Original Article

Steroid Receptor Expression in Thymomas and Thymic Carcinomas

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BACKGROUND: Although protein expressions of glucocorticoid receptor (GR), estrogen receptors (ERα and ERβ), progesterone receptor A (PgR-A), and androgen receptor (AR) were shown to play roles in the growth and differentiation of normal thymus and thymic tumors, to the authors' knowledge their association with patient characteristics and prognosis has yet to be determined. **METHODS:** A series of 140 thymic epithelial tumors (57 type A + AB thymomas, 40 type B1 + B2 thymomas, 6 type B3 thymomas, and 37 thymic carcinomas) were examined for GR, ERα, ERβ, PgR-A, and AR expression using immunohistochemistry. In addition, the correlation between expression of these hormone receptors and clinicopathologic factors and overall survival (OS) was assessed. **RESULTS:** GR and ERβ demonstrated a high rate of expression in thymomas and thymic carcinomas (82.9% and 76.4%, respectively), whereas rates of ERα, PgR-A, and AR expression were low (13.6%, 0.71%, and 23.6%, respectively). A significant correlation ($P < .05$) was found between ERα expression and tumor size and between ERβ expression and tumor stage. Multivariate analyses revealed that histologic subtype ($P = .0039$), tumor stage ($P = .0012$), and GR expression ($P = .0025$) were significantly correlated with the 10-year OS rate. **CONCLUSIONS:** GR and ERβ demonstrated high rates of expression in thymomas and thymic carcinomas. Furthermore, multivariate analysis revealed that GR expression was associated with better prognosis in patients with surgically resected thymomas and thymic carcinomas. ***Cancer*** **2011;117:4396–405.** © *2011 American Cancer Society.*

KEYWORDS: glucocorticoid receptor, estrogen receptor, progesterone receptor, thymoma, thymic carcinoma.

Thymomas and thymic carcinomas, the most common epithelial tumors of the anterior mediastinum, are comprised mainly of various percentages of lymphocytes and epithelial cells. The normal thymus is primarily comprised of lymphocytes and thymic epithelial cells. These lymphocytes are comprised mainly of immature T cells called thymocytes. During T-cell ontogeny in the thymus, thymocytes undergo a process of positive (maturation) or negative (apoptosis) selection. Epithelial cells play an active role in promoting T-cell maturation, either through the action of their humoral substances or through direct contact with thymocytes.

Glucocorticoids (GCs), a class of steroid hormones, are important regulatory molecules that control inflammation, cell growth, and differentiation through the activity of a specific intracellular glucocorticoid receptor (GR).[1-3] In the normal thymus, GR is expressed in not only immature thymocytes but also epithelial cells.[4,5] In thymomas, GR expression is also observed in both epithelial cells and lymphocytes by immunohistochemical analysis.[4] The administration of GCs induces apoptosis in thymocytes.[6] The administration of prednisone, the most potent GC, has demonstrated dramatic responses in patients with refractory thymoma.[7-13]

Other steroids such as estrogen or progesterone regulate cell proliferation and other biological functions in various neoplasms derived from hormone-dependent tissues, such as breast and endometrial cancers.[14] These biological effects are in general mediated through initial interactions with native receptors. Estrogen receptor (ER) and progesterone receptor (PgR), 2 representative sex steroid receptors, have been detected in homogenates of the mature human thymus.[15,16] In

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We would like to thank Sachiko Miura and Chizu Kina for their skillful technical assistance.

DOI: 10.1002/cncr.26061, **Received:** October 21, 2010; **Revised:** December 27, 2010; **Accepted:** January 31, 2011, **Published online** March 22, 2011 in Wiley Online Library (wileyonlinelibrary.com)

addition, previous reports have indicated that ERs are intimately involved in the regulation of thymic tumor development and progression.[17-19] Therefore, it is important to examine the expression of GR and other steroid receptors in thymic tumors.

