

Invasion, Recurrence, and Progression Relationship of CD47 and CD138 Staining Levels in Bladder Tumors: A Pilot Study

Uğur Akgün¹, Taşkın Erkinüresin², Efe Önen¹, Özgür Ekici¹, Volkan Çağlayan¹, Abdullah Erdoğan¹, Metin Kılıç³, Sinan Avcı¹, Turgut Kaçan⁴, Sedat Öner¹

¹University of Health Sciences Türkiye, Bursa City Hospital, Department of Urology, Bursa, Türkiye

²University of Health Sciences Türkiye, Kanuni Sultan Süleyman Education and Research Hospital, Department of Pathology, İstanbul, Türkiye

³University of Health Sciences Türkiye, Bursa High Specialization Education and Research Hospital, Department of Urology, Bursa, Türkiye

⁴Atlas University Medical Faculty, Department of Internal Medicine and Medical Oncology, İstanbul, Türkiye

What's known on the subject? and What does the study add?

CD138 (syndecan-1) is expressed in normal urothelium, and its loss has been linked to aggressive behavior in several carcinomas, while CD47 helps tumor cells evade macrophages. Data on both markers in urothelial carcinoma are limited and conflicting. In this pilot study of 116 transurethral resection specimens, CD138 expression decreased with increasing T stage and grade, and lower CD138 was associated with higher progression risk. CD47 expression increased with T stage but was not associated with grade, recurrence, or progression. CD138 may be a candidate prognostic marker warranting validation in larger prospective studies.

Abstract

Objective: This study aimed to evaluate the relationship between cluster of differentiation 138 (CD138) and CD47 expression levels in urothelial carcinoma of the bladder and their association with tumor stage, grade, recurrence, and progression.

Materials and Methods: A total of 116 patients (mean age: 67.8±10.5 years) diagnosed with bladder urothelial carcinoma who underwent transurethral resection of bladder tumor were retrospectively analyzed. The slides obtained from transurethral resection specimens were re-evaluated by the same pathologist. Immunohistochemical staining for CD138 and CD47 was performed, and staining levels were evaluated for correlation with pathological stage, grade, recurrence, and progression.

Results: Of the 116 patients, 34 (29.4%) were in the Ta stage, 35 (30.2%) were in the T1 stage, 45 (38.7%) were in the T2 stage, and 2 (1.7%) were in the carcinoma in situ stage. In addition, 39 patients (34%) were classified as low-grade and 75 (66%) were classified as high-grade. CD138 staining levels significantly decreased with increasing tumor stage and grade. Higher CD138 expression was associated with a lower risk of progression (p=0.003). CD47 expression levels significantly increased with tumor stage but showed no significant correlation with tumor grade or recurrence. While CD47 staining was associated with advanced T stage, no correlation was found between CD47 levels and disease progression.

Conclusion: CD138 may serve as a useful prognostic marker in bladder cancer, with lower expression levels indicating a higher risk of tumor progression. CD47 expression is positively associated with tumor stage.

Keywords: Bladder tumor, CD47, CD138, immunohistochemistry

Introduction

Bladder cancer is the most common malignancy of the urinary system, accounting for 6-8% of all cancers in men and 2-3% in women. It is frequently observed in the 6th and 7th decades of life

(1). Urothelial carcinomas account for 90-95% of bladder cancer cases. Approximately 75% of bladder cancers are confined to the mucosa or lamina propria of the bladder at the time of initial diagnosis. Some of these may progress to invade the muscle layer.

Correspondence: Uğur Akgün MD, University of Health Sciences Türkiye, Bursa City Hospital, Department of Urology, Bursa, Türkiye

E-mail: ugurakgun@hotmail.com **ORCID-ID:** orcid.org/0000-0003-0436-7451

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Extensive research is being conducted using various markers to determine the diagnosis and prognosis of bladder tumors (2). Studies have been conducted on oncogenes, cell cycle regulators, and markers associated with apoptosis (3,4). Cluster of differentiation 138 (CD138) is universally expressed in plasma cells and plasma cell tumors, serving as a representative immunomarker for these cells (5). CD138 immunohistochemical expression is generally observed in various epithelial lesions of the urinary tract and in normal urothelial epithelium (6).

