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Case Report / Olgu Sunumu

A thymic neuroendocrine carcinoma presenting with upper gastrointestinal bleeding: A case report

Üst gastrointestinal kanama ile birlikte seyreden timik nöroendokrin karsinom: Olgu sunumu

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ABSTRACT

Neuroendocrine carcinomas of the thymus are rare clinical entities, which can be complicated by endocrine abnormalities. These tumors are frequently associated with ectopic adrenocorticotropic hormone production giving rise to Cushing's syndrome. Herein, we describe a 23-year-old male case with upper gastrointestinal bleeding as the initial presentation of a thymic neuroendocrine carcinoma. This case was reported due to its extremely exceptional occurrence.

Keywords: Gastrointestinal bleeding; thymic carcinoma; thymus.

ÖZ

Timusun nöroendokrin karsinomları nadir klinik durumlar olup, endokrin anormallikler ile komplike olabilir. Bu tümörler sıklıkla ektopik adrenokortikotropik hormon salgısı ile ilişkili olup, Cushing sendromuna neden olabilirler. Bu çalışmada, timik nöroendokrin karsinomun ilk bulgusunun üst gastrointestinal kanama olduğu 23 yaşında bir erkek olgu sunuldu. Bu olgu, son derece nadir olması nedeniyle sunuldu.

Anahtar sözcükler: Gastrointestinal kanama; timik karsinom; timus.

Most thymic neuroendocrine tumor cases are completely asymptomatic initially and imaging studies for other reasons often incidentally detect thymic neuroendocrine tumors.[1] Clinical symptoms usually occur at a later stage of the disease, including chest discomfort, superior vena cava syndrome, dyspnea, and cough.[1] Occasionally, they may present with symptoms related to an associated endocrinopathy.[2] Herein, we describe a 23-year-old male case with upper gastrointestinal bleeding as the initial presentation of a thymic neuroendocrine carcinoma.

CASE REPORT

A 23-year-old man was admitted to the hospital with abdominal pain and blood in the vomit. Laboratory testing revealed normochromic-normocytic anemia with positive results of occult blood in the stool, hyperglycemia, and hypokalemia. Upper endoscopy revealed active gastric ulcer, likely causing gastrointestinal bleeding. Serum cortisol, adrenocorticotropic hormone (ACTH), and urinary free cortisol levels were analyzed due to hypokalemia. At presentation, his serum cortisol level was 81.46 µg/dL (reference range: 2.3-19.4 µg/dL), ACTH was 1,237 pg/mL (reference range: 5-46 pg/mL), and urinary free cortisol was 22,000 µg/24 h (reference range: 0-60 µg/24 h). Thoracic computed tomography (CT) revealed a 4 cm anterior mediastinal mass on thymic location (Figure 1), and abdominal CT demonstrated bilateral adrenal hyperplasia. Thyroid

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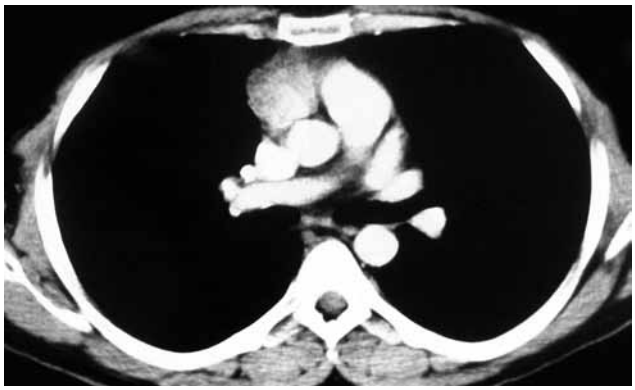

Figure 1. Computed tomography showing an anterior mediastinal mass.

Figure 2. An intraoperative view of the lesion.

ultrasonography (USG) and pituitary magnetic resonance imaging (MRI) findings were normal. On physical examination, hypertension was noted without a Cushingoid appearance. The patient was scheduled for surgery.

