

Case Report

Cushing's syndrome with Carcinoid Tumor: A Case Report and Literature Review

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Submitted: 30 June 2018

Accepted: 18 August 2018

Published: 20 August 2018

ISSN: 2373-9282

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Keywords

- Cushing's syndrome
- Carcinoid tumor
- neuroendocrine tumor

Abstract

Thymic Neuroendocrine Tumor (TNET) is rare and its incidence rate is approximately 2–5%. Carcinoid tumor of thymus with Cushing's syndrome (CS) is a rare co-morbid condition. We report a 19-year-old girl with CS who had 8-months history of 10-15 kg weight gain, acne on face and back of the hands, menstrual irregularity, depression, fatigue and fatigability, moon faces, buffalo hump, truncal obesity and cutaneous striae. Initial laboratory tests revealed a serum cortisol level of 78 µg/DL, morning serum cortisol of 130 µg/DL, the ACTH level of 440 pg/ml and a 24 hour urinary free cortisol level of 11000 µg/24 hours. Thorax computed tomography showed a heterogeneous well defined mass measuring about 18×15 mm in the anterior compartment of the mediastinum. An extended thymectomy was performed by a median sternotomy. Report of pathologist was "Well-differentiated neuroendocrine neoplasm (Typical carcinoid tumor of thymus, grade 1) without lymphatic and vascular invasion".

ABBREVIATIONS

TNET: Thymic Neuroendocrine Tumor (TNET); CS: Cushing's syndrome; ACTH: Adrenocorticotropic Hormone

INTRODUCTION

Thymic Carcinoid Tumors are divided in three groups: typical carcinoid, atypical carcinoid and small-cell carcinoma of the thymus. They may be originated from the argyrophil cells in the normal thymus [1]. Thymic neuroendocrine carcinomas account for approximately 2% - 4% of all anterior mediastinal tumors [1-3]. Thymic neuroendocrine tumour (TNET) is rare; with incidence rate of approximately 2–5%. Among all thymic epithelial tumors, NETs originated from thymus account for only 0.4%. The most common histological type of TNET is atypical carcinoid tumor (ATC) [2].

Thymus neuroendocrine carcinomas which are associated with Cushing's syndrome can occur at any age between 4 to 64 years, but their peak prevalence is between the second and the fourth decades of a patient's life [1,4] as frequently in men as in women [1,5,6]. Thymic carcinoid, as well as pulmonary carcinoid, may rarely be associated with an ectopic Cushing's syndrome [1,5]. Once the ectopic nature of the Cushing's syndrome is established by exclusion of a pituitary adenoma, adrenal adenoma or hyperplasia, or some other ectopic site, the thorax should be

investigated for either a pulmonary or thymic carcinoid [1,5,7]. In most circumstances, the thymic tumor is readily detected, but occasionally the carcinoid tumor is quite small and may easily be undetected by standard radiographic studies. Spiral CT (computed tomography) of chest followed by high-resolution CT of any suspicious area is indicated [1]. If a lesion is not found or is indeterminate, an Octreotide Radio labeled Scan should be indicated (111In-DTPA) [6]. Here we report a rare case of Cushing's syndrome with typical carcinoid tumor of the thymus which is very rare in review of literatures.

CASE PRESENTATION

A 19-year-old girl was referred to Razi Educational Remedial Research Center for evaluation of Cushing's syndrome. She had experienced 10-15 kg weight gain within a few months, acne on face and back of hands and menstrual irregularity. She felt depression, fatigue and was only able to sleep 3-4 hours at night. Her blood pressure and a pulse rate were 130/80 mmHg and 76 beats per minutes respectively, and she had a cushingoid appearance (moon face, supraclavicular fat, acne on face and back of hands and purplish striae on the elbow and abdomen) (Figure 1). Initial laboratory tests revealed serum cortisol level of 78 µg/DL, morning serum cortisol of 130 µg/DL, and the ACTH level of 440 pg/ml and 24 hours urinary free cortisol level of 11000 µg/24 hours. Thyroid stimulating hormone (T.S.H) and total T4 and T3

levels were within normal range. Work up for multiple endocrine neoplasm type 1 was negative. Abdominal and pelvic computed tomography scan with contrast showed no adrenal masses. Brain magnetic resonance imaging with gadolinium was negative. Thorax computed tomography demonstrated a heterogeneous well defined mass measuring about 18×15 mm in the anterior compartment of the mediastinum (Figure 2). The octreotides can showed pathological uptake in the right side of the anterior mediastinum (Figure 3,4). An extended thymectomy was performed by a median sternotomy. Intraoperatively, the tumor location was in the body of the thymus gland (2-2cm) without any invasion to the adjacent organs (Figure 5). Microscopically, the tumor manifested well-differentiated neuroendocrine neoplasm (typical carcinoid tumor of thymus, grade 1) without lymphatic and vascular invasion (Figure 6). After 14 months follow-up patient is in good condition.

DISCUSSION

A thymic neuroendocrine tumor (TNET) is rare and its incidence rate is approximately 2-5% among all thymic epithelial tumors. Pulmonary NET (PNET) and TNETs are classified as low grade for typical carcinoids (TCs), intermediate grade for atypical



Figure 1 Abdominal wall striae.

