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Case Report / Olgu Sunumu

Simultaneous resection of thymic and bronchial carcinoid tumors in a patient diagnosed with multiple endocrine neoplasia type 1

Multipl endokrin neoplazi tip 1 tanılı bir hastada timik ve bronşiyal karsinoid tümörlerin eş zamanlı rezeksiyonu

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ABSTRACT

Thymic carcinoid tumors are rare tumors which may be associated with multiple endocrine neoplasia type 1. Bronchial carcinoids are also rare tumors and associated with multiple endocrine neoplasia type 1. Coexisting of thymic and bronchial carcinoid tumors in this case is extremely rare. Herein, we report a unique case of coexistence of thymic and bronchial carcinoid tumors which were simultaneously resected via thoracotomy.

Keywords: Carcinoid tumor, multiple endocrine neoplasia type 1, resection.

ÖZ

Timik karsinoid tümörler nadir tümörler olup, multipl endokrin neoplazi tip 1 ile birlikte görülebilirler. Bronşiyal karsinoidler de nadir tümörler olup, multipl endokrin neoplazi tip 1'e eşlik edebilirler. Bu durumda timik ve bronşiyal karsinoid tümörlerin birlikteliği oldukça enderdir. Bu yazıda, torakotomi ile eş zamanlı rezeke edilen timik ve bronşiyal karsinoid tümörlerin benzersiz bir birlikteliği olgusu sunuldu.

Anahtar sözcükler: Karsinoid tümör, multipl endokrin neoplazi tip 1, rezeksiyon.

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant disease characterized by the occurrence of the tumors involving the endocrine glands usually parathyroid glands, pancreas, and pituitary gland.[1] Less frequently, several other tumors of neuroendocrine origin may emerge in the course of the disease. Thymic carcinoid tumors are rare tumors which may be associated with MEN1.[2] Bronchial carcinoid (BC) tumors have also been rarely described and associated with MEN1.[3,4] In addition, coexistence of thymic and BC tumors in MEN1 is extremely rare.

Herein, we report a unique case of coexistence of thymic and BC tumors which were simultaneously resected via thoracotomy.

CASE REPORT

A 36-year-old male patient with a history of nephrolithiasis presented with abdominal pain and flatulence. Hand-foot enlargement, facial coarsening and multiple skin tags were noted on physical examination. Abdominal computed tomography (CT) revealed two pancreatic lesions suggesting a neuroendocrine tumor. Multiple renal stones and a hypoattenuating cystic adrenal mass in the left adrenal gland were also detected. Laboratory analysis demonstrated hypercalcemia and hypophosphatemia due to primary hyperparathyroidism. Pituitary hormone profile confirmed growth hormone excess and revealed hyperprolactinemia due to putative pituitary stalk

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Table 1. Laboratory test results

Parameter	Value	Reference range
Corrected calcium (mg/dL)	12.3	8.4-10.5
Phosphorus (mg/dL)	2.3	2.5-4.5
25-OH vitamin D (µg/dL)	20.7	20-30
Parathormone (pg/mL)	198	12-88
GH (ng/mL)	8.1	0-3
IGF-1 (ng/mL)	1092	140-405
Prolactin (ng/mL)	128	1.9-17.2
ACTH (pg/mL)	11	0-46
Cortisol (µg/dL)	1.5	6.7-22.7
TSH (µIU/mL)	0.3	0.4-5.3
fT4 (pmol/L)	7.0	7.9-14.4
fT3 (pmol/L)	4.0	3.8-6
FSH (mIU/mL)	3.6	0.7-18
LH (mIU/mL)	2.7	2.4-10
Testosteron (ng/dL)	132	240-871

25(OH) vitamin D: 25- hidroksi vitamin D; GH: Growth hormone; IGF: Insulin-like growth factor; ACTH: Adrenocorticotropic hormone; TSH: Thyroid stimulating hormone; fT4: Free thyroxine; fT3: Free triiodothyronine; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone.

compression. Other pituitary axes were affected as well, and the patient had panhypopituitarism (Table 1). All parathyroid glands were enlarged as assessed by ultrasonography, and magnetic resonance imaging indicated a 31-mm macroadenoma located in the pituitary gland. Based on confirmatory medical history, presenting symptoms and imaging findings, the patient was clinically diagnosed with MEN1 syndrome. To determine the extent of neuroendocrine system involvement, positron emission tomography (PET)/CT was performed. Multiple accumulations in the pancreas (SUV_{max}: 6.4), pituitary (SUV_{max}: 7.4), right lobe of the thyroid (SUV_{max}: 4), thymic tissue (SUV_{max}: 6.7), and left adrenal gland (SUV_{max}: 2.7) were observed.

