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CD15 and CEA expression in thymic epithelial neoplasms

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ABSTRACT

The aim of this study was to evaluate the expression of CD15 and CEA in thymic epithelial neoplasms and assess their correlation with various World Health Organisation (WHO) subclasses of thymic epithelial neoplasms. A total of seventy cases of thymic epithelial neoplasm seen between 1981 and 2001 were retrieved from the archives of the Department of Pathology at Hacettepe University. Hematoxylene and Eosin stained sections were evaluated and reclassified according to the WHO classification. Representative sections from each case were stained for CD15 and CEA by immunohistochemical technique. CD15 was strongly positive in 4 of 5 (80%) WHO type A cases and specifically stained the A component in all of mixed (AB) thymomas. While 3 of 5 (60%) WHO type C cases strongly expressed CD15, none of WHO type B cases demonstrated strong positivity. Strong CEA expression was not seen in any of the cases. Heterogeneous staining pattern (+2) was seen in only WHO type C cases and not in any of type A or B cases. Thus, CD15 expression highly correlates with type A component of thymic epithelial neoplasms. CEA expression on the other hand can be seen in type C thymic epithelial neoplasms. [Turk J Cancer 2008;38(3):113-117]

KEY WORDS:

Thymoma, thymic epithelial neoplasms, CD15, CEA

INTRODUCTION

Thymic epithelial neoplasms are uncommon neoplasms with distinctive morphological features. Histological classification of these neoplasms is one of the most controversial subjects in surgical pathology. In the last century more than twenty classifications have been proposed for thymomas (1). Lastly, in 1999, WHO classification was proposed which subdivided thymic epithelial neoplasms as types A, AB, B1, B2, B3 and C, based on epithelial cell morphology, epithelial-lymphocyte ratio and cytological atypia (2).

The Lewis blood group and CEA related antigens are cell surface carbohydrates which have adhesive functions in human tissues. They play roles in organogenesis, differentiation and protection of normal mucosal tissues, migration of neutrophils, bacterial binding, and tumor differentiation and dissemination (3). Lewis blood group antigens form the terminal carbohydrate chains on a CEA related glycoprotein backbone. They are structurally related to the major blood group antigens ABH which were discovered on the surface of erythrocytes. CD15 (Lewis X, X hapten, Stage Specific Embryonic Antigen-I) is a member of this family and plays important roles in embryonic organisation, granulocyte migration and tumor invasiveness (3-5). CEA was first described in human colon cancer tissue extracts. After that, its expression was also shown in fetal tissues. It was referred to as oncofetal antigen, since it was believed that its expression is restricted to neoplastic and fetal tissues. CEA is approximately 200 kDa in molecular

weight and rich in carbohydrate content. CEA gene family is composed of 29 different genes/pseudogenes which is present on chromosome 19q13.2. We currently know that CEA is also expressed in many adult tissues. Because of the stability and accumulation in blood in various cancer patients this molecule is widely used as a tumor marker (3,6,7).

MATERIALS AND METHODS

Tissues

Seventy cases of formalin-fixed, paraffin-embedded specimens of thymic epithelial neoplasms seen between 1981 and 2001 were retrieved from the archives of the Department of Pathology at Hacettepe University. Hematoxylen&Eosin stained sections were evaluated and reclassified according to the WHO classification (Table 1).

Formalin-fixed, paraffin-embedded specimen of one colon adenocarcinoma obtained from surgical files for positive control, and two cases of thymectomy -one showing normal thymus and another showing involution- were also included as controls.

Immunohistochemistry

A representative block was chosen for each case and immunohistochemical staining was performed using a streptavidin-biotin-peroxidase complex procedure. After deparaffinization and dehydration with xylene and alcohol, peroxide blockage and protein blockage were performed. After antigen retrieval with citrate buffer (pH 6.0) and microwave oven the sections were incubated for 1 hour with anti-CD15 antibody (Clone MMA, Leu-M1, 1/50 dilution, Neomarkers, Fremont, CA, USA) and anti-CEA (Clone COL-1, 1/75 dilution, Neomarkers, Fremont, CA, USA). Detection was carried out using the LSAB kit and DAB as chromogen (DAKO, Denmark). Two pathologists evaluated immunostaining simultaneously (AA, AÜ). Staining intensity and pattern was scored from 0 to +3, as follows: 0; no staining, +1; staining in less than 5% of the neoplastic cells (weakly positive), +2; staining in 5-90% of the neoplastic cells (heterogeneously positive) and +3; staining in more than 90% neoplastic cells (strong positivity).

