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E-CADHERIN ADHESION MOLECULE AND SYNDECAN-1 EXPRESSION IN VARIOUS THYROID PATHOLOGIES

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Cadherins and syndecans are transmembrane glycoproteins implicated in cell-cell and cell-matrix adhesion. Impairment of cadherin and syndecan mediated adhesion is likely to constitute one of the main factors leading to the reduced cell-cell and cell-matrix adhesion characteristics of tumor cells and play a pivotal role in the acquisition of invasive and metastatic proprieties by neoplastic epithelial cells. ***Aim:*** **To elucidate the role and alterations of syndecan-1 expression in comparison with those of E-cadherin in normal and pathological thyroid glands (TG).** ***Methods:*** **A total of 55 TG carcinomas, 40 TG adenomas, 40 cases of hyperplastic TG disorders and 20 cases of normal TG autopsy samples, were evaluated by immunohistochemistry. The staining intensity, and localization of syndecan-1 and E-cadherin in sequential sections were examined, and semi-quantified.** ***Results:*** **Immunostaining of syndecan-1 and E-cadherin was strong in normal follicular TG epithelial cells, and located mainly in basolateral membrane. No significant change was seen in either molecule in hyperplastic TG disorders compared with TG adenomas. A significant reduction in expression of both syndecan-1 and E-cadherin was seen in well-differentiated TG carcinomas as compared with normal TG epithelium ($p = 0.0001$ and $p = 0.032$, respectively). Similarly, there was a significant reduction of both molecules expression in poorly differentiated and anaplastic TG carcinomas compared to well differentiated tumors (syndecan-1: $p = 0.0037$; and E-cadherin: $p = 0.075$).** ***Conclusion:*** **Decreased E-cadherin and syndecan-1 expression along with decreasing cellular differentiation may be involved in the complex mechanism of progression of TG pathology.**

Key Words: **adhesion molecules, cadherin, syndecan, thyroid cancer.**

Follicular cell-derived thyroid carcinoma is the most common endocrine malignancy, representing almost 2% of all reported human cancers. Papillary carcinoma is the most common, and it accounts 65% to 80% of the 15,000 annual thyroid cancer cases in the United States [1]. Because, at the time of clinical presentation, most of the tumors are still confined to the thyroid gland (TG), appropriate surgical treatment achieves a 95% — 5-year survival [1, 2]. Follicular carcinomas account between 4% and 39% of all malignant tumors, and medullary thyroid carcinoma, a relative rare cancer, account up to 10% of all thyroid cancers, is composed of C (parafollicular) cells [1, 3]. Several prognostic factors have been reported to be significant in thyroid cancers, such as age of presentation, local tumor size, extrathyroidal spread, distant metastasis, and histology [3]. Although certain histologic variants of papillary carcinoma are recognized to behave in a more aggressive fashion, routine histopathologic parameters fail to prospectively identify the subset of conventional papillary carcinomas that is associated with unusually aggressive biological potential. Therefore, early markers to predict patients with a low risk of suffering a poor outcome from those with a higher risk of suffering a poor outcome are lacking.

The ability of malignant tumors to metastasize depends on various factors such as the capacity to degrade the extracellular matrix (ECM), to enter or exit the blood circulation, and to proliferate in different microenvironments. At present, some families of adhesion receptors are known to exist, which comprise the cadherins, syndecans, integrins, selectins, immunoglobulin supergene familiy, and CD44 [4]. Syndecan-1 is a membrane proteoglycan which functions in cell-extracellular matrix adhesion, cell-cell adhesion, cell migration, as well as in regulation of cell morphology [5, 6]. It binds via heparin sulfate chains to both insoluble molecules within the ECM including interstitial collagens, fibronectin, tenascin, thrombospondin and growth factors such as FGF2 [5]. During organogenesis, syndecan-1 is expressed on both epithelial and mesenchymal cells, predominantly on the surface of epithelial cells [7], while in the adult syndecan-1 expression is found predominantly on the surface of epithelial cells, including those of the skin [8], vagina [9], cervix [10], gastric [7] and colonic mucosa [11].

