Primary adrenal carcinoid: An unusual localization

Primer adrenal karsinoidi: Mutad olmayan bir lokalizasyon

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ÖZET: *Karsinoid tümörlerin mutad lokalizasyonları apendiks ve terminal ileumdur. Karsinoid tümörler, nadiren, gastrointestinal sistemin diğer bölgelerinde, çok daha nadiren de timüs, gonadlar, ve bronş ağacı gibi gastrointestinal sistem dışındaki organlarda lokalize olabilmektedirler. Venöz dreajı karaciğerden geçmeyen karsinoid tümörlerde erken devrede karsinoid sendrom gelişebilmektedir. Adrenal gland karsinoid tümörler için oldukça mutad-dışı bir lokalizasyondur. Biz burada daha önceki devrede ishali olan ve bize sağ hipokondriumda, sonuçta adrenal karsinoid olduğu anlaşılan, bir kitle ile müracaat eden hastayı bildiriyoruz. Hasta sağ adrenalektomi ile, başarılı olarak, tedavi edildi. Karsinoid tümörün yerleşebileceği başka bir alan bulunamadığından ve adrenalektomi sonrasında hastanın ishali tümüyle kaybolduğundan saptanan tümörün primer olduğu kabul edildi.*

Anahtar kelimeler: **Karsinoid tümör, adrenal**

SUMMARY: *The usual locations of carcinoid tumors are appendix and terminal ileum. Carcinoid tumors may rarely arise from other parts of gastrointestinal tract as well, and very rarely from extragastrointestinal organs such as thymus, gonads, and bronchial tree. Carcinoid syndrome may develop early in carcinoid tumors where their venous drainage is not entering the liver. Adrenal gland is a very unusual localization for carcinoid tumors. We describe here a patient presented with diarrhea and a right hypochondrial mass which was proved to be a carcinoid tumor. The patient was successfully treated by right adrenalectomy. Because no other site of carcinoid was found. The diagnosis of primary adrenal carcinoid was made.*

Key words: **Carcinoid tumor, adrenal**

OVER 90% of carcinoid tumors originate in the gastrointestinal tract, the most frequent enteral sites are the appendix, terminal ileum and rectum. The colon, stomach, duodenum, and Meckel's diverticulum are less frequently involved. Carcinoid tumors rarely arise in the biliary tract, pancreatic duct, esophagus, and thymus and gonads. Bronchial carcinoids, originating from the enterochromaffin cells in the epithelium of the bronchial tree were also reported (1).

We report here a case of primary adrenal carcinoid, successfully managed by adrenalectomy.

CASE REPORT

75 yr-old woman was admitted with a continuous right hypochondrial pain and intermittent colic type abdominal pain radiating to the back associated with diarrhea for the last three months. The patient was otherwise well. In physical examination the right hypochondrium was tender to palpation and a mass was palpable just under the right costal margin. Blood pressure was 140/90 mmHg. Physical examination was otherwise normal. Her past history was negative. In laboratory examination: The red blood cell sedimentation rate: 11 mm/h, hematocrit: 43%, hemoglobin: 132 g/l, platelets: $211X10^9/1$, WBC: $4.6X10^9/1$, WBC differential count: normal, MCV: 106, BUN: 19 mg/dl, creatinine: 1.2 mg/dl, glucose: 105 mg/dl, albumin: 35 g/l, globulin: 32 g/l, alkalen phosphatase: 10.5 KAU (Normal: 3-10 KAU), cholesterol: 311 mg/dl, Bilirubin: 0.88 mg/dl, AST: 8 U/l, ALT: 12 U/l, Sodium: 145 meq/l, Potassium: 4.5 meq/l. No abnormality was found in urinalysis. Ultrasonographic examination revealed a 5X4X3 cm. solid mass in right adrenal gland. Computed tomography confirmed this finding (Fig 1). The mass was initially considered as a metastatic lesion and a search for a possible primary focus was undertaken: Chest X-ray, thorax CT, upper and lower GI series did not reveal any lesion. Sigmoidoscopic examination was also negative. In the 5 days period of hospitalization, the main complaint of the patient was worsening right hypochondrial pain. The patient passed one or two unformed stools daily preceded by a colicky abdominal pain. Daily stool volume was 280 g and examination of stool revealed no ova or parasites. There was neither mucus nor white blood cells and culture of the stool revealed no pathogenic bacteria. In the sixth day, exploration of the right adrenal was performed by a right lombotomy incision under general anesthesia. The mass was closely adjacent to right adrenal gland and it was extirpated