CD47 is a transmembrane protein that inhibits phagocytosis by delivering a “don’t eat me” signal to macrophages. While minimally expressed in normal tissues, CD47 is overexpressed in various solid and hematologic malignancies, where it facilitates immune escape and tumor progression. The functions of the cell membrane receptor CD47 include neutrophil migration, T-cell co-stimulation, and neuronal regeneration. CD47 interacts with signal regulatory protein- α (SIRP- α), a specific receptor in macrophages that regulates their functions by downregulating signals (7,8). Its overexpression has been associated with poor clinical outcomes in glioblastoma and in breast, colon, and lung cancers. However, studies evaluating CD47 expression in urothelial carcinoma are limited, although early evidence suggests a potential role in tumor aggressiveness and treatment resistance (9,10). In our study, we aimed to investigate the relationship between the expression levels of CD138 and CD47, immunohistochemical markers, in pathology specimens from bladder cancer patients and various factors, including T stage, histological grade, recurrence, and progression status. Additionally, we aimed to assess their potential clinical utility.

Materials and Methods

This retrospective study was conducted in accordance with the Declaration of Helsinki, patient rights regulations, and ethical principles and was approved by the University of Health Sciences Türkiye, Bursa High Specialization Education and Research Hospital Clinical Research Ethics Committee (approval number: 2011-KAEK-25 2018/06-37, date: 06.06.2018). The study was carried out between 1 September 2018 and 1 March 2019. Patients included in our study underwent transurethral resection of bladder tumor (TUR-BT) between 2013 and 2017 at our urology clinic and were diagnosed with bladder cancer for the first time. The informed consent form was obtained from the patients.

The inclusion criteria for our study were patients who had undergone TUR-BT and been diagnosed with urothelial carcinoma at pathological stages Ta, T1, T2, or carcinoma *in situ* (CIS). Exclusion criteria included patients with bladder tumors other than urothelial carcinoma (e.g., adenocarcinoma and

squamous cell carcinoma), patients with autoimmune diseases, patients with malignancies outside the bladder, patients who received radiotherapy or chemotherapy for any reason, and patients lacking sufficient clinical data.

The patients’ demographic characteristics were age and gender. Histological grades and stages were recorded after TUR-BT. The numbers of TUR-BT procedures and cystoscopies that patients underwent, as well as subsequent pathological diagnoses, were documented. Recurrence was defined as detection of recurrence on subsequent cystoscopic examinations, whereas progression was defined as advancement in stage or development of metastases during follow-up.

Slides obtained from transurethral resection specimens of 116 cases of bladder urothelial carcinoma, examined between 2013 and 2017 at the Pathology Clinic of University of Health Sciences Türkiye, Bursa High Specialization Education and Research Hospital, were re-evaluated by the same pathologist (Taşkın Erkinürsün). For each case, two sections were taken from the paraffin block corresponding to the most suitable slide (where invasion was most common and stage-defining) for immunohistochemical examination: one stained with CD47 and the other with CD138.

Immunohistochemical examination: Transurethral resection specimens were fixed in 10% neutral-buffered formalin for 24-48 hours. After macroscopic examination, the materials were blocked and embedded in paraffin following overnight tissue processing. A paraffin block containing sufficient tumor tissue and the area of deepest invasion was selected for each case. Slides were deparaffinized by heating in an oven and by immersion in xylene, then gradually rehydrated in a series of ethanol-water mixtures. Immunohistochemical staining was performed according to the manufacturer’s instructions for the Leica Bond-Max automated immunohistochemistry staining machine, using the monoclonal antibodies CD47 (B6H12 clone) (Santa Cruz eBioscience, San Diego, CA, USA) and BOND™ Ready-to-Use Primary Antibody CD138 (MI15) (University Department of Cellular Science, John Radcliffe Hospital, Oxford, UK). Heat-induced epitope retrieval was performed using BOND Epitope Retrieval Solution 1 for 30 minutes.

Evaluation of immunohistochemistry: For each case, a block containing the densest carcinoma tissue obtained by TUR-BT was selected after examination of routine hematoxylin and eosin-stained sections under a microscope. Immunohistochemical staining for CD47 and CD138 was performed using 4 μ m thick sections obtained from these blocks. In all these techniques, 3,3'-diaminobenzidine was used as a chromogen. Monoclonal antibodies were used. Hematoxylin stain was used as a counterstain. Samples with known positive reactivity for each antibody were used as positive controls. Based on personal observations and findings from previously reported literature

(for CD138 and CD47), the staining pattern was defined as positive or negative, as follows:

CD138 and CD47 positive: More than 5% staining in malignant cells (+, ++, +++, ++++),

CD138 and CD47 negative: Membranous staining in less than 5% of malignant cells.