A written informed consent was obtained from the patient and he underwent partial pancreatectomy with retroperitoneal lymphadenectomy, splenectomy, hemithyroidectomy, and parathyroidectomy. Postoperative thoracic CT revealed a partially calcified thymic mass (Figure 1a) and an additional three lung nodules in the lower lobe (Figure 1b and c), compatible with a BC tumor. The patient underwent extended thymectomy and right lower lobectomy combined with mediastinal lymph node dissection via a right thoracotomy (Figure 2). On histopathological examination, all tumors showed neuroendocrine features. Neoplasms were composed of monotonous population of cells with a scant-to-moderate amount of cytoplasms, bland-looking, round-to-oval nuclei with a salt-and-pepper chromatin pattern. A delicate capillary network surrounding the tumor nests and trabeculae was seen (Figure 3a). No necrosis was present. However, the peripheral pulmonary tumor and the thymic tumor were mitotically active (8 and 7 mitoses per 10 high power fields (hpf) with a Ki-67 proliferation index of 10% and 8%, respectively) (Figure 3b). These tumors were diagnosed as intermediate-grade neuroendocrine neoplasms, which could be considered as atypical carcinoid tumors. Bronchial tumors showed no mitotic activity and revealed a Ki-67 proliferation index of 1%, which is consistent with a typical carcinoid tumor. Neuroendocrine nature of neoplasms was also confirmed by immunohistochemical stain for CD56 (Figure 3c). The postoperative course was uneventful, and the patient was discharged on the postoperative ninth day. He is still on the waiting list for pituitary surgery.

DISCUSSION

Thymic carcinoid tumors, which usually occur in the third or fourth decade of life, are associated with

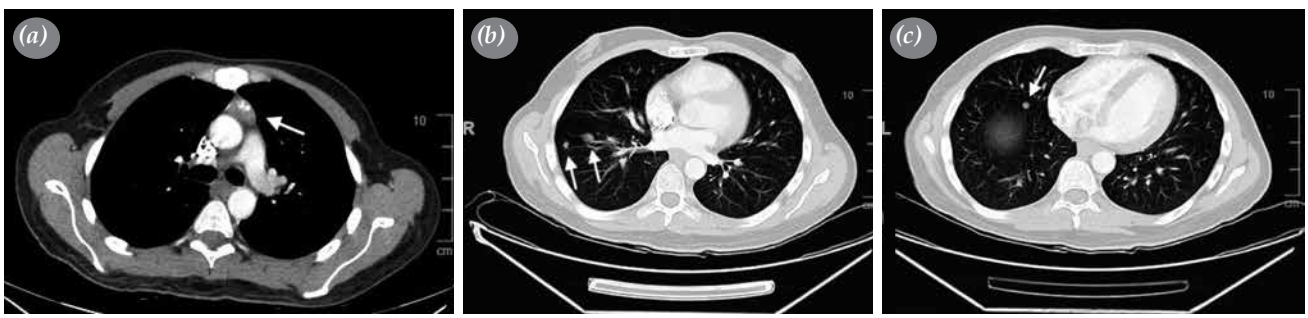

Figure 1. (a) Thoracic computed tomography revealing a partially calcified thymic mass and **(b, c)** an additional three lung nodules in lower lobe.

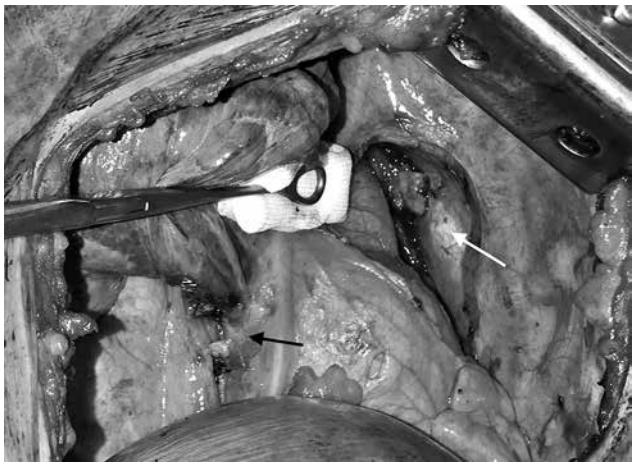

Figure 2. A right thoracotomy view following extended thymectomy (white arrow) and right lower lobectomy (black arrow).

smoking and male gender. They are associated with MEN1 in 3.1 to 8% of cases.[5-7] The prevalence of BC tumors in patients with MEN1 has been reported to be between 5 and 31% with a variable gender predominance.[3,4,8] Thus, the simultaneous occurrence of these tumors in patients with MEN1 is unique. To the best of our knowledge, this is the second reported case of coexistence of thymic and BC tumors associated with MEN1.