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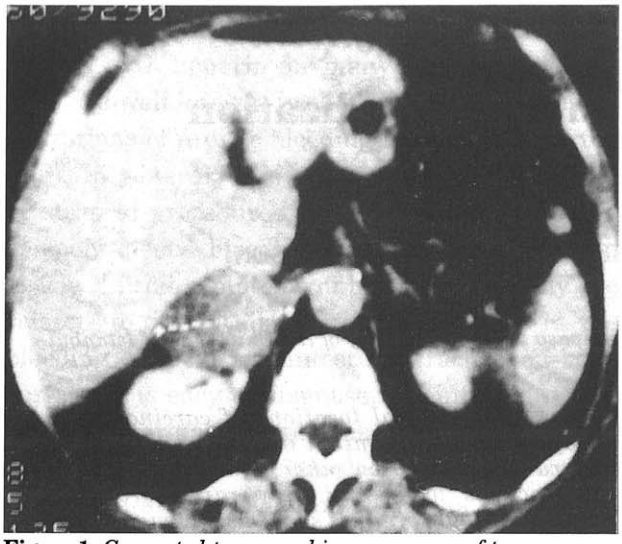

Figure 1. *Computed tomographic appearance of tumour.*

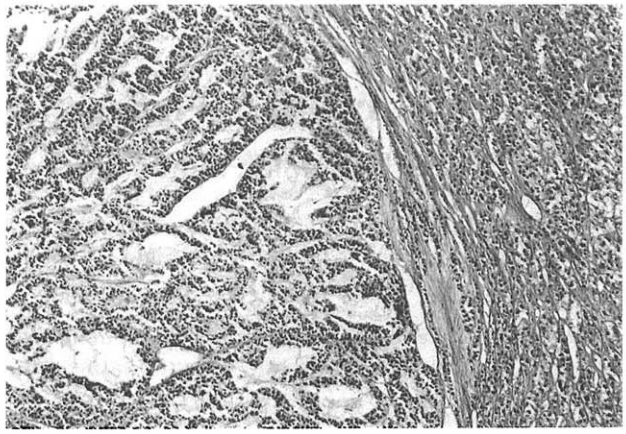

Figure 2. *Carcinoid tumour in the adrenal gland: Montoneous tumour cells forming trabecular and glandular structure. H/E X 80.*

with it. Pathologic examination revealed a tumor in the adrenal gland measuring 5 cm, well demarcated and encapsulated. The adrenal tissue was compressed by the tumor and was 3X2X1 cm. In the cut surface of the tumor, there were necrotic and haemorrhagic areas. Histologic examination showed carcinoid tumor composed of monotonous appearing cells of trabecular and glandular like pattern (Fig 2). The acidic mucosubstance in the glandular spaces was demonstrated with Alcian Blue pH 2.5/PAS and Mayer's mucicarmine stains (Fig 3). In the immunohistochemical investigation, tumor cells were stained with neuron specific enolase (NSE), (Dako Corporation), (Figure 4). The tumor had invaded the adrenal medulla. The adrenal cortex around the tumor was intact. Pathologic diagnosis was carcinoid tumor. After the diagnosis of carcinoid tumor was made in the post-operative period, serum serotonin and urinary 5-hydroxyindolacetic acid (5-HIAA) levels were measured and both were in the normal range. The patient was free of pain and diarrhea in the first week following operation. In a repeated test, urinary 5-HIAA and VMA and serum serotonin levels were in the normal range. There was neither abdominal pain nor diarrhea. The patient was discharged on the 12th post-operative day in excellent health.

DISCUSSION

Carcinoid tumors arise from the enterochromaffin cells. Enterochromaffin cells belong to a larger family that shares the features of amine content, precursor aptake, and decarboxylation, hence the term of APUD (1). The complex of symptoms and signs that comprise the carcinoid syndrome includes diarrhea, abdominal cramps, borborygmi, episodic flushing, telangiectasia, cyanosis, pellegra-like skin lesions, bronchospasm with wheezing and asthma-like attacs, dyspnea, and murmurs of valvular lesions of the heart. These signs and symptoms result from increased production of a variety of substances with pharmacologic and physiologic functions represented principally by.

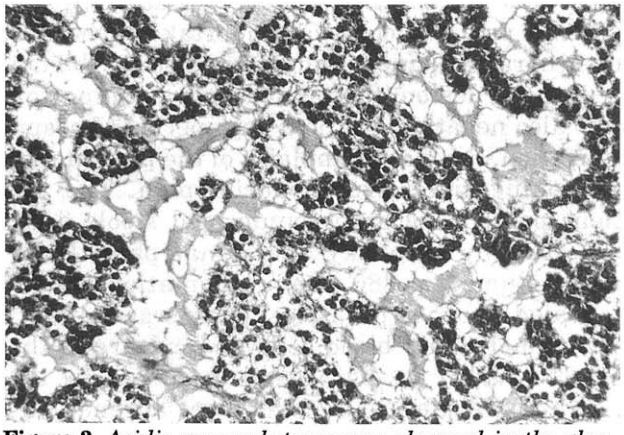

Figure 3. *Acidic mucosubstance was observed in the glandular space. Mayer's mucicarmine X 200.*