Positivity for CD47 and CD138 in urothelial carcinoma was categorized into three groups according to the percentage of stained cancer cells: 1+: membranous staining in 6-35% of cells; 2+: membranous staining in 36-65% of cells; and 3+: membranous staining in 66-100% of cells (Figures 1 and 2).

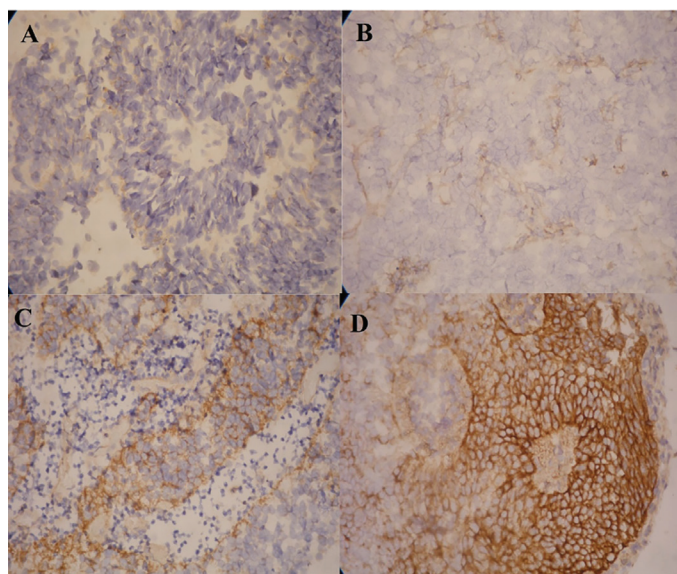


Figure 1. CD47 staining levels (40X). A) Negative (-), B) 1+ (+), C) 2+ (++), D) 3+ (+++)

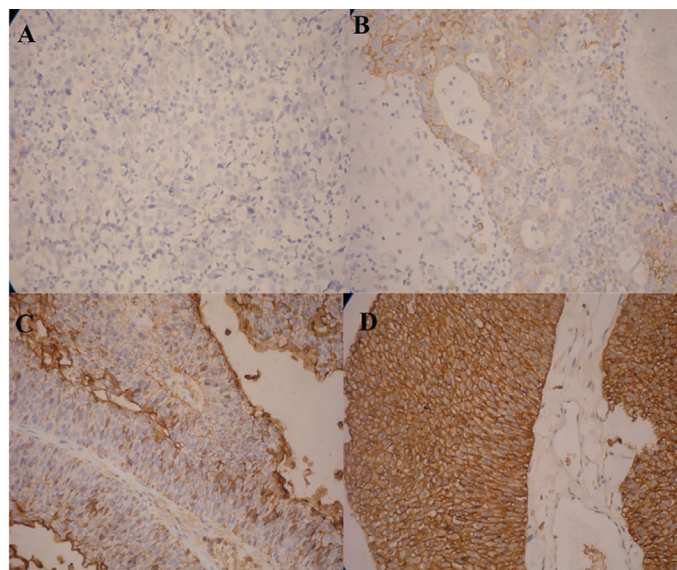


Figure 2. CD138 staining levels (40X). A) Negative (-), B) 1+ (+), C) 2+ (++), D) 3+ (+++)

Statistical Analysis

In our study, the SPSS version 21.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Frequencies and percentages were used to describe categorical data. Differences between groups with respect to categorical variables and associations between variables were examined using Fisher's exact test. For quantitative data analysis, data distribution was assessed using the Kolmogorov-Smirnov test, and correlations between variables were evaluated using the Spearman test. The significance level for all analyses was set at $p < 0.05$.