A written informed consent was obtained from the patient. Surgical resection was performed by a median sternotomy and the thymic tumor was excised with all the anterior mediastinal adipose and thymic tissues (Figure 2). Histopathological examination revealed a neoplasm composed of fairly uniform, small, round or oval cells with a narrow cytoplasm, organized either in diffuse sheets or trabeculae and in somewhat an organoid pattern (Figures 3a, b). Tumor cells were positive for cytokeratin AE-1/AE-3, synaptophysin, chromogranin, and neuron-specific enolase (NSE) (Figures 4a-d) and negative for thyroid transcription factor-1 (TTF-1). Based on these findings, the patient was diagnosed with a well- differentiated neuroendocrine carcinoma (typical carcinoid tumor), pigmented variant. Although apparently tymic elements were not seen, the age of the patient, the localization of

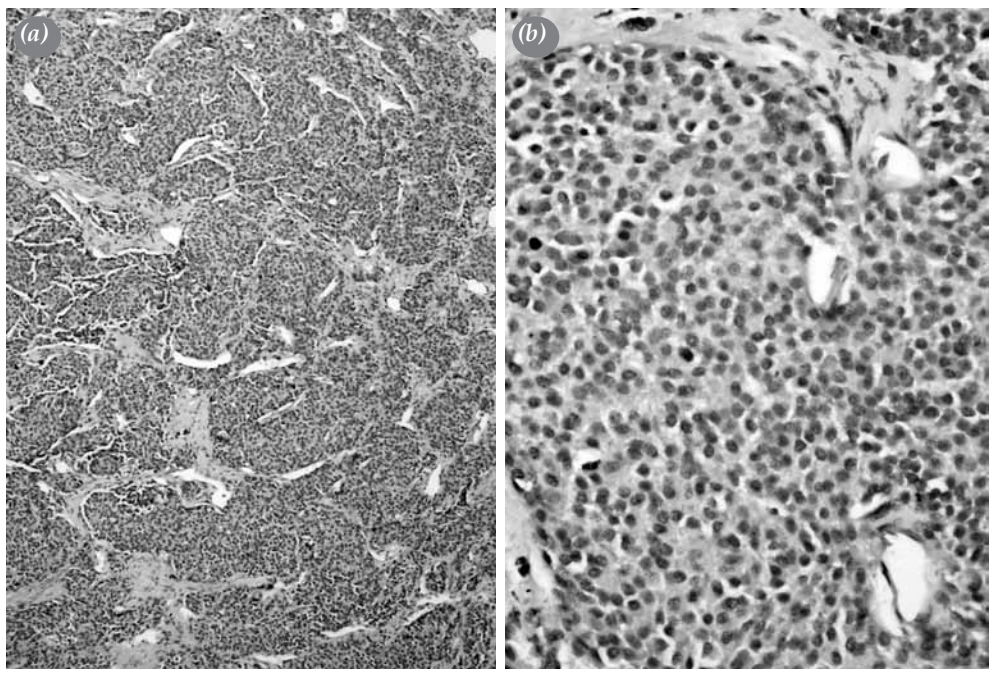

Figure 3. (a) Organoid pattern of the tumor composed of diffuse sheets and trabeculae in hyalinized stroma with delicate vascular structures (H-E × 100), **(b)** made up of small and fairly uniform cells with a narrow cytoplasm (H-E × 200).

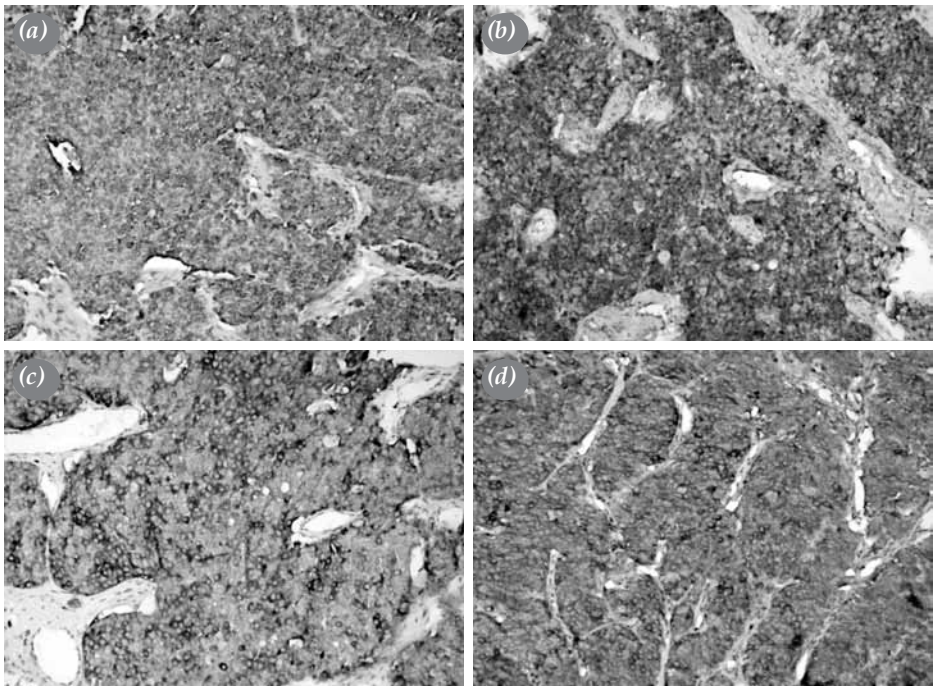

Figure 4. (a) Tumor cells were positive for CK AE-1/AE-3 (DAB × 100), **(b)** synaptophysin (DAB × 100), **(c)** chromogranin and (DAB × 100), **(d)** neuron-specific enolase (DAB × 100).