E-cadherin, a 120 kDa glycoprotein is a calcium-dependent homophilic cell adhesion molecule [12], which plays a central role in maintaining epithelial integrity, functioning in intercellular adhesion and differentiation, as well as in establishing and maintaining cell polarity and tissue architecture [13, 14]. The prototypic E-cadherin (also called LCAM, uvomorulin) has been mapped on chromosome 16q22.1 [4, 15]. A mechanical linkage at the zonula adherens between E-cadherin and cytoskeleton actin filaments mediated by catenins is critical for normal E-cadherin function [4, 12]. Failure of E-cadherin/catenin complex assembly and failure of proper actin cytoskeleton connection results in loss of adhesion [16]. Changes in E-cadherin function are evident in morphogenetic events asso-

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Abbreviations used: ECM – extracellular matrix; FCs – follicular carcinomas; PCs – papillary carcinomas; TG – thyroid gland; UCs – undifferentiated or anaplastic carcinomas.

ciated with cellular rearrangement, movement and wound healing [17].

Malignant epithelial neoplasms develop with concomitant changes in cellular adhesion, cell motility and changes in the ECM environment [16]. This suggests that the function and expression of adhesion molecules may also change during malignant transformation as it has been previously reported [8, 18]. Syndecan-1 may play a pivotal role in limiting tumor growth and invasive capacity through its action as a receptor for ECM. The ability to invade the ECM is important to neoplastic cells [19]. During malignant progression, syndecan-1 expression is lost on cells exhibiting an invasive phenotype [20]. In addition, cells which normally invade type I collagen gels, *in vitro*, are rendered non-invasive following their transfection with a cDNA for syndecan-1, thus providing direct evidence that loss of syndecan-1 expression may be an essential element in the process of invasion [21]. Loss of E-cadherin mediated intercellular adhesion is also important factor in tumor pathogenesis [22]. E-cadherin deficiency in tumors leads to changes in motility and morphology, and, as such, E-cadherin is considered to have a tumor suppressor function [16]. Numerous studies have shown that E-cadherin function is frequently inactivated in cancers of the breast [23], colon [12], ovarian [24], stomach [25], liver [12], esophagus [12], endometrium [26], kidney [12], lung [27] and thyroid [28]. E-cadherin has been found to stain moderately, and in some cases strongly in well-differentiated carcinomas, which maintain their intercellular adhesion and thus are less invasive, and to stain weakly in poorly differentiated carcinomas, which have lost their adhesivity [22].

The purpose of this study was to clarify the role and alterations of syndecan-1 expression in comparison with those of E-cadherin in different cellular phenotypes of thyroid neoplasms, by using immunohistochemical staining.

MATERIAL AND METHODS

Representative histological slides and paraffin blocks were retrieved from the files of the Departments of Forensic Pathology and Pathology, of the Medical School of the University of Ioannina. The mean age of patients was 54 (range 21–86 years). Samples included in this study consisted of normal thyroid gland (n = 20), hyperplastic disorders (nodular hyperplasias, n = 23; adenomatous hyperplasias, n = 17), adenomas (microfollicular type, n = 10; macrofollicular type, n = 18; 7 cases of mixed adenomas, and 5 cases of Hurthle's adenomas) and carcinomas (papillary, n = 18; papillary microcarcinomas n = 14; follicular, n = 7; medullary carcinomas, n = 3 cases; Hurthle's carcinomas, n = 2, poorly differentiated carcinomas, n = 5, and finally, anaplastic carcinomas, n = 6) were collected and classified according to histopathological criteria by the World Health Organization committee (WHO) [29]. Normal thyroid tissue samples were obtained from autopsies with their relatives' consent. The average of the tumor size was 2.5 cm (1.8 to 3.1 cm) from conventional papillary carcinomas; 0.7 cm (0.3–1.0 cm) from papillary microcarcinomas; 2.3 cm (1.5–2.8 cm) from follicular and medullary carcinomas; and 3.5 cm (3.5–6.4 cm) from poorly differentiated and anaplastic carcinomas.