Results

Our clinic obtained data from 120 patients who underwent TUR-BT between 2013 and 2017. Four patients were excluded from the study due to insufficient data. A total of 116 patients were included in the study. The median age of the 116 patients included in the study was 69 years (range, 38-89). Of these patients, 12.06% were female and 87.94% were male. Following TUR-BT, tumor stages were distributed as follows: Ta, 34 patients (29.4%); T1, 35 patients (30.2%); T2, 45 patients (38.7%); and CIS, 2 patients (1.7%). The two patients with CIS were excluded from further statistical analysis. Among the 34 patients with tumor-node-metastasis (TNM) stage Ta, 14 developed recurrence during follow-up, while no recurrence was observed in 20 patients. Only one patient with recurrence exhibited progression. Among the 35 patients with TNM stage

Table 1. Demographic characteristics of the patients (n=116)	
Variables	n (%)
Sex	
Male	102 (87.94%)
Female	14 (12.06%)
Tumor T stage	
Ta	34 (29.4%)
T1	35 (30.2%)
T2	45 (38.7%)
CIS	2 (1.7%)
Histological grade	
Low grade	39 (34.2%)
High grade	75 (65.8%)
Recurrence	
Absence	44 (64%)
Presence	25 (36%)
Progression	
Absence	65 (94%)
Presence	4 (6%)
Follow up time (month) (min-max)	3-36
CIS: Carcinoma <i>in situ</i> , Min-max: Minimum-maximum	

T1, 11 developed recurrence during follow-up, while 24 did not. Three patients with recurrence showed progression. Patients with TNM stage T2 who underwent radical cystectomy, radiotherapy, or chemotherapy after TUR-BT were excluded from further evaluation of recurrence and progression because of the complexity of the treatment regimen. Therefore, these patients were not included in the recurrence and progression analysis (Table 1).

Correlation analysis between T stage and CD138 staining levels showed that CD138 staining decreased significantly as T stage increased ($p=0.005$, correlation coefficient= -0.259) (Tables 2 and 3).

Correlation analysis between tumor T stage and CD47 staining levels showed that CD47 staining levels increased significantly with increasing T stage ($p=0.047$, correlation coefficient= $+0.186$) (Tables 2 and 3).

The correlations of CD138 and CD47 with T stage and grade are shown in Table 3.

When stages are compared, no statistically significant difference is observed in CD138 staining levels between the Ta-T1 and T1-T2 stages. However, T2 patients exhibit a significant decrease in CD138 staining levels compared with Ta patients ($p=0.049$). CD47 staining levels are significantly higher in T1 and T2 patients than in Ta patients (Ta-T1: $p=0.048$, Ta-T2: $p=0.041$). No significant difference was observed between T1 and T2 patients. In terms of pathological grade, 39 patients (34%) were classified as low grade, while 75 patients (66%) were classified as high grade. Correlation analysis between tumor pathological grade

and CD138 staining levels showed a statistically significant negative association, with CD138 staining decreasing as grade increased ($p=0.02$, correlation coefficient= -0.288) (Table 4). No statistically significant correlation was observed between tumor pathological grade and CD47 staining levels ($p=0.577$) (Table 4).

Regardless of the stage, no statistically significant correlation was found between the presence of recurrence and CD138 staining levels. However, as CD138 staining levels increase, a statistically significant reduction in progression is observed ($p=0.003$, correlation coefficient= -0.259). There was no statistically significant relationship found between CD47 staining levels and recurrence or progression.

Analysis of the correlation between CD138 and CD47 staining levels and the T stage revealed a negative correlation for CD138 and a positive correlation for CD47.

Discussion

Intensive studies have been conducted on various markers to determine diagnosis and prognosis of bladder tumors. Research has focused on oncogenes, cell cycle regulators, and markers associated with apoptosis (11,12). Although some of them have shown promise, no suitable marker has been found for routine clinical use. In our study, we investigated the relationship between the expression levels of CD138 and CD47—both immunohistochemical markers—in pathology specimens from patients with bladder tumors and the clinicopathological features T stage, histological grade, recurrence, and progression. According to our results, higher CD47 staining levels are associated with higher T stage, but not with grade, recurrence, or progression. CD138 staining levels, on the other hand, decrease as the T stage and grade increase, and this decrease is associated with an increased risk of progression.

The demographic characteristics of the 116 patients included in the study were consistent with the literature. The mean age at diagnosis was 67.8 years, which is in line with findings from a study by the European Organisation for Research and

Table 2. Distribution of staining levels according to T stages (n=114)

T stage, n (%)	CD138 staining levels			
	Negative	+	++	+++
Ta	1 (2.9%)	1 (2.9%)	3 (8.8%)	29 (85.3%)
T1	0 (0%)	2 (5.7%)	8 (22.9%)	25 (74.1%)
T2	2 (4.4%)	8 (17.8%)	9 (20%)	26 (57.8%)
	CD47 staining levels			
	Negative	+	++	+++
Ta	23 (67.6%)	7 (20.6%)	3 (8.8%)	1 (2.9%)
T1	14 (40%)	14 (40%)	7 (20%)	0 (0%)
T2	21 (46.7%)	11 (24.4%)	9 (20%)	4 (8.9%)