However, to the best of our knowledge, currently, the clinicopathological significance of GR, ER, and PgR expression in thymoma and thymic carcinoma is unknown. In the current study, we immunohistochemically analyzed the expression of GR, ERα, ERβ, PgR-A, and androgen receptor (AR) in thymic epithelial tumors (thymomas and thymic carcinomas). We also analyzed the correlation between the expression of these steroid receptors and clinical features. These data will serve as background information for studies assessing the predictive value of molecular markers of sensitivity to antihormone therapy.

MATERIALS AND METHODS

Patient Population

This study included 140 patients who underwent surgical resection for a thymic tumor at the National Cancer Center Hospital in Tokyo, Japan between 1973 and 2009 for thymic carcinoma and between 1999 and 2009 for thymoma (Table 1). An institutional review board approved this study.

All hematoxylin-and-eosin–stained slides, special stains, and the immunohistochemical analyses available were reviewed. Histologic diagnosis was based on the classification schema of the latest edition of the World Health Organization classification.[20]

Microarray Construction

The most representative tumor areas were sampled for the tissue microarray (TMA). The TMAs were assembled with a tissue-arraying instrument (Azumaya, Tokyo, Japan). To reduce sampling bias because of tumor heterogeneity, we used 2 replicate cores measuring 2.0 mm in diameter from different areas of individual tumors.

Immunohistochemical Analysis

For immunohistochemical staining, 4 μm-thick sections were routinely deparaffinized. The sections were exposed to 3% hydrogen peroxide for 15 minutes to block endogenous peroxidase activity and then washed in deionized water for 2 to 3 minutes. Heat-induced epitope retrieval was performed with citrate buffer solution (pH 6.0) (Muto Pure Chemicals Co., Tokyo, Japan) for GR and PgR-A or with Target Retrieval Solution (pH 9.0) (Dako Corporation, Carpinteria, Calif) for ERβ and AR. After the slides were allowed to cool at room temperature for approximately 30 minutes, they were rinsed with deionized water. The slides were then incubated with primary antibodies against GR (1:200, H8004; Perseus Proteomics, Tokyo, Japan), ERβ (1:100, EMR02; Leica, Wetzlar, Germany), PgR-A (1:400, 636; Dako Corporation), and AR (1:100, AR441; Dako Corporation) for 1 hour at room temperature. Immunoreactions were detected using the Envision-Plus system (Dako Corporation) and visualized with 3,3′-diaminobenzidine; counterstaining was performed with hematoxylin. Immunohistochemistry (IHC) for the ERα antibody (1:100, CONFIRM Estrogen Receptor SP1; Ventana, Tucson, Ariz) was processed by the BenchMark XT automated slide processing system (Ventana) according to the manufacturer's protocol.

IHC Scoring System

The IHC signal was evaluated using the Allred score, which assessed ERα status in breast carcinoma by IHC.[21] This system was used because it was easy to learn and highly reproducible.[21] Briefly, a proportion score was assigned, which represented the estimated proportion of positively staining tumor cells (0 indicates none; 1, $\leq$ 1/100; 2, 1/100 to $<$ 1/10; 3, 1/10 to $<$ 1/3; 4, 1/3 to $<$ 2/3; and 5, $\geq$ 2/3). An intensity score was assigned based on the average estimated intensity of staining in positive cells (0 indicates none; 1, weak intensity [immunoreactivity was only observed at $\times$ 100 magnification]; 2, intermediate intensity [immunoreactivity was detected at $\times$ 40 magnification but was weaker compared with positive controls]; and 3, strong intensity [immunoreactivity was easily detected at $\times$ 40 magnification]). The proportion score and intensity score were added to obtain a total score that ranged from 0 to 8. A total score of $\geq$ 3 was defined as positive for ERα, ERβ, PgR-A, and AR (Fig. 1). For GR, the Allred score was determined using 3 criteria (ie, total scores of $\geq$ 3, $\geq$ 4, and $\geq$ 5, to explore the best threshold).

