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Histologic characteristics of thymic adenocarcinomas: Clinicopathologic study of a nine-case series and a review of the literature

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ABSTRACT

Primary thymic adenocarcinoma is an extraordinarily rare malignancy; only 49 cases have been reported in the medical literature to date. Because of its rarity, clinical and pathologic characteristics of thymic adenocarcinoma are unclear. We present nine cases of primary thymic adenocarcinoma and discuss clinicopathologic findings in the context of the existing literature.

Two-hundred twenty-six thymic carcinoma cases were diagnosed at Samsung Medical Center in Korea, from January, 2001 to July, 2016. Nine of these 226 cases were primary thymic adenocarcinomas. The mean age of primary thymic adenocarcinoma patients was 53.6 years, slightly younger than the mean age of patients with thymic squamous cell carcinomas. The male to female ratio was 2:1. Symptoms, if present, were usually due to compression by the tumor. Tumors showed an extra- or intra-cellular mucin and tubular growth pattern, with CK20- and CDX2-immunoreactivity, similar to adenocarcinomas of the lower intestinal tract.

Twenty-five previously reported cases, classified as mucinous adenocarcinoma and adenocarcinoma, not otherwise specified, also had similar characteristics to enteric-type adenocarcinoma and generally expressed CK20, CDX2, CEA, and/or MUC2. Some of these cases had a thymic cyst. These characteristics are different from those of papillary thymic carcinomas, which are morphologically similar to papillary thyroid carcinomas, express CK7 but not CK20, and are often associated with thymoma. The prognosis of thymic adenocarcinoma, enteric type appeared to be worse than the prognosis of papillary thymic carcinoma or carcinoma with adenoid cystic carcinoma-like features.

In summary, we demonstrated that common primary thymic adenocarcinomas show enteric-type differentiation with mucin. This tumor type has distinct clinical, pathological, immunohistochemical and prognostic characteristics and is different from other subtypes of thymic adenocarcinoma, papillary thymic carcinoma, and carcinoma with adenoid cystic carcinoma-like features.

1. Introduction

Primary thymic adenocarcinoma is an extraordinarily rare malignancy. It is classified as papillary adenocarcinomas, mucinous adenocarcinomas, carcinomas with adenoid cystic carcinoma-like features, and not otherwise specified (NOS) types by the World Health Organization based on histologic morphology [1]. A total of 49 cases of primary thymic adenocarcinoma have been reported in the medical literature to date. Due to the rarity of this tumor, the clinical and pathologic characteristics of thymic adenocarcinoma are not well defined.

We present here nine cases of primary thymic adenocarcinoma. To identify the pathologic characteristics of primary thymic adenocarcinomas, we also reviewed the medical literature. We focused

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Table 1
Clinical features of the nine thymic adenocarcinomas cases.

	Sex	Age	Symptoms	History	Smoking history	Tumor size (cm)	Masaoka Stage	Metastasis	Associated findings	Treatment	Follow-up	Status
#1	F	56	cough sputum	N-S	never smoker	7.6	III		Normal serum CEA	CTx	5yr 3mon	DOD
#2	M	46	N-S	HTN	20PY, current	10	III		Elevated serum CEA	S + CTx + RTx	2yr 9mon	DOD
#3	M	51	shoulder and back pain	HTN DM	30PY, current	6.4	IVB	liver, lung, spine	Elevated serum CEA	RTx	1yr 2mon	AWD
#4	M	34	N-A	N-S	3PY, ex-smoker	11.9	IVB	spine	N-S	CTx	1yr	AWD
#5	F	56	N-S	Colon adeno-carcinoma	8.5PY, current	4.6	III		N-S	S	1yr 5mon	Progression (1yr), AWD
#6	M	70	chest wall pain	HTN DM CVA	40PY, ex-smoker	9.6	II		N-S	CCRT	8mon	Progression (5mon), AWD
#7	M	50	chest discomfort, weight loss (8 kg/2 mon)	Angina	20PY, ex-smoker	8.1	IVB	lung, spine	N-S	CTx + RTx	7mon	Progression (5mon), AWD
#8	M	62	chest discomfort	HTN DM	5PY, current	3.2	IVB	bone (scalp)	Elevated serum CEA	CTx	5mon	AWD
#9	F	57	dyspnea rib pain	HTN	never smoker	5	IVB	bone (sacrum)	N-S	CTx	5mon	Progression (3mon), AWD