RESULTS

The patients consisted of 38 male (54.3%) and 32 female (45.7%) with a mean age of 43.4 ± 14.1 (Range17 - 73 years). The distribution of cases according to WHO classification is shown in table 1. Specific diagnosis of 5 type C thymomas were as follows; 2 cases of epidermoid non-keratinizing carcinoma, 2 cases of lymphoepithelioma-like carcinoma and one case of undifferentiated carcinoma.

Table 1
Distribution of 70 thymic epithelial neoplasms according to the WHO classification and CEA and CD15 staining properties scored 0 to 3, respectively

		Histological subtypes according to the WHO classification						
Antibody	**Score**	**A**	**AB**	**B1**	**B2**	**B3**	**C**	**Total**
CEA	0	5	5	1	24	29	2	66
	1	0	0	0	0	1	0	1
	2	0	0	0	0	0	3	3
	3	0	0	0	0	0	0	0
CD15	0	0	0	1	22	22	0	45
	1	1	1	0	2	5	0	9
	2	0	3	0	0	3	2	8
	3	4	1	0	0	0	3	8
Total (%)		5 (7.1)	5 (7.1)	1 (1.4)	24 (34.3)	30 (42.9)	5 (7.1)	70 (100)

The immunohistochemical profiles of CD15 and CEA expression of thymic epithelial neoplasms are demonstrated in table 1. Colon adenocarcinoma which was used as a positive control stained strongly with both CD15 and CEA.

In normal thymus, CD15 staining was observed in Hassal's corpuscles, medullary epithelium, and focally in cortical epithelium. Additionally leukocytes showed strong positivity. The staining characteristic of CD15 in involuted epithelium was heterogenous and patchy. In the thymic epithelial neoplasms CD15 was strongly expressed in 4/5 (80%) WHO type A cases and specifically stained the A component in all of AB (mixed) thymomas. Three of 5 (50%) WHO type C cases strongly expressed CD15 and other 2 cases of type C thymoma stained heterogeneously. None of WHO type B cases stained strongly with CD15 whereas only 3/30 cases of B3 (10%) were heterogeneously immunoreactive (Figure 1).

CEA staining was observed only in Hassal's corpuscles of normal thymus, whereas no positivity was seen in involuted thymus. In thymic epithelial neoplasms, strong CEA positivity was not seen in any of the cases. Heterogenous staining pattern (+2) was observed in only 3 of 5 (60%) WHO type C cases (Figure 1).

DISCUSSION

In this study, CD15 expression was observed in WHO type A and type C thymic epithelial neoplasms but not in type B. We observed strong positivity in 4 of 5 cases of type A thymomas. The fifth case that showed +1 staining appeared morphologically different than the other cases. This weakly CD15 positive type A case had a prominent microcystic character and was composed of short spindle cells. Strongly CD15 positive cases had typical type A morphology. In all type AB cases the spindle cell component was positive for CD15. In the light of these findings it can be suggested that CD15 expression is a characteristic of medullary differentiation. Previously, CD15 expression was studied in fetal thymus by Engel et al. (8) which demonstrated that in normal thymus, Hassals' cor-