Table 3. Correlation between parameters and CD138 and CD47 (n=116)

(n=114)		CD138		CD47	
		r*	p	r*	p
	T stage	-0.259	0.005	0.186	0.047
	Grade	-0.288	0.02	0.099	0.577

*: Spearman's correlation coefficient

Table 4. Distribution of staining levels according to histologic grades (n=114)

Grade, n (%)	CD138 staining levels			
	Negative	+	++	+++
Low grade	0 (0%)	0 (0%)	5 (12.8%)	34 (87.2%)
High grade	3 (4%)	11 (14.7%)	15 (20%)	46 (61.3%)
	CD47 staining levels			
	Negative	+	++	+++
Low grade	22 (56.4%)	11 (28.2%)	5 (12.8%)	1 (2.6%)
High grade	36 (48%)	21 (28%)	14 (18.7%)	4 (5.3%)

Treatment of Cancer, in which the median age was 65 years among patients with bladder tumors. Furthermore, the male-to-female ratio was 4.1 in the aforementioned study, compared with 7.2 in our study. This difference in the ratio might be attributed to geographical and sociocultural variations (13). Shimada et al. (14) demonstrated that CD138 is upregulated in CIS and invasive urothelial carcinoma and promotes cancer cell survival via the long JunB-FLIP [cellular FLICE (FADD-like IL-1 β -converting enzyme)-inhibitory protein] signaling pathway by increasing resistance to apoptosis and enhancing cell growth. They also found lower levels of CD138 expression in low-grade and non-invasive urothelial lesions (14).

Increased CD47 expression has been observed in many malignancies in humans. Studies have shown that high CD47 expression serves as a diagnostic marker and a negative prognostic factor in patients with leukemia and ovarian cancer (15,16). In a multicenter study conducted by Willingham et al. (17), CD47 expression was increased in several solid cancers, including bladder, prostate, lung, kidney, gastric cancer, hepatocellular carcinoma (HCC), and sarcoma, compared with normal tissue. This condition was identified as a negative prognostic factor (17).

Circulating tumor cells (CTCs) have been detected in the peripheral blood of many cancer types (18). A self-renewing subpopulation has been identified among these CTC groups. These cells, referred to as metastasis-initiating cells and cancer stem cells (CSC), have been demonstrated in breast, prostate, lung, and colorectal cancers (19). It has been shown that CSCs are positive for CD44, CD47, CD123, epithelial cell adhesion molecule, CD133, and insulin-like growth factor 1 receptor. CSCs have been demonstrated to play a significant role in resistance to modern cancer therapies, and targeting the receptors mentioned above is anticipated to increase success rates in cancer treatment (20). In patients with HCC, increased expression of CD47 in tumor-initiating cells has been demonstrated in chemotherapy-resistant compared with chemosensitive patients (21).

Recent studies have investigated CD138 (syndecan-1) as a diagnostic and prognostic marker in urothelial carcinomas. Kind et al. (6) reported that CD138 expression is frequently observed in urothelial tissues and a wide spectrum of epithelial malignancies, including bladder cancer, which supports its role as a universal epithelial marker. Furthermore, Sanaee et al. (5) demonstrated that patients with moderately differentiated bladder tumors have elevated serum levels of soluble CD138, suggesting a potential role for CD138 both in tissue-based evaluation and as a serum biomarker for disease surveillance. Our findings are consistent with these results, as we observed a significant decrease in CD138 expression with advancing tumor stage and grade. This inverse relationship may reflect a loss of epithelial characteristics during tumor progression, including epithelial-mesenchymal