Statistical Analysis

We analyzed thymomas and thymic carcinomas and categorized the former into 3 groups: type A + AB, type B1 + B2, and type B3 thymomas because although type A and AB and type B1 and B2 have similar clinical behaviors, type B3 differs from the other types of thymoma. In addition, we combined Masaoka stage into 2 groups for the analysis: stage I + II and stage III + IV according to the

Table 1. Patient Characteristics According to ERα, ERβ, PgR-A, AR, and GR IHC Score[a]

	All Patients	GR IHC			ERα IHC			ERβ IHC			PgR-A IHC			AR IHC		
Variable		Positive	Negative	*P*	Positive	Negative	*P*	Positive	Negative	*P*	Positive	Negative	*P*	Positive	Negative	*P*
Sex				.62			.15			.15			.20			.84
Male	53	45	8		10	43		44	9		1	52		13	40	
Female	87	71	16		9	78		63	24		0	87		20	67	
Age, y				.69			.67			.18			.36			.15
Median	57.4	58.0	54.9		57.1	57.5		59.0	52.2		67	57.4		56.3	57.8	
Range	25-84	25-84	32-74		25-79	28-84		25-84	28-76		67	25-84		25-79	28-84	
Histology (WHO)				.43			<.001			<.001			.47			.029
Type A +AB	57	47	10		2	55		54	3		0	57		14	43	
Type B1+B2	40	36	4		11	29		25	15		1	39		13	27	
Type B3	6	5	1		3	3		2	4		0	6		3	3	
Thymic carcinoma	37	28	9		3	34		26	11		0	37		3	34	
Masaoka stage				.17			.48			.008			.51			.21
I + II	98	84	14		12	86		81	17		1	97		26	72	
III + IV	42	32	10		7	35		26	16		0	42		7	35	
Tumor size, cm				.030			.021			.16			.37			.87
Median	6.01	6.03	5.92		6.24	5.97		5.79	6.72		8	6.01		6.16	5.97	
Range	1.5-13	1.5-13	1.5-9.0		1.5-13	1.5-12.5		1.5-12.5	3.5-13		8	1.5-13		1.5-12	1.5-13	

Abbreviations: AR, androgen receptor; ER, estrogen receptor; GR, glucocorticoid receptor; IHC, immunohistochemistry; PgR-A, progesterone receptor A; WHO, World Health Organization.
[a] Missing data were excluded from the analysis.