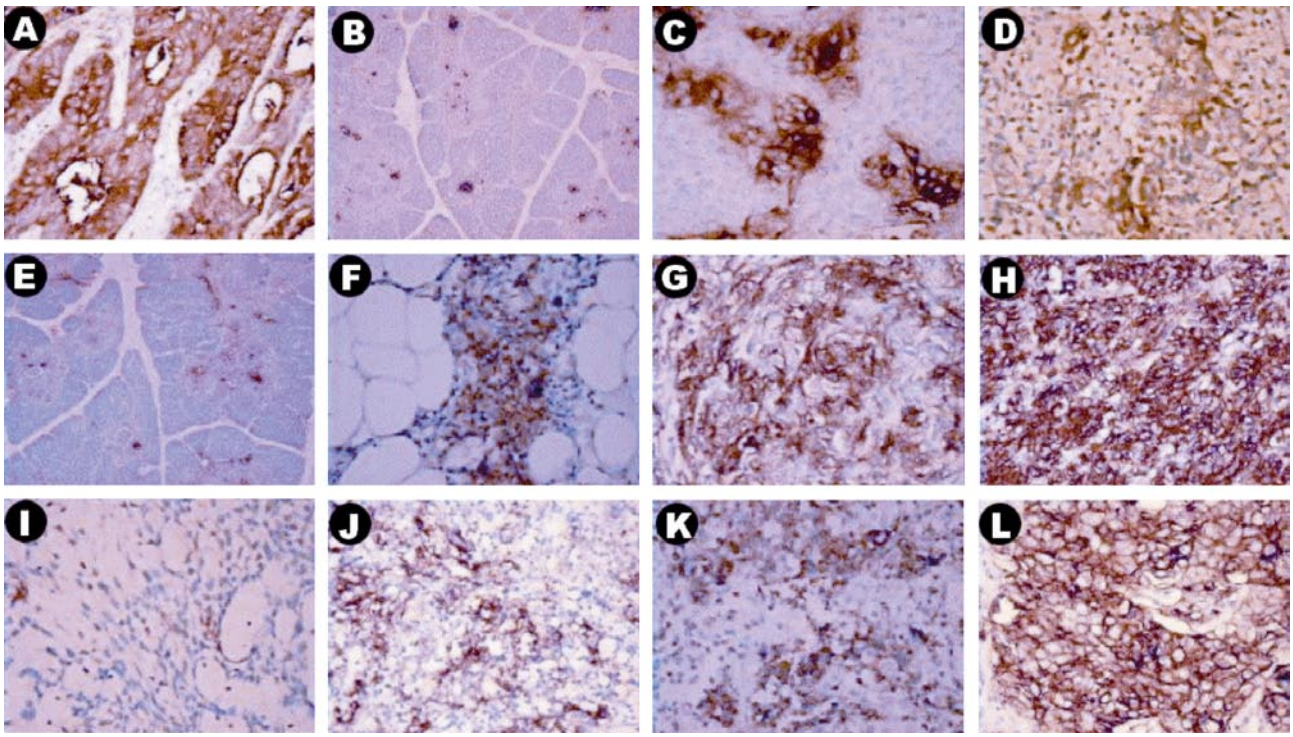

Fig 1 (A-L). CEA (A-D) and CD15 (E-L) staining. (A): Strong membranous staining of colon adenocarcinoma as a positive control for CEA, (B): Hassal corpuscles showed positivity in non-neoplastic thymus, (C&D): Epidermoid non-keratinizing carcinoma and lymphoepithelioma like thymic carcinoma showed immunoreactivity with CEA, (E): CD15 positivity in Hassal corpuscles and medullary epithelium in non-neoplastic thymus, (F): Positivity in epithelial remnants of involuted thymus tissue, (G, H): Strong immunoreactivity in type A thymomas, (I): Weak staining (score 1) in cystic thymoma, (J): Staining of A component in type AB thymomas, (K, L): Strong membranous staining in thymic carcinomas

puscles, medulla and rare cortical epithelial cells are positive. However, thymomas were to a great extend negative or showed weak expression with only thymic carcinomas showing stronger positivity with antibodies against Lewis-x and sialyl-Lewis-x. The findings in our study and that of Engel et al. are in accordance. The identification of Le-x in fetal medulla in Engel et al.'s study also suggests that this may be a feature of medullary differentiation in thymomas. While we observed strong CD15 expression in Type A thymomas they have reported weak expression in their study. The differences observed between the two studies may in part be due to composition of thymic epithelial neoplasms included in the studies and the use of different monoclonal antibodies to detect CD15.

Differential expression among thymic epithelial neoplasms with medullary and cortical differentiation has been shown for two other markers namely CD20 and CD57 (9-11). CD20, a pan-B-cell marker can be useful in the differentiation of spindle cell and mixed thymomas from cortical thymomas (9,10). CD57 (Leu-7) expression has been shown in subcapsular cortical epithelium in normal thymic tissue and in spindle and mixed thymomas, but not in thymic carcinomas (11).

The results of CEA staining of our study are in agreement with other reports (12-15). Troung et al. (14) demonstrated CEA positivity in 5 of 13 thymic carcinomas. Papillary carcinoma of thymus was described by Matsuno et al. (15) and 4 cases of these neoplasms were positive with CEA. Our findings and other reports pointed out that CEA expression can be seen in thymic carcinomas in a heterogeneous pattern, but there is no positivist in WHO type A, AB or B thymomas. This property of thymic carcinomas is also similar to CD5 immunoreactivity (2,16). So in addition to the CD5 expression, positivity with CEA may favor malignancy in thymic epithelial neoplasms.

Our study and previous studies which are related with immunohistochemical characteristic of thymic epithelial neoplasms demonstrates that CD5, CD15, CD20, CD57 and CEA are useful markers for subclassification of these neoplasms. CD5 and CEA are generally positive in thymic carcinomas, CD57 positivity is seen in medullary differentiation not in cortical. CD15 and CD20 share similar staining characteristics in that they are expressed in type A and C cases.

As a conclusion CD15 positively stains A component of WHO type A and AB thymomas and WHO type C thymomas. So it is a useful marker for subclassification of thymomas to highlight the A component and determination of malignancy potential. CEA expression can be seen in type C thymomas but not in any cases of A, AB or B thymomas.

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