasia" refers to three autosomal dominant disorders: MEN 1, MEN 2A, and MEN 2B.

MEN 1 is an autosomal dominant disorder caused by germline mutations of the MEN1 gene, a tumor suppressor gene located on chromosome 11q13 that encodes the protein menin. The exact function of menin is unknown, but it is involved in DNA replication and repair, transcription, and chromatin modification. Affected individuals are predisposed to develop tumors primarily of the anterior pituitary, parathyroid, and endocrine pancreas. However, combinations of over 20 various endocrine and nonendocrine tumors have been described in patients with MEN 1. Other clearly associated endocrine tumors include foregut carcinoids (thymic, bronchial, gastric, and duodenal) and adrenocortical lesions. The initial manifestation of individuals with MEN 1 usually occurs during late adolescence or early adulthood. The specific endocrine gland involved and the age of onset is variable among individuals and families, but primary hyperparathyroidism is commonly the initial endocrinopathy. The high penetrance of MEN 1 is evident in that half of affected patients show biochemical manifestations of the disease by 20 years of age. Nearly 100% of patients are symptomatic by age 60 years.

MEN 1 is diagnosed clinically for patients who develop two or more of the classic tumors associated with the disease (pituitary, parathyroid, or endocrine tumors of the pancreas or duodenum), or for

![Figure 4 - Pedigree. His sister, son and daughter also have some features of MEN 1.](image-url)
patients who have one of the classic tumors and at least one close relative with a clinical diagnosis of MEN 1.4

Approximately 90% of patients with classic, familial MEN 1 have an identifiable mutation.5 There is a wide range of mutation types within the MEN1 gene and often specific mutations are unique to each family. To date, no genotype-phenotype correlations have been established as many as 10% of patients are found to have a de novo mutation of the MEN1 gene, in which case the family history is noncontributory.7

REFERENCES