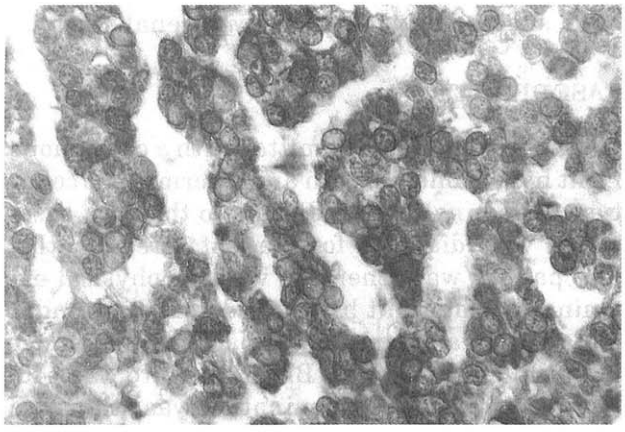

Figure 4. *Tumour cells reacted positively with NSE. X 500.*

5- hydroxytriptamine (serotonin), 5-hydroxytryptophan (5-HTP), kinin peptides, histamine, catecholamines, and prostaglandins. Insulin, adrenocorticotropic hormone (ACTH), melanophore-stimulating hormone (MSH), glucagon, gastrin, parathormone, vasoactive intestinal peptide (VIP), gastric-inhibiting polypeptide (GIP), ACTH releasing factor (CRF), calcitonin, vasopressin (ADH), substance P, neuropeptide K, neurokinin A (substance K), motilin, methionine enkephalin, and beta-endorphin are also secreted excessively in this syndrome (1).

Our patient initially presented with a mass in abdomen and pain related to it. At the admission to the hospital, unexplained diarrhea was present as well, but we failed to suspect carcinoid syndrome (CS), because, the main concern was the mass adjacent to right adrenal gland and, the other systemic signs and symptoms suggestive of CS were absent. Given to our failure to suspect carcinoid in the pre-operative period, we did not have the levels of serum serotonin and urinary 5-HIAA measured. Normal levels of this substances in blood and urine in the post-operative period shows successful extirpation of carcinoid tumor.

In a study reporting the localization of this tumor in 2837 cases (2), the main location was appendix (77.3%), followed by small intestine (33.7), rectum and rectosigmoid (1.3%), lung and bronchi (0.6), and stomach (0.3%). In another study evaluating 103 metastatic carcinoid tumor cases (3), the main location was ileum (73%), followed by bronchi (6.8%), jejunum (3.9%), cecum (2.9%), appendix (1.9%), mediastinum (0.9%), duodenum (0.9%), and rectum (0.9%).

The histologic differential diagnosis of the carcinoid tumor in the adrenal gland includes medullary paraganglioma and pheochromocytoma. All these tumors derive from neuroendocrine cell-line and ultrastructurally they contain neurosecretory granules. Immunohistochemically they are stained with NSE. A carcinoid tumor with a dominating solid pattern may be confused with paraganglioma and pheochromocytoma. However, in the latter two tumors, typically Zellbalen pattern is observed, tumor cells are larger than carcinoid tumors and mucosubstance is never observed. Furthermore pleomorphism between the tumor cells is frequently seen in pheochromocytoma (4). In the presented case positive reaction of the tumor cells with NSE revealed neuroendocrine origin. However the lack of Zellbalen pattern and the presence of mucosubstance containing glandular pattern and the general monotonous structure eliminated the possibilities of paraganglioma and pheochromocytoma. Carcinoid tumors in the adrenal gland are generally metastatic (4). However in the presented case, no evidence of an underlying primary tumor was found. Besides serum serotonin and urinary 5-HIAA levels were in the normal range in the early postoperative period in repeated tests and patient's diarrhea subsided accordingly. The origin of the carcinoid tumor of the gastrointestinal tract and many other organs are the endocrine cells. It has been widely accepted that these cells and the cells of other endocrine glands share the same neuroendocrine cell-line (5). The origin of gastrointestinal carcinoid tumor is the endocrine cells localized in the mucosa and submucosa (6). Endocrine cells in the submucosa have been regarded as Schwanien cell origin (7,8). Although rare, there are tumors of gastrointestinal tract and adrenal medulla, like ganglioneuroma and paraganglioma, that show Shwanien cell differentiation (9,10). Since the carcinoid tumors and adrenal medulla share the same phylogenetic background and in the view of the above discussion, it can be concluded that the presence of carcinoid tumor in the adrenal medulla is also possible.

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