Immunohistochemistry. For immunohistochemical analysis the specimens were cut at 4 μm on poly-l-lysine slides. Syndecan-1 was stained using mouse monoclonal antibody against human syndecan-1 (DL-101; Santa Cruz Biotechnology, USA). In the study, E-cadherin, a monoclonal mouse antibody, which recognizes an epitope of human E-cadherin, was used (Biotechnology, Santa Cruz, USA). The deparaffinized and rehydrated sections were heat treated in 10 mmol citrate buffer (pH = 6.0) for 40 min at 95 °C for antigen retrieval before staining. After endogenous peroxidase blocking and incubation in normal goat serum for 20 min, these sections were incubated at 4 °C overnight with primary antibodies (syndecan-1 antibody (1 : 100 dilution) and E-cadherin (1 : 100 dilution)). After rinsing in PBS, they were treated with streptavidin — biotin — peroxidase complex technique (DAKO Co., Glostrup, Denmark). The peroxidase reaction was visualized by incubating the section with 3,3′-diaminobenzidine tetrahydrochloride (DAB, from DAKO). The sections were counterstained with Harri's haematoxylin. Sections of normal skin were used as positive controls. Omission of the primary antibodies in a matched serial normal tissue section (which lacks the specific staining of the respective primary antibody) was used as a negative control.

Scoring of immunostaining. All sections were first screened to disclose the areas with well-preserved tissue architecture and cell morphology for scoring of immunoreactivity. Necrotic tumor areas or areas with deterioration of tissue morphology due to processing were discarded in the analysis. Immunoreactivity for syndecan-1 and E-cadherin was assessed by two observers, (AM, EI) independently, and using microscope (Olympus, x 40 objective) and scored using a semi-quantitative approach. Assessment of syndecan-1 and E-cadherin expression was done without any knowledge of the slide examined. Differences in interpretation were reconciled by re-review of slides separately or jointly at a double-headed microscope. The specimens were classified according to intensity, the localization, and the distribution of staining. Staining intensity was classified as absent (–), weak (+), moderate (++), and strong (+++). Cellular localization of staining was noted as diffuse cytoplasmic or staining of cell-cell contact sites or in both. Distribution of staining was classified as homogeneous (uniform staining of cells), focal (areas of positively stained cells) or heterogeneous (scattered positively and negatively stained cells).

Statistical analysis. To compare morphological features and proteins expression data Superior Performance Software System (SPSS), software 10.0 for windows Inc., (1999) was used. Significant differences

between the expression of the target protein was computed by the *Fisher* test for paired or non-paired values or ANOVA test. *P* values ⩽ 0.05 were considered statistically significant.

RESULTS

Syndecan-1, E-cadherin immunoreactivity in normal thyroid tissue. The epithelial cells in all normal thyroid tissue specimens examined showed distinct to moderate syndecan-1 and E-cadherin immunoreactivity. The staining intensity was strong in 85% and 75% of the cases respectively. This immunoreactivity was less intense in the flat cell lining large follicules than in cuboidal or columnar cells lining medium-size or small follicules. The lateral borders of epithelial cells exhibit more intense staining than the basal borders. With respect to localization of immunostaining, syndecan-1 and E-cadherin were expressed both in cell membrane and cytoplasm of the thyrocytes, with homogeneous distribution. In our study the stromal components of normal thyroid tissue, were completely un-reactive for both molecules. The results are shown in Tables 1 and 2.

Table 1. Immunoreactivity for syndecan-1 in normal, hyperplastic, and neoplastic thyroid tissue

Histology	Number of cases	Total	Intensity of immunostaining (%)			
			–	+	++	+++
Normal tissue	20	13.3			15	85
Hyperplasias:	40	26.6				
Nodular	23	15.3			21.7	78.2
Adenomatous	17	11.3			35.3	64.7
Adenomas:	40	26.6				
Macrofollicular	18	12	11.1	27.8	27.8	33.3
Microfollicular	10	6.6	10	20	30	40
Mixed	7	4.6		14.3	42.8	42.8
Hurtle cell	5	3.3		20	60	20
Carcinomas:	55	33.3				
Papillary	18	12	5.5	16.6	50	27.7
Micropapillary	14	6.6	7.6	23.1	61.5	7.6
Follicular	7	4.6	14.3	28.5	57.1	
Hurthle	2	1.3		100		
Medullary	3	2.0	100			
Poorly differentiated	5	9.09		33.3		
Anaplastic	6	4.0	66.6	33.3		