transition, which contributes to increased invasiveness. In 2009, Chan et al. (22) determined that tumor-initiating cells in bladder cancer express high levels of CD47. Additionally, these cells have been shown to be associated with poor prognosis (22). In their 2016 study, Goto et al. (23) demonstrated that CD138 expression is widely observed in all variants of urothelial carcinomas and various other epithelial tumors of the urinary tract. Furthermore, it was noted that CD138 expression is not specific to plasmacytoid urothelial carcinoma (23). In the study conducted by Shimada et al. (14) in 2009, a positive correlation was observed between CD138 expression and T stage, grade, and tumor recurrence. In their studies, Shimada et al. (14) obtained the anti-syndecan-1 antibody from Dako, Japan. However, the specific clone number of the antibody was not specified in the article. Shimada et al. (14) report a positive correlation between the percentages of syndecan-1 immunopositive cells and both tumor grade and T stage. ImageJ software was used for image analysis. However, the exact method used to determine the percentages of immunopositive cells (e.g., how many cells were counted in a specific magnification field or what the intensity thresholds were) is not detailed in the provided citations. In general, the reasons for the contrasting results between our study and that of Shimada et al. (14) include differences in the antibody clones used (which bind different epitopes), differences in sample preparation and fixation methods, tissue processing protocols, scoring methodologies (e.g., differing interpretations of positivity in terms of intensity, proportion, or distribution), and heterogeneity in the patient populations or tumor subtypes studied.

Contrary to the findings mentioned above, studies indicate that loss of CD138 expression may be a significant step in the progression of carcinoma cells towards a metastatic phenotype. In head and neck Squamous cell carcinoma (SCC), the level of CD138 expression has been shown to decrease significantly as tumor aggressiveness increases (24,25). In our study, decreased CD138 expression was associated with a statistically significant increase in T stage and grade, consistent with findings in head and neck SCCs but contrary to Shimada et al. (14).

In our study, although no relationship was observed between CD138 staining levels and recurrence, a statistically significant increase in the risk of progression was observed as CD138 staining levels decreased. In our study, CD138 expression was observed in bladder tumors and decreased with increasing tumor stage. It is thought that this could be explained by decreased CD138 expression as the tumor becomes less differentiated with increasing invasion. Additionally, CD138 staining levels may serve as a marker of tumor progression. It may be necessary to approach patients with low CD138 staining levels cautiously, considering the possibility of advanced tumor stage and potential progression during follow-up.

CD47 has emerged as a critical immune checkpoint molecule that allows tumor cells to escape macrophage-mediated clearance. Its overexpression has been reported in several solid tumors, and novel immunotherapeutic strategies targeting the CD47-SIRP α axis are under investigation (7,8). In our study, we found that CD47 expression significantly increased with higher T stage, aligning with prior reports indicating a link between CD47 upregulation and tumor aggressiveness (9,10). While we did not observe a statistically significant correlation with tumor grade or progression, the stage-dependent increase suggests that CD47 may play a more prominent role in local invasion rather than in histological dedifferentiation. As highlighted by Kiss et al. (10), CD47-targeted photoimmunotherapy showed promising results in preclinical bladder cancer models, suggesting that CD47 may serve as both a prognostic biomarker and a therapeutic target.

In the study conducted by Olcucuoglu et al. (26) in 2017, the first in the literature to investigate the relationship between CD47 staining levels and bladder tumor stage, a statistically significant difference in CD47 staining was observed between Ta stage and T1 stage patients, and between Ta stage and T1-4 patients. However, no correlation was found between T stage or pathological grade and CD47 staining levels. Additionally, a statistically significant difference was observed between CIS-positive patients and other patients, whereas no relationship was found between lymph node involvement and CD47 positivity (26). Our study, on the other hand, is the second in the literature to investigate the relationship between CD47 staining levels and bladder tumor stage. Consistent with Olcucuoglu et al. (26), our results showed a statistically significant positive correlation between CD47 staining levels and T stage. However, no statistically significant correlation was observed between pathological grade and CD47 staining levels. CD47 staining levels were significantly higher in T1 and T2 patients compared with Ta patients, with no significant difference observed between T1 and T2 patients. Yu et al. (16) investigated the expression of CD47 in ovarian cancer, its relationship with the tumor immune microenvironment, and its prognostic value using various bioinformatics databases. According to the Oncomine, GEPIA, and TIMER databases, CD47 was found to be highly expressed in various cancer types, including head and neck cancer, kidney cancer, myeloma, ovarian cancer, pancreatic cancer, and sarcoma. In ovarian cancer, CD47 expression did not differ significantly between stages. The UALCAN database also indicated that CD47 expression was not associated with cancer stage, tumor grade, patient race, patient age, or TP53 mutation status. Similarly, Willingham et al. (17) investigated CD47 expression and its prognostic significance in solid tumors. The study evaluated CD47 expression by flow cytometry in tumor cells of ovarian, breast, colon, bladder, glioblastoma, HCC, and prostate origin. CD47 expression was

detected in almost all primary patient tumor and xenograft samples.