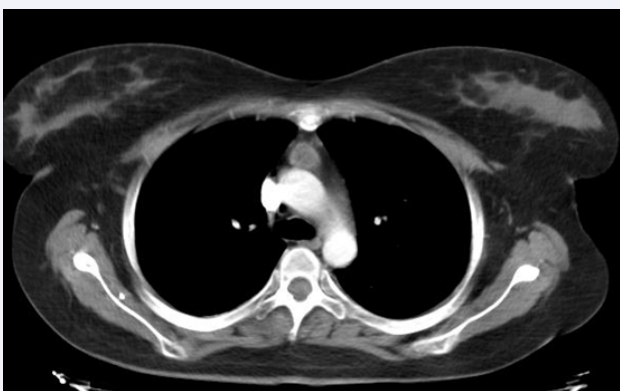


Figure 2 CT-scan of chest with heterogeneous well defined mass in the anterior mediastinum.



Figure 3 Octreotide scan which showed pathological uptake in the right side area of anterior mediastinum.

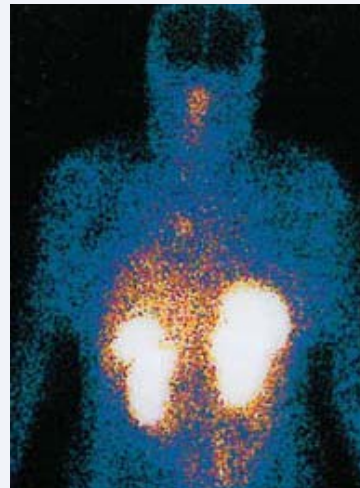


Figure 4 Octreotide scan which showed pathological uptake in the right side area of anterior mediastinum.

carcinoids (ATCs) and high grade for large-cell neuroendocrine carcinoma and small-cell carcinoma tumors. The most common histological type of TNET reported to be atypical carcinoids tumors. Epidemiological findings have shown that a TNET occurs more frequently in men with a mean age of 50 years, and nearly all TNETs have been reported to be non-functional [2]. But some reports show as frequently in men as in women [1,5,6]. Our case was a woman. Thymic carcinoma is a rare aggressive neoplasm. In the thymus, neuro-endocrine carcinoma accounts for approximately 2-4% of all anterior mediastinal tumors. Its peak incidence is between the second and fourth decades of life [1]. They may be presented with symptoms due to mass effect or with endocrinopathy [1,2]. Cushing syndrome is the most common endocrine manifestation of these tumors [8]. Optimal treatment and accurate pretherapeutic diagnosis are important. Diagnosis must be confirmed by increased cortisol level in the serum or in the 24 hours urine collection, which must remain high despite a low dose dexamethasone suppression test [1,4]. The presence of elevated ACTH levels excludes the possibility of an autonomous secretion of cortisol by an adrenal tumor [9]. Radiographic and nuclear imaging play important roles in the diagnosis



Figure 5 Mass of thymus after operation.

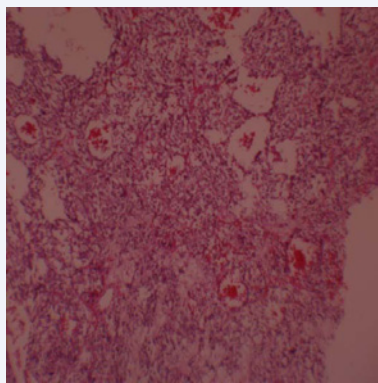


Figure 6 Microscopically, well-differentiated neuro-endocrine neoplasm (Typical carcinoid tumor of thymus, grade 1) without lymphatic and vascular invasion is shown.

and management of carcinoid tumors [6,9]. Spiral computed tomography, magnetic resonance imaging and ultrasonography are used for determining the precise location of tumors and for monitoring of response to treatment [1]. Octreotide scan can recognize early advanced lesions which were not revealed by the other diagnostic procedures [1,6]. The result of treatment is particularly helpful if surgery is being considered. All patients should have an octreoscan as a baseline and patients who have undergone curative surgery should have manual octreoscan [6,9]. Surgery is the cornerstone of the treatment of thymic carcinoma, although chemotherapy and radiotherapy also have been reported to be effective in some cases [1,2]. The most common chemotherapy regimens for thymic carcinoma are platinum based. However these interventions do not significantly affect survival or recurrence rates. Nakamura found no association between histological subtypes and prognosis in patients with advanced thymic carcinoma who received chemotherapy and showed that platinum based chemotherapy is only marginally effective for advanced thymic carcinoma [7]. Suster and Rosai similarly found no beneficial effect. The prognosis is reported a five years survival of approximately 50% for patients with

well defined thymic carcinoid tumor and 27% for those with moderately differentiated thymic carcinoid tumors [10]. High histological grade, tumor extension, incomplete resection and distant metastasis predict a poor prognosis. Most patients present with local recurrence or metastasis within 5 years after surgery and die within 10 years [1]. In the first year after surgery patients should be monitored with serum and urinary free cortisol testing as well as conventional imaging as our patient [4]. If a baseline octreoscan is positive, an octreoscan is recommended either once a year or earlier if evidence of disease is seen [9]. Our patient initially presented with weight gain and fatigue and was eventually diagnosed with Cushing's syndrome. We decided on an aggressive approach of resection without adjuvant chemotherapy and radiotherapy. She discharged with good condition. In follow-up, she did not complain. As in our case, long term follow up is recommended though complete resection was achieved.

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Cite this article

Aghajanzadeh M, Alavi CE, Rimaz S, Mohamadi F, Geranmayeh S, et al. (2018) Cushing's syndrome with Carcinoid Tumor: A Case Report and Literature Review. *Ann Clin Pathol* 6(4): 1145.