the tumor, and TTF-1 negativity suggested that that the tumor was originated from the thymus, rather than to be metastatic. All removed lymph nodes were tumor-free. Due to the aggressive nature of the tumor with a high incidence of locoregional recurrence following surgery, postoperative radiotherapy with thoracic fields (45-60 Gy) was added. The patient recovered well, and six months after resection, ACTH level was 36.9 pg/mL and serum cortisol level was 7.76 μg/dL. Serum potassium and phosphorus levels also returned to normal values. Three years after resection, there are no signs of recurrence, and the laboratory results are still normal.

DISCUSSION

Primary neuroendocrine tumors of the thymus are capable of producing a variety of biogenic amines.[2] Since 1972, approximately 400 primary neuroendocrine tumor cases of the thymus have been reported, and only 46 of them presented with ACTH production and Cushing syndrome.[2,3] Sapmaz et al.[4] reported an atypical carcinoid tumor arising from the thymus complaining of difficulty in breathing, hypertension, and Cushing's syndrome with elevated ACTH and cortisol.

These tumors typically manifest in one of the following four ways: They may be asymptomatic and found incidentally on routine chest radiography, they may produce symptoms of thoracic structure displacement or compression, they may present with symptoms related to associated endocrinopathy, or they may manifest with signs and symptoms relating to a distant metastasis, most commonly to the liver, lung, pancreas, pleura, and bone.[5] It has been estimated that over one-third of patients are asymptomatic and are incidentally diagnosed. Most patients present with signs and symptoms related to a rapidly expanding mediastinal mass, such as cough, chest pain, and superior vena cava syndrome.[5] Indeed, our case presented with upper gastrointestinal bleeding due to associated endocrinopathy along with an underlying thymic carcinoid. There are some thoughts on how corticosteroids may compromise the gastric mucosa. Reduction of gastric mucus secretion, inhibition of mucosal prostaglandin synthesis, and gastric cell hyperplasia resulting in increased acid secretion have been proposed.[6] Therefore, in patients with peptic ulcer disease, clinician should be alert to the possible endocrine pathologies.

Surgery remains the gold standard for the treatment of thymic neuroendocrine tumors which usually involves en-bloc resection of the tumor with the pericardium, pleura, and/or great vessels. In our case, the thymic tumor due to gastrointestinal bleeding was

early detected, and the tumor was localized and did not reach to a size to create invasion. The tumor and all the anterior mediastinal adipose tissues between the phrenic nerves were resected. It is important to excise the anterior mediastinal adipose tissue as much as possible, as ectopic thymic tumors often distribute in any part of the anterior mediastinal adipose tissue.

Thymic carcinoid tumors are sometimes associated with multiple endocrine neoplasia (MEN) syndromes, particularly MEN-1.[4] Parathyroid, pancreatic, and pituitary tumors are the major components of the disease. In our case, thyroid USG and pituitary MRI findings were normal and no adrenal and pancreatic adenoma was identified on abdominal CT. There was also no family history, and no association with MEN syndromes was suspected.

The overall five- and 10-year survival rates of patients with thymic neuroendocrine tumors are reported to be 28% and 10%, respectively.[7] These tumors tend to be very aggressive, and over 70% of patients develop locoregional or distant metastasis within five years of diagnosis, despite resection and adjuvant therapy. Additionally, about 35% of patients have systemic symptoms at the time of presentation, due to associated endocrinopathies and paraneoplastic syndromes.[7]

The role of either adjuvant radiotherapy or chemotherapy still remains controversial and no established criteria are available for adjuvant treatment. As local recurrence occurs relatively often, there may be a benefit of adjuvant radiotherapy.[7] In our case, all removed lymph nodes were tumor-free and no distant metastasis was detected. Therefore, no adjuvant chemotherapy was considered. Temozolomide and platinum-based chemotherapy may be used in patients with distant metastases or unresectable tumors.[8] Three years after resection, our patient has no evidence of recurrence and laboratory results are still normal.

In conclusion, thymic carcinoid tumors may present with symptoms of associated endocrinopathies and endocrine background may be the first presentation of the disease. Even rare, suspicion regarding this possibility should be kept in mind.

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