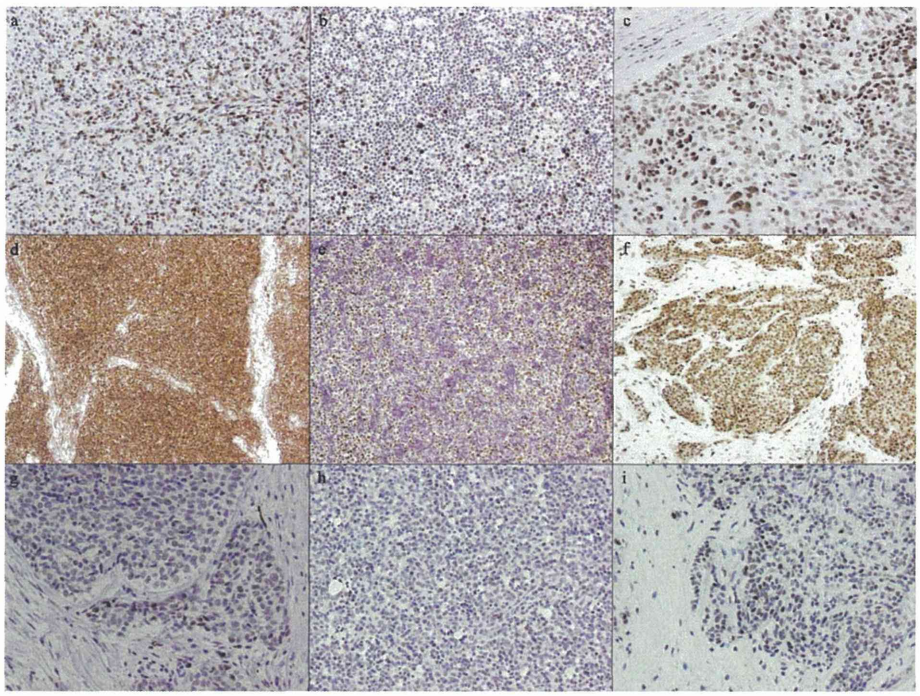

Figure 1. Representative images of positive immunohistochemical staining for glucocorticoid receptor (GR), estrogen receptor β (ERβ), and androgen receptor (AR) are shown. (a) GR expression in type A thymoma is shown (× 20). (b) GR expression in type B2 thymoma is shown (× 20). (c) GR expression in thymic carcinoma is shown (× 20). (d) ERβ expression in type A thymoma is shown (× 10). (e) ERβ expression in type B1 thymoma is shown (× 10). (f) ERβ expression in thymic carcinoma is shown (× 10). (g) AR expression in type AB thymoma is shown (× 20). (h) AR expression in type B2 thymoma is shown (× 20). (i) AR expression in thymic carcinoma is shown (× 20).

presence of invasion or metastasis to other organs. The Mann-Whitney *U* test for continuous variables and chi-square tests for categorical variables were used. A *P* value $\leq .05$ was regarded as statistically significant. Overall survival (OS) curves were calculated using the Kaplan-Meier method. Univariate survival analysis was performed with the log-rank test and Cox proportional hazards regression. Each variable was analyzed using the multivariate Cox model that was suitable for the variables with $P < .10$ from a Wald test of the univariate model. Statistical significance was set at $P \leq .05$.

RESULTS

Clinicopathologic Findings

A total of 140 cases of thymic epithelial tumors were studied, including 57 type A + AB, 40 type B1 + B2, and 6 type B3 thymomas and 37 thymic carcinomas. The patient cohort included 53 males and 87 females. The mean age of the patients at the time of diagnosis was 57.4 years (range, 25 years-84 years). Tumor size ranged from 1.5 cm to 13.0 cm (mean, 6.01 cm) (Table 1). The median follow-up was 64.6 months (range, 0.03 months-356.1 months). The 10-year survival rate in this patient cohort was 74.0% (95% confidence interval, 63.0%-85.0%), with 112 patients still alive at the time of last follow-up.

GR, ERα, ERβ, PgR-A, and AR Expression

Representative cases of positive expression of GR, ERβ, and AR for each histologic subtype are shown in Figure 1. For GR expression, we used 3 criteria: Allred scores of ≥ 3, ≥ 4, and ≥ 5. For any of the criteria, no significant differences were detected between GR expression and sex, age, histologic subtype, or tumor stage (data not shown). The difference between GR expression and tumor size was significant for total scores ≥ 5 and ≥ 4 ($P = .030$ and $P = .043$, respectively), but not for a total score ≥ 3 ($P = .110$). GR expression and OS were found to have a significant correlation only for a total score ≥ 5 ($P = .0125$). Thus, we adopted the total score ≥ 5 as being indicative of positive GR expression.

GR expression was detected in 116 (82.9%) patients, which included 47 (of 57 patients 82.5%)

Table 2. Coexpression Status for GR and ERβ, GR and AR, or ERβ and AR

	ERβ			AR		
	Positive	Negative	*P*	Positive	Negative	*P*
GR positive: TS ≥3			.75			.22
GR positive	102	31		30	103	
Negative	5	2		3	4	
GR positive: TS ≥4			.48			.48
GR positive	101	30		30	101	
Negative	6	3		3	6	
GR positive: TS ≥5			.22			.22
GR positive	91	25		25	91	
Negative	16	8		8	16	
AR positive: TS >3			.72			—
AR positive	26	7		—	—	
Negative	81	26		—	—	

Abbreviations: AR, androgen receptor; ER, estrogen receptor; GR, glucocorticoid receptor; TS, total score for Allred score.

patients with type A + AB thymoma, 36 (of 40 cases; 90%) with type B1 + B2 thymoma, 5 (of 6 cases; 83.3%) with type B3 thymoma, and 28 (of 37 cases; 75.7%) with thymic carcinoma ($P = .426$). No significant difference was recognized among the histologic subtypes.