The natural history of MEN 1-related carcinoids and their management strategies have not been clearly understood yet, due to the limited number of cases in the literature. Based on the results of previous studies, MEN1-associated carcinoid tumors are important determinants of long-term survival. Although these tumors are associated with poor prognosis, bronchial subtypes have a more indolent natural history, taking the potential for metastasis and recurrence after resection into consideration.[9-11] In addition, BC tumors may be multicentric and may develop both synchronously and metachronously in the same patient.[4] Therefore, these patients should be closely followed postoperatively for potential occurrence of recurrent or metachronous disease. On the other hand, thymic carcinoids carry poor prognosis.[5,7,8,10] In their study, Ospina et al.[3] reported that only one of seven patients was free of recurrence after a five-year follow-up, and the cause of death was related to a thymic carcinoid in 43% of the remaining patients.[3] Therefore, close follow-up should be the mainstay of the management strategy following thymic carcinoid resection. Also, thymic carcinoid tumors are typically a late manifestation of MEN1 and, thus, its occurrence during the initial

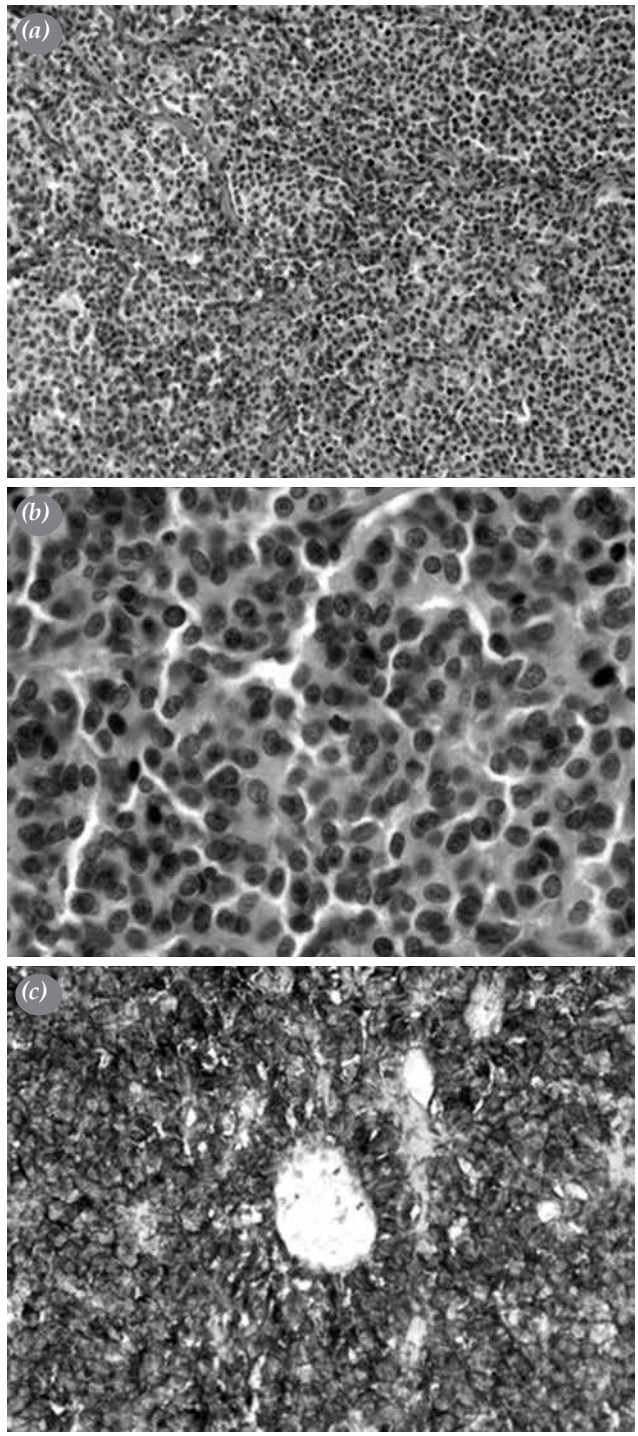

Figure 3. (a) Histopathological features of tumors. A delicate capillary network surrounding tumor nests and trabeculae were seen. **(b)** Both tumors were mitotically active. **(c)** Immunohistochemical staining of the tumor cells with CD56.

manifestation is unexpected.[5] However, in our case, thymic lesion was detected with PET/CT during the initial screening and was, then, confirmed by

thoracic CT. Early detection of thymic carcinoids before invading the neighboring structures increased the likelihood of R0 resection in our case.

From the surgical standpoint, management of synchronous thymic and pulmonary lesions is challenging due to the limited number of cases and lack of surgical guidelines. The appearance of the thymus and lungs in anatomically adjacent compartments make a simultaneous resection of both lesions technically feasible.[12-14] Although video-assisted thoracoscopic surgery (VATS) has become the main technique for the resection of both thymic and pulmonary diseases in recent years, the operation can be successfully carried out via a thoracotomy. The main determinant of survival for all thymic neoplasms is *en-bloc* resection of the tumor either via thoracoscopy or thoracotomy.[12,15] Due to our limited institutional experience in VATS resections, we preferred simultaneous resection of both the lower lobe and thymus via a thoracotomy approach.

In conclusion, it should be kept in mind that thymic and bronchial carcinoid tumors can coexist and simultaneously can be resected in patients with multiple endocrine neoplasia type 1. Early detection with thoracic screening and prompt treatment may improve survival, particularly in thymic carcinoids, and close follow-up during the postoperative period is considerably important for detecting recurrences. However, prospective and large-scale series are needed to clearly identify the optimal management of this uncommon multiple endocrine neoplasia type 1- associated tumors.

Declaration of conflicting interests

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