The invasion of the lamina propria and muscularis propria is crucial for treatment decisions in bladder tumors. In our study, we also found a positive correlation between CD47 staining levels and stage. Future studies targeting CD47 may be valuable for assessing the effectiveness of therapeutic approaches for bladder tumors.

Our findings provide important insights into the roles of CD138 and CD47 in bladder tumor progression. The observed inverse relationship between CD138 expression and tumor stage and grade suggests that the loss of CD138, a transmembrane heparan sulfate proteoglycan, may be indicative of a significant phenotypic shift during tumor development. This decline in CD138 expression is a hallmark feature often associated with epithelial-mesenchymal transition, a critical process in which epithelial cells lose their polarity and cell-to-cell adhesion and gain increased migratory and invasive properties (27,28). The downregulation of CD138, or syndecan-1, has been widely recognized as a pivotal event contributing to the aggressive metastatic potential of various carcinomas (27). Our data, therefore, align with the established understanding that the loss of epithelial markers like CD138 facilitates the transition to a mesenchymal-like phenotype, thereby promoting tumor invasion and metastasis (27).

In parallel, our study revealed that CD47 expression increased significantly with increasing tumor T stage, indicating its potential role in advanced disease. CD47, a widely expressed transmembrane glycoprotein, acts as a crucial “don’t eat me” signal by binding to signal regulatory protein alpha on phagocytic cells, thereby inhibiting their ability to engulf and clear tumor cells (29,30). This immune evasion mechanism is a major contributor to tumor progression and has been identified as a negative prognostic factor in various cancers (30). The overexpression of CD47 allows malignant cells to escape destruction by the innate immune system, promoting tumor survival and proliferation (29). Furthermore, CD47 has been implicated in directly enhancing tumor cell invasion and metastasis through mechanisms beyond immune evasion, affecting cellular plasticity and metabolic processes that contribute to tumor aggressiveness (30). The increased expression of CD47 in more advanced bladder tumors, observed in our study, underscores its multifaceted contribution to cancer progression and its potential as a therapeutic target (30).

Study Limitations

This study has several limitations. Its retrospective design, coupled with a relatively small single-center sample and limited data on patient progression, inherently restricts the generalizability of our findings. We assessed tumor tissue only

and did not include a healthy patient control group, which particularly limits the interpretability of CD138 and CD47 expression. Relying on a single time-point measurement limits understanding of longitudinal changes in clinical behavior. Furthermore, the exclusion of metastatic cases means our results may not reflect marker behavior in advanced-stage disease. Methodological shortcomings also include the absence of logistic regression analysis and comparative evaluations with existing prognostic nomograms. There was an unavoidable sampling limitation due to tumor heterogeneity during tissue collection. Limited long-term follow-up data precluded survival analysis, and the omission of molecular and genomic analyses restricted mechanistic insights into CD47 and CD138 expression patterns. Consequently, given these methodological constraints, the present findings do not provide sufficient evidence to support any direct clinical diagnostic or prognostic application for CD138 or CD47. Further large-scale prospective studies are therefore crucial to clarify their full clinical relevance and therapeutic potential.

Conclusion

In this study, CD138 and CD47 expression levels were evaluated in relation to clinicopathological characteristics of bladder urothelial carcinoma. A significant inverse correlation was observed between CD138 expression and both tumor stage and tumor grade, and lower CD138 levels were associated with an increased risk of progression. Conversely, CD47 expression was positively correlated with tumor stage but did not show a significant association with tumor grade or recurrence. Our study presents preliminary findings suggesting that CD138 may play a role in bladder cancer prognosis, and CD47 may play a role in tumor burden.

Ethics

Ethics Committee Approval: Ethical principles and was approved by the University of Health Sciences Türkiye, Bursa High Specialization Education and Research Hospital Clinical Research Ethics Committee (approval number: 2011-KAEK-25 2018/06-37, date: 06.06.2018).

Informed Consent: The informed consent form was obtained from the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.E., V.Ç., S.A., S.Ö., Concept: E.Ö., Ö.E., M.K., T.K., Design: E.Ö., A.E., T.K., Data Collection or Processing: T.E., Ö.E., S.A., Analysis or Interpretation: U.A., T.E., E.Ö., M.K., Literature Search: U.A., V.Ç., A.E., Writing: U.A., Ö.E., S.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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