N-A, not available; N-S, non-specific; HTN, hypertension; DM, diabetes; S, surgical excision; CTx, chemotherapy; RTx, radiotherapy; CCRT, concurrent chemoradiotherapy; DOD, dead of disease; AWD, alive with disease; PR, partial regression.

on clinical characteristics, microscopic morphology, and immunohistochemical profiles of primary thymic adenocarcinomas.

2. Methods and materials

All 226 cases of thymic carcinoma were identified from the files of patients treated at Samsung Medical Center in Korea, from January, 2001 to July, 2016. Cases with the possibility of metastatic carcinoma or primary lung cancer were excluded based on clinical findings and pathologic review of a tumor in another organ or in the lungs or a TTF-1 positive-adenocarcinoma. A total of nine cases of primary thymic adenocarcinoma were identified. Clinical data, such as symptoms, history, and follow-up, were obtained by reviewing the respective clinical charts. Hematoxylin and eosin (H-E)-stained sections were reviewed, and immunohistochemical staining was performed using a Ventana automated immunostainer (Ventana, USA) if tissue sections were available. Primary antibodies used were CK7 (M7018; DAKO, Denmark), CK20 (M7019; DAKO), CDX2 (PA0535; Novocastra, UK), MUC2 (NCL-MUC-2; Leica Biosystems, UK), TTF-1 (M3575; DAKO), carcinoembryonic antigen (CEA, M7072; DAKO), CD5 (NCL-L-CD5-4C7; Leica Biosystems), and c-kit (A4502; DAKO). Kaplan-Meier survival analysis was used to compare survival among the subtypes of thymic adenocarcinoma. The study was approved by the Institutional Review Board of Samsung Medical Center.

3. Results

3.1. Epidemiology of thymic carcinomas

Two hundred twenty-six cases of thymic carcinoma were diagnosed at Samsung Medical Center from January, 2001 to July, 2016. One hundred ninety cases (84.1%) were diagnosed as thymic squamous cell carcinoma. Other cases were classified as large cell neuroendocrine carcinoma (10/226, 4.4%), small cell carcinoma (4/226, 1.8%), spindle cell neuroendocrine carcinoma (1/226, 0.4%), mucoepidermoid carcinoma (3/226, 1.3%), lymphoepithelioma-like carcinoma (2/226, 0.9%), clear cell carcinoma (1/226, 0.4%), sarcomatoid carcinoma (2/226, 0.9%), pleomorphic carcinoma (3/226, 1.3%), and undifferentiated carcinoma (1/226, 0.4%). Nine patients had thymic adenocarcinomas (9/226, 4.0%).

3.2. Clinical features of thymic adenocarcinoma

The clinical features of the nine cases are summarized in Table 1. Patients comprised six men and three women between 34 and 70 years of age. Mean age was 53.6 years. The chief complains were a non-symptomatic incidental mass (two cases) or non-specific symptoms of cough, dyspnea, or chest discomfort/pain. Some patients had chronic illnesses, such as hypertension (4/9), diabetes (3/9), and/or arrhythmia (1/9). One patient had undergone a right hemicolectomy due to colonic adenocarcinoma 3 years before discovery of the thymic mass. We reviewed the clinical evaluations and H-E slides of the colonic adenocarcinoma case to confirm the diagnosis of primary thymic mucinous adenocarcinoma. Seven patients had a smoking history (3–40 PYs, mean 18.07 PYs) and two were never-smokers.

Diagnostic imaging revealed an infiltrative mass in the anterior mediastinum, ranging in size from 3.2 to 11.9 cm (mean 7.4 cm). In four of nine cases, the mediastinal masses contained calcification, and two of nine cases had a cystic portion on computed tomography (CT).

At the time of diagnosis, clinical stage was III or IV. Four patients had nodal metastasis (cN1) and five cases had distant metastasis (cM1) based on CT and whole-body positron emission tomography