Table 2. Immunoreactivity for E-cadherin in normal, hyperplastic and neoplastic thyroid tissue

Histology	Number of cases	Total	Intensity of immunostaining (%)			
			–	+	++	+++
Normal tissue	20	13.3			25	75
Hyperplasias:	40	26.6				
Nodular	23	15.3		13.1	56.5	30.4
Adenomatous	17	11.3		23.5	64.7	11.8
Adenomas:	40	26.6				
Macrofollicular	18	12	5.5	44.4	38.8	11.1
Microfollicular	10	6.6		30	60	10
Mixed	7	4.6		28.5	57.1	14.2
Hurtle cell	5	3.3		40	60	
Carcinomas:	55	33.3				
Papillary	18	12	16.6	27.7	38.8	16.6
Micropapillary	14	6.6	23.1	38.5	30.7	7.7
Follicular	7	4.6	28.5	28.5	42.9	
Hurthle	2	1.3		100		
Medullary	3	2.0	100			
Poorly differentiated	5	9.09		33.3		
Anaplastic	6	4.0	83.3	16.6		

Syndecan-1and E-cadherin immunoreactivity in hyperplasias. The intensity of syndecan-1 and E-cadherin immunostaining in hyperplasias was usually homogeneous and in some cases heterogeneous, and less intense than in normal follicular epithelium. The reduction of immunoreactivity for both molecules may be due to flat cells lining large follicules fullfilled with colloid. We found a statistically significant difference between normal thyroid tissue and nodular hyperplasias ($p < 0.0001$), indicating that the intensity of expression of syndecan-1 and E-cadherin was stronger in normal tissue than in hyperplasias. There was no statistically significant difference among the types of hyperplasia. Therefore, E-cadherin expression was reduced in nodular hyperplasias in comparison with the adenomatous ones ($p = 0.0048$).

Syndecan-1 and E-cadherin expression in adenomas. Membranous and cytoplasmatic staining of syndecan-1 and E-cadherin was displayed in the cases of adenomas examined. Differences in intensity were seen, as well as with the distribution of immunostaining. The immunoreactivity was weak to moderate in 83.2% of the cases for E-cadherin and 55.5% of the cases for syndecan-1, and strong in 11.1% and 33.3% respectively. Reduced expression of both molecules was associated with the different histological type of adenomas.

A statistically significant difference between adenomas and normal thyroid tissue (syndecan-1, $p = 0.001$, and E-cadherin $p = 0.0001$) was found. In addition, no significant difference of syndecan-1 and E-cadherin localization among the types of adenomas was observed. Generally the distribution of syndecan-1 and E-cadherin in adenomas was rather irregular than homogeneous. In the cases of microfollicular adenomas the distribution of syndecan-1 and E-cadherin staining was more homogeneous than in macrofollicular adenomas in which the staining pattern was irregular.

Syndecan-1 and E-cadherin expression in thyroid cancer. Immunoreactivity for syndecan-1 was observed at the cell-cell boundaries and cytoplasm in papillary carcinomas (PCs), with weak expression in 27.7% of the specimens, intermediate expression in 38.8%, and high expression in 16.6%. The lateral borders exhibited more intense staining than their basal borders (Fig. 1). Immunoreactivity for E-cadherin was observed at the cell-cell boundaries in PCs (Fig. 2). The expression of E-cadherin showed high variability in PCs specimens, with no expression in 27.03% of the cases, low expression in 38.5%, intermediate expression in 30.7% and high expression in 3 cases (7.7%). Expression of syndecan-1 and E-cadherin was observed in the cell-cell contact areas and in the cytoplasm in follicular carcinomas (FCs) cells with moderate expression in 42.9% for E-cadherin and 54.1% for syndecan-1. None of the medullary carcinomas specimens showed any immunoreactivity for syndecan-1 and E-cadherin. Poorly differentiated carcinomas showed weakly immunostaining of both syndecan-1 and E-cadherin, in the same proportion (only 2 samples). Undifferentiated or anaplastic carcinomas (UCs) are composed of varying proportions of spindle, polygonal and giant cells. Immunoreactivity

for syndecan-1 and E-cadherin was observed weakly in only one case of UCs (16.6%) for E-cadherin, and in two cases (33.3%) for syndecan-1. Therefore, in areas with differentiation of PCs the immunoreactivity was more markedly positive. A small number of the polygonal or giant carcinoma cells showed very low expression on their membranes. None of the spindle-shaped tumor cells expressed both molecules.