ERα expression was detected in 19 (13.6%) patients, which included 2 (of 57 cases; 3.5%) patients with type A + AB thymoma, 11 (of 40 cases; 27.5%) with type B1 + B2 thymoma, 3 (of 6 cases; 50%) with type B3 thymoma, and 3 (of 37 cases; 8.1%) with thymic carcinoma ($P < .001$). Significant differences were detected between type A + AB thymoma and other histological subtypes; type B1 + B2 thymoma ($P = .002$), type B3 thymoma ($P = .006$), and thymic carcinoma ($P = .046$); and type B3 thymoma and thymic carcinoma ($P = .019$).

ERβ expression was detected in 107 (76.4%) patients, which included 54 (of 57 cases; 94.7%) patients with type A + AB thymoma, 25 (of 40 cases; 62.5%) with type B1 + B2 thymoma, 2 (of 6 cases; 33.3%) with type B3 thymoma, and 26 (of 37 cases; 70.3%) with thymic carcinoma ($P < .001$). Significant differences were detected between type A + AB and type B1 + B2 thymoma ($P = .001$), type B3 thymoma ($P = .002$), and thymic carcinoma ($P = .021$).

PgR-A expression was detected in only 1 (0.71%) patient. The thymoma was type B1 + B2 (1 of 46 cases; 2.2%). No significant difference was observed compared with the other histologic subtypes.

AR expression was detected in 33 (23.6%) patients, which included 14 (of 57 cases; 24.6%) patients with type A + AB thymoma, 13 (of 40 cases; 32.5%) with type B1 + B2 thymoma, 3 (of 6 cases; 50%) with type B3 thymoma, and 3 (of 37 cases; 8.1%) with thymic carcinoma ($P = .029$). A marginal difference was detected between type B1 + B2 thymoma and thymic carcinoma ($P = .054$).

With regard to coexpression status, no significant differences were detected among the subtypes (Table 2).

In the association analysis between clinicopathologic factors and hormone receptor expression, significant correlations were observed between ERα expression and tumor size ($P = .021$) and between ERβ expression and tumor stage ($P = .008$). The other clinicopathologic factors demonstrated no statistically significant correlation with the expression status of any of the hormone receptors (Table 1). In addition, no significant differences were detected in the expression levels of GR, ERβ, and AR between type A and type AB thymomas or between type B1 and type B2 thymomas (data not shown).

Correlation of OS With Clinicopathologic Factors and Steroid Receptor Expression

We investigated whether there was a correlation between OS and clinicopathologic factors or hormone receptor expression (Fig. 2). The 10-year OS rates for patients with type A + AB, type B1 + B2, and type B3 thymomas and thymic carcinoma were 92.6%, 89.5%, 75.0%, and 42.5%, respectively (thymoma vs thymic carcinoma; $P < .0001$) (Fig. 2a). Significant differences were found between thymic carcinoma and type A + AB thymoma and between thymic carcinoma and type B1 + B2

