CCKoma

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ABSTRACT

Cholecystokinin (CCK)-secreting neuroendocrine tumors (CCKomas) are very rare neuroendocrine tumors of the pancreas. CCKomas can present with persistent non-watery diarrhea, weight loss combined with more specific symptoms of gallbladder disease and duodenal ulcer disease. The diagnosis is based on elevated circulating CCK levels in the absence of elevated circulating gastrin concentrations.

INTRODUCTION

In 1928, the famous US physiologist Andrew Conway Ivy and the neurosurgeon Eric Oldberg isolated the hormone cholecystokinin (CCK) from jejunal extracts. CCK belongs to a large peptide family, but in humans CCK and gastrin are the only family members. Both peptides are ligands for the CCK1 and CCK2 receptors (1).

PHYSIOLOGY OF CHOLECYSTOKININ

CCK peptides have local acute digestive effects including stimulation of gallbladder contraction and gut motility, stimulation of pancreatic enzyme secretion, and stimulation of acid secretion from the stomach (1). CCK also is a growth factor and neurotransmitter in the brain and peripheral neurons (1). CCK stimulates calcitonin, insulin, and glucagon secretion, and may act as a natriuretic peptide in the kidneys, sperm fertility factor, cytokine, and marker of heart failure. CCK is derived from proCCK and its plasma forms are CCK-58, -33, -22, and -8, whereas CCK-8 and -5 are neurotransmitters (1). CCK expression has also been encountered at variable amounts in different neuroendocrine tumors, like corticotroph pituitary tumors, medullary thyroid carcinomas, and pheochromocytomas and other neoplasms such as Ewing's sarcomas, cerebral gliomas, astrocytomas, and acoustic neuromas. However, its expression in these tumors has never been associated with increased concentrations of CCK in plasma or the presence or symptoms thereof (1).

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A few case reports of patients with metastatic neuroendocrine pancreatic tumors presenting with a specific CCKoma syndrome were recently published; the first case being described by the Danish biochemist Jens Rehfeld and his clinical colleagues (2). These case reports further suggest that circulating CCK may be a useful tumor marker in neuroendocrine tumor patients (2,3). For proper CCKoma diagnosis, assays that distinguish sulfated CCK from nonsulfated CCK and gastrin are required (1).

Symptoms that should raise CCKoma suspicion are: 1. persistent non-watery diarrhea; 2. weight loss, 3. combined with more specific symptoms of gallbladder disease and duodenal ulcer disease (1-3). Since the

clinical presentation of CCKoma could mimic gastrinomas, because CCK peptides are full agonists of the gastrin/CCK-B receptor, circulating gastrin concentrations should not be elevated in the presence of elevated circulating CCK levels in CCKoma patients (1-3). The CCKoma syndrome is very rare. It has been suggested that some gastrinoma patients with nondetectable serum gastrin levels might represent misdiagnosed CCKoma patients awaiting correct diagnosis. However, in a series of 284 patients with neuroendocrine tumors of the gastrointestinal tract and pancreas, and/or with metastases in the liver, only one CCKoma patient could be identified who also presented with typical symptomatology (3).

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