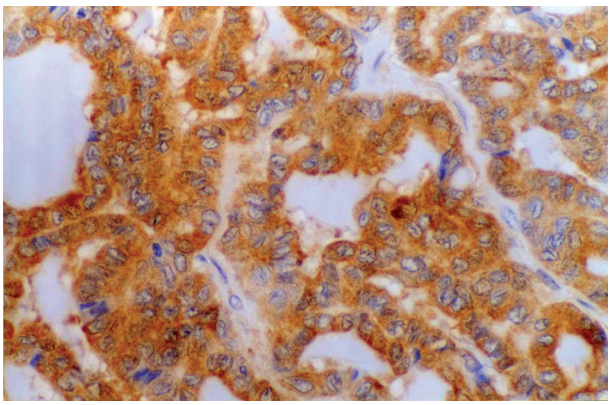

Fig. 1. A case of papillary carcinoma with moderate syndecan-1 immunoreactivity. Note the cell surface expression with prominent cell-cell junction staining and cytoplasmic staining in some tumour cells. x 400

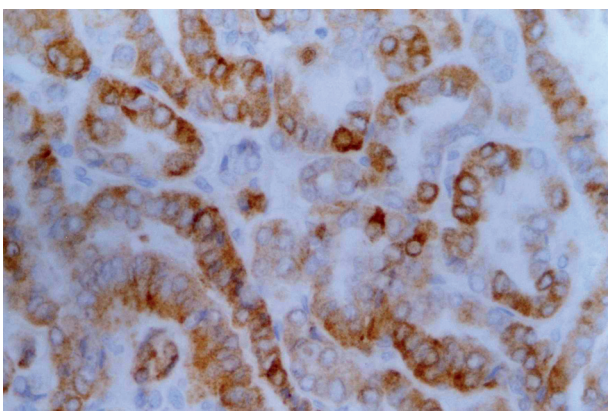

Fig. 2. E-cadherin immunoreactivity was observed at the cell-cell boundaries in the same case of papillary thyroid carcinoma. x 400

In carcinomas, changes in the proportion of cells with positive staining were seen, as well as changes in the intensity of the membranous staining. Analysis of the weighted scores showed a significant reduction in staining for both syndecan-1 and E-cadherin in carcinomas compared with normal thyroid tissue (syndecan-1, $p = 0.004$ and E-cadherin, $p = 0.0004$), hyperplasias (syndecan-1, $p < 0.0001$ and E-cadherin, $p = 0.0001$) and finally with adenomas (syndecan-1, $p = 0.0068$ and E-cadherin, $p = 0.006$). The intensity of E-cadherin was reduced in all studied malignancies. We observed that the intensity of syndecan-1 expression was moderate to strong in some cases of well-differentiated carcinomas, and very weak or absent in poorly differentiated and anaplastic (undifferentiated) carcinomas. Some tumor epithelial cells showed a membrane-dominant expression pattern of syndecan-1 staining, in which the staining was stronger in a cell membrane than in cytoplasm. No statistical difference among the papillary and follicular types of carcinoma was found. A statistically significant difference between moderate to strong immunoreactivity of PCs with UCs ($p = 0.0084$) for syndecan-1 and E-cadherin ($p = 0.0015$), was observed.

Correlation between syndecan-1 and E-cadherin expression. A statistically significant relationship in the intensity of syndecan-1 and E-cadherin ($p < 0.0001$) was found, due to reduction of E-cadherin expression in all the examined samples, as well as in the localization of the staining pattern ($p = 0.002$) and finally with the distribution ($p = 0.068$) of immunoreactivity in both molecules.