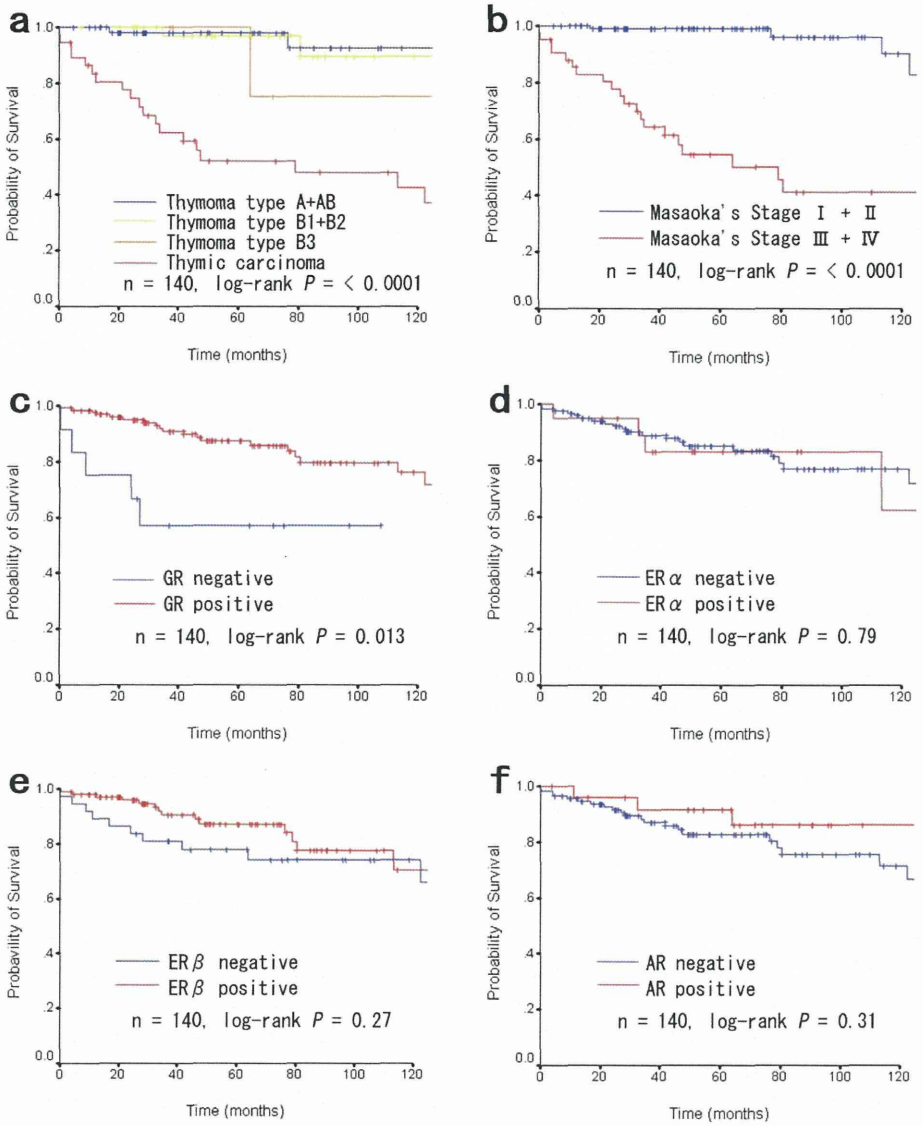

Figure 2. (a) Overall survival (OS) is shown according to histologic subtype (ie, type A + AB thymoma, type B1 + B2 thymoma, type B3 thymoma, and thymic carcinoma). (b) OS is shown according to Masaoka stage (ie, stage I + II and stage III + IV). (c) OS is shown according to glucocorticoid receptor (GR) immunohistochemistry (IHC) score (positive indicates a total score ≥ 5; negative, total score ≤ 4). (d) OS is shown according to estrogen receptor α (ERα) IHC score (positive indicates a total score ≥ 3; negative, total score ≤ 2). (e) OS is shown according to ERβ IHC score (positive indicates a total score ≥ 3; negative, total score ≤ 2). (f) OS is shown according to androgen receptor (AR) IHC score (positive indicates a total score ≥ 3; negative, total score ≤ 2).

thymoma (both $P < .0001$), whereas no significant difference between thymic carcinoma and type B3 thymoma was detected ($P = .15$). In addition, no significant difference was detected between type B1 + B2 and type B3 thymomas with regard to the 10-year OS rates ($P = .30$) (data not shown). The 10-year OS rates for Masaoka stage I + II and stage III + IV were 82.5% and 41.0%, respectively ($P < .0001$) (Fig. 2c). With regard to negative and positive hormone receptor status (Figs. 2c-2f), the 10-year OS rates for GR were 65.7% and 75.6%, respectively ($P = .013$); 76.8% and 62.2%, respectively, for ERα ($P = .79$); 74.3% and 71.9%, respectively, for ERβ ($P = .27$); and 71.1% and 85.0%, respectively, for AR ($P = .31$).

Multivariate analysis revealed that histologic subtype ($P = .0039$), tumor stage ($P = .0012$), and GR expression ($P = .0025$) were significantly correlated with the 10-year OS, whereas no significant correlation was detected between the other variables and OS (Table 3).

Table 3. Univariate, Multivariate, and Bootstrap Analysis of Survival

	Univariate Analysis			Multivariate Analysis		
Variable	HR	95% CI	*P*	HR	95% CI	*P*
Histology (WHO)						
Thymoma vs thymic carcinoma	11.6	4.3-31.3	<.0001	5.69	1.8-18.5	.0039
Masaoka stage						
I + II vs III + IV	14.9	5.1-43.2	<.0001	2.66	1.5-4.8	.0012
Sex						
Male vs female	0.81	0.38-1.7	.59	—	—	—
Age, y						
Continuous	1.0	0.97-1.0	.94	—	—	—
Tumor size, cm						
Continuous	1.1	0.89-1.2	.58	—	—	—
GR protein expression						
Negative vs positive	0.35	0.15-0.83	.013	0.24	0.10-0.61	.0025
ERα protein expression						
Negative vs positive	1.2	0.40-3.4	.79	—	—	—
ERβ protein expression						
Negative vs positive	0.64	0.29-1.4	.27	—	—	—
AR protein expression						
Negative vs positive	0.58	0.20-1.7	.31	—	—	—

Abbreviations: 95% CI, 95% confidence interval; AR, androgen receptor; ER, estrogen receptor; GR, glucocorticoid receptor; HR, hazard ratio; WHO, World Health Organization.

DISCUSSION

In the current study, high rates of GR and ERβ expression were observed in thymoma and thymic carcinoma. Furthermore, multivariate analysis revealed that GR expression was associated with better prognosis in those patients with surgically resected thymoma and thymic carcinoma. In addition, we established possible criteria for GR expression in IHC.

To our knowledge, the underlying mechanism of the better prognosis noted for patients with GR protein-expressing tumors, including thymic epithelial tumors, remains unknown. However, it has been shown that GCs contribute in eliciting a positive clinical response in patients with pediatric acute lymphoblastic leukemia or metastatic prostate cancer.[22,23] Moreover, some studies have reported that the administration of GC demonstrated a dramatic response among patients with thymic epithelial tumors, indicating that GC acts a tumor suppressor through the GR in thymic epithelial tumors.[7-13] There have been conflicting results concerning the antitumor effects of GCs. In some tumors, GCs assist tumor progression by inhibiting chemotherapy-induced or immunoresponse-induced apoptosis, promoting tumor growth[24] and increasing cancer invasiveness.[25-27] Conversely, GC induces tumor apoptosis by negatively affecting the transcription of nuclear factor kappaB (*NF-κB*), an important regulator of the immune system and antiapoptotic mechanisms, in various cell lines and lymphocytes.[28-30] In vitro analysis revealed that GCs induce cell cycle arrest and apoptosis in epithelial cells of thymic neoplasms.[4]

Similar to the results of the current study, some tumors that express GR in other organs have shown favorable outcomes and a statistically significant correlation with OS.[31,32] In the correlation analysis of the current study between GR expression score and clinicopathologic factors, the patients with a higher GR expression score demonstrated a more favorable outcome. This result suggested that a low level of physiologic GCs may exert antineoplastic effects. The possible effects of physiologic sex steroids have been demonstrated in the progression of breast and prostate cancers.[33-37] Physiologic steroid hormones can also affect systemic organs. Thus, the results of the current study indicate that physiologic GCs may also play a role in the inhibition of tumorigenesis of thymic epithelial tumors.