DISCUSSION

Syndecan-1 plays an important role in cell-cell adhesion, and many studies have examined the role of syndecan-1 in oncogenesis [19, 25, 30]. Recent reports suggest a decreased expression of syndecan-1 in different types of cancers such as hepatocellular carcinoma [31], lung cancer [32], infiltrating breast cancer [33], laryngeal cancer [34], and carcinoma of the uterine cervix [10]. On the other hand, there are many examples of carcinomas in which the occurrence of altered E-cadherin expression has been correlated with low histological differentiation, increased risk of local invasion and metastatic disease, recurrence, and poor prognosis [23, 24, 26, 27, 35, 36]. Although E-cadherin has been extensively studied in thyroid pathologies [28, 35, 37], syndecan-1 has not been addressed thoroughly. To our knowledge, there is no data that compare syndecan-1 and E-cadherin expression in each cellular phenotype in thyroid pathologies.

We studied a series of tissue samples representing normal TG, hyperplastic lesions, adenomas as well as different histiotypes of carcinomas. The present results demonstrate that the cell-cell adhesion molecules, syndecan-1 and E-cadherin, are expressed strongly in normal TG. This is an expected finding because thyrocytes are typical epithelial cells for which E-cadherin and syndecan-1 are considered to be specific. The surface expression of syndecan-1 and E-cadherin was confined to the basolateral domain of the plasma membrane, the area of cell-cell contact. Thus, there is both biochemical and functional evidence that syndecan-1 and E-cadherin may be important in cell-cell adhesion in the thyroid follicular epithelium.

In tissue of various benign thyroid diseases, included in the present study, e.g. hyperplasias, E-cadherin expression were moderate to strong, (25% and 75% of the cases, respectively) and are accordingly to other reports [28, 37, 38]. In our report, we found that syndecan-1 immunoreactivity was strong in normal epithelium and moderate in hyperplasias (85% and 78.5% of the cases, respectively). In follicular adenomas syndecan-1 and E-cadherin immunostaining was reduced in comparison with the normal tissue. The thyroid follicular adenoma consisting of Hurthle cells displayed a reduced immunostaining, which was mainly cytoplasmic and its localization might be impaired due to abnormal subcellular targeting of the molecules.

In the present report, the both molecules, syndecan-1 and E-cadherin were expressed and impaired in thyroid carcinomas. The staining was clearly detectable in the majority of well-differentiated papillary carcinomas and microcarcinomas. By contrast, in medullary, poorly differentiated, and anaplastic thyroid carcinomas the immunoreactivity was, in conformity with differentiated tumors, only weakly positive or most often, unreactive, indicating that syndecan-1 and E-cadherin are markers of thyroid differentiation. This is further supported by the fact that most PCs, are generally known as rather slowly growing tumors, although PCs have a highly metastatic rate to the regional lymph nodes [3, 39].

This is analogous to the simultaneous disappearance of both E-cadherin and syndecan-1 from the embryo during loss of the epithelial phenotype [40]. Loss of cell surface syndecan-1 in normal murine mammary gland epithelia is accompanied by reduced E-cadherin expression [20]. Manipulation of either syndecan-1 or E-cadherin expression seems to suggest that E-cadherin regulates syndecan-1 or, conversely, syndecan-1 regulates E-cadherin in epithelial cells [40]. When syndecan-1 is down regulated by anti-sense, transfection in mammary epithelial tumor cells, E-cadherin expression is lost from the cell surface, and when E-cadherin is expressed following transfection, syndecan-1 is upregulated. [6]. It may be that E-cadherin and syndecan-1 act in concert, being regulated together, and that suppression of both leads to malignant transformation of epithelial cells.

Our results are in contrast to findings in the study of Ito et al. [41], in which syndecan-1 was expressed in both stromal and neoplastic epithelial cells. The authors found that stromal syndecan-1 expression was observed more frequently in larger papillary carcinomas and in poorly differentiated than in well-differentiated carcinomas. These contradictory results may be probably due to the difference in the sampling of the cases, techniques, methods of analysis, and besides the use of a different antibody. Our present results demonstrated the reduced expression of syndecan-1 in the epithelia, from normal to benign and malignant lesions, and the absence of syndecan-1 reaction in the stromal components; syndecan-1 has been regarded as an inhibitor of cell migration and metastasis [5].