The observed immunohistochemical positivity of ERα was low (19 cases; 13.6%) compared with a previous report in which approximately two-thirds of thymoma

cases were positive.[38] One possible reason for this discrepancy is that because ERα expression was heterogeneously distributed, areas with positive ERα expression could not be easily detected on TMA, which was a tiny area compared with the whole section. Another possible reason is the differences in the specificity and sensitivity of the antibodies used for ERα. The clone 6F11 that was used in the previous study was not highly specific for ERα. Clone 6F11 recognizes the full-length protein. Because the full-length ERβ protein is homologous to the full-length ERα protein, clone 6F11 may recognize ERβ as ERα, with particular binding in the DNA binding domain . Furthermore, we used a highly sensitive rabbit monoclonal antibody (clone SP1) that demonstrated an 8-fold higher affinity than the mouse antibody.[39] Thus, the results of the current study indicate that the immunohistochemical positivity of ERα is not very high in both thymoma and thymic carcinoma.

Unlike ERα expression, we detected high expression of the ERβ protein (76.4%). In addition, the results of the current study demonstrated a high positivity (94.7%) in type A + AB thymoma and a decreased positivity (33.3%) in type B3 thymoma. This result indicates that the high expression of ERα noted in the earlier mentioned study may be because of a cross-reaction with ERβ. To the best of our knowledge, there was only 1 report published to date analyzing ERβ expression in thymomas, and the expression rate was extremely low (7%)[38] compared with that observed in the current study. This discrepancy may be because of differences in the patient population, source of antibody, dilution, method of antigen retrieval, and scoring system. Among these, the most likely factor was the difference in the source of antibody. The clone EMR02, which was used in the current study, recognizes the C-terminus, whereas the clone 06-629 that was used in the previous study recognizes the N-terminus. Another possibility was the difference in the patient population.

The issue of whether ERβ is a target in tumor therapy is controversial. However, there is increasing evidence in several studies that ERβ is significantly related to cancer invasiveness. ERβ expression has been frequently observed in metastases of prostate cancer using IHC.[40] In addition, in vivo and in vitro studies have demonstrated that ERβ exerts stimulative effects on breast cancer development and metastasis.[41] It has also been shown that ERβ negatively affects malignant cell tumorigenesis.[19,42,43] Although to our knowledge the exact correlation between ERβ expression and tumor progression in thymic epithelial tumors is still unclear, ERβ is suggested as a potential target in the treatment of ERβ-positive thymomas and thymic carcinomas.

In the current study, we found that PgR-A and AR proteins were expressed at low levels in thymomas and thymic carcinomas. The previous study also demonstrated low expression rates of PgR-A (4%) and AR (15%).[38] These results indicate that PgR-A and AR have low potential as targets for therapy and have little involvement in thymoma and thymic tumorigenesis.

The results of the current study also demonstrated a significant correlation of histologic subtype and tumor stage with OS. There have been conflicting results concerning prognosis among the histologic subtypes of thymic epithelial tumors.[44-49] Some reports have shown that patients with type B3 thymoma have a worse prognosis than those with type B2 thymoma,[44,45] whereas others have reported no significant difference in survival between these 2 groups.[46-49] The results of the current study indicated no difference in the 10-year OS rates between patients with type B1 + B2 (89.5%) and type B3 (75.0%) thymomas ($P = .30$), whereas significant differences ($P < .001$) were noted between patients with type B1 + B2 (86% and 85%, respectively) and type B3 (38%) thymomas in a previous report from our institution.[44] A possible reason is the difference in the period of analysis; the analysis of the current study was conducted between 1999 and 2009 for thymoma, whereas that of the previous report was performed between 1962 and 2000.

The results of the current study demonstrated a high rate of GR and ERβ expression in thymomas and thymic carcinomas. Furthermore, multivariate analysis revealed that GR expression was associated with better prognosis in patients with surgically resected thymomas and thymic carcinomas. These associations should be validated through prospective studies that include greater numbers of cases.

FUNDING SOURCES

No specific funding was disclosed.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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