The potential mechanisms for syndecan-1 deregulation in malignant progression include increased protease activity, transcriptional regulation and post-transcriptional regulation. Active shedding of syndecan-1 occurs from the cell surface and may be due to increased protease activity within the tumor [42]. Changes in syndecan-1 expression can also be regulated by post-transcriptional mechanisms, including suppression and alteration of glycosylation, although these are not well understood [6].

The disturbance in E-cadherin-mediated cell adhesion, evident in the current study of well-differentiated and undifferentiated tumors, is likely to be attributable to alterations in the E-cadherin/catenin complex. Possible mechanisms for interfering with E-cadherin function include transcriptional downregulation, tyrosine phosphorylation of catenins, mutations of the E-cadherin or catenin genes and abnormal recycling of E-cadherin [12, 17, 43]. Surface expression of E-cadherin may be influenced by a balance between endocytosis of membrane E-cadherin and transport of the protein to the cell surface. Le et al. [17] found that even at steady state in confluent monolayers, surface E-cadherin is subject to endocytosis and recycling. The proportion of the protein in the recycling pool is increased in the absence of stable cell-cell contacts [17, 20]. This may be the explanation for the other interesting finding resulting from our investigation, namely the abnormal location of syndecan-1 and E-cadherin in some normal follicules and in some tumor cells. In some of them with homogeneous and heterogeneous syndecan-1 and E-cadherin expression, immunoreactive molecules were located diffusely in the cytoplasm. These findings suggest that functional disorders may occur in syndecan-1 and E-cadherin expression. Further study of the significance of cytoplasmic staining, may reveal new insights into biology of cancer.

In conclusion, the present study assessed the expression of E-cadherin and syndecan-1, which are only one part of the cell-cell and cell-matrix adhesion system in the tumors of the TG. Both proteins expression decreased with decreasing cellular differentiation. The concomitant reduction of the content of these molecules along with tumor dedifferentiation may be correlated with more aggressive phenotype.

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ЭКСПРЕССИЯ Е-КАДГЕРИНА И СИНДЕКАНА-1 В ТКАНИ ЩИТОВИДНОЙ ЖЕЛЕЗЫ ПРИ ЕЕ РАЗЛИЧНОЙ ПАТОЛОГИИ

Кадгерины и синдеканы — это трансмембранные гликопротеины, участвующие в межклеточной адгезии и адгезии клеток к матриксу. Изменения экспрессии этих молекул играют главную роль в приобретении инвазивного и метастатического потенциала злокачественно трансформированными эпителиальными клетками. *Цель:* оценка роли экспрессии синдекана-1 и Е-кадгерина в ткани щитовидной железы в норме и при патологии. *Методы:* образцы ткани для иммуногистохимического исследования взяли у 55 больных раком щитовидной железы (ЩЖ), 40 пациентов — с аденомой ЩЖ, 40 — с гиперпластическими процессами ЩЖ, контролем служили 20 образцов неизмененной ткани ЩЖ (аутопсия). *Результаты:* экспрессия синдекана-1 и Е-кадгерина в нормальных фолликулярных эпителиальных клетках ЩЖ выражена интенсивно, с преимущественной локализацией в базолатеральной мембране. Не отмечали существенных различий в экспрессии обеих молекул при гиперпластических процессах по сравнению с аденомами ЩЖ. Однако таковая значительно снижена в образцах высокодифференцированной карциномы по сравнению с нормальным эпителием ЩЖ ($p = 0{,}0001$ и $p = 0{,}032$ соответственно), а также при низкодифференцированном и анапластическом раке по сравнению с высокодифференцированными опухолями ЩЖ ($p = 0{,}0037$ для синдекана-1 и $p = 0{,}075$ для Е-кадгерина). *Выводы:* снижение экспрессии синдекана-1 и Е-кадгерина, сопровождающееся снижением способности клеток к дифференциации, может быть частью механизма прогрессирования заболеваний ЩЖ.

Ключевые слова: **молекулы адгезии, кадгерин, синдекан, рак щитовидной железы.**