

RESEARCH ARTICLE

Significance of CA19-9 in Predicting the Prognosis of Urothelial Carcinoma: A Hospital Based Study from Nepal

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Abstract

Background: The present study was undertaken to establish any correlation of elevated levels of CA19-9 with tumor stage or grade of urothelial carcinoma. **Materials and Methods:** This hospital based study was carried out in the Department of Biochemistry of Nepalese Army Institute of Health Sciences between 1st July 2012 and 31st December 2012. Approval for the study was obtained from the institutional research ethical committee. CA19-9 was assayed with an ELISA reader for all cases and expressed in U/ml with 37U/ml taken as the cut-off upper value for normal. **Results:** Out of 20 cases enrolled, 15 were of urothelial carcinoma and the remaining 5 were controls. There was marked difference between the mean values of CA19-9 in cases 40.2 ± 19.3 U/ml of urothelial carcinoma and controls 7.98 ± 7.34 U/ml. The number of cases in Ta, T1, T2, T3, T4 stages of urothelial carcinoma were 2, 6, 3, 3, 1 respectively. The percentage rise in CA19-9 was less with low grade tumors (22.2%) when compared with high grade tumors (66.6%) (p value 0.001*). The percentage of rise in CA19-9 for muscle invasive tumors was very high when compared to superficial tumors. Similarly, the percentage of rise in CA19-9 for metastatic disease was very high when compared to non-metastatic disease and it was found statistically significant (p value 0.001*). **Conclusion:** Serum CA19-9 levels predicts the prognosis of urothelial carcinoma as it is almost invariably raised in tumors having metastatic spread.

Keywords: CA 19-9 - urothelial carcinoma - prognosis - Nepal

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Introduction

Transitional cell carcinoma is the second commonest malignancy of the genitourinary tract worldwide after prostate cancer (Salehi et al., 2011). The 90 % of bladder cancer is transitional cell carcinoma that accounts for 2.9% and 1.5% of all cancer deaths in men and women, respectively in USA (Kong et al., 2010). The majority of urothelial tumors are on the surface but reappearance rate is predominantly elevated regardless of sufficient resection of the primary lesion. The greatest confront in the management of superficial bladder cancer is to thwart succession to invasive disease. The thriving management of transitional cell carcinoma of urinary bladder is principally reliant upon usual observation and early finding of importunate or recurrent carcinoma (Badar et al., 2009). The different investigative groups studying extensively monitoring measures such as periodic cystoscopic examination and urine cytology previously for bladder cancer but these investigations have lot of restraint as they necessitate ample number of exfoliated cells in the urine (Terris et al., 1990). Tumor markers such as the bladder tumor antigen (BTA), nuclear matrix proteins (NMP22), and fibrinogen degradation have high false positive rates

(Kikuchi., 2004). CA 19-9 is a cancer-related carbohydrate antigen and is recognized by using a monoclonal antibody against the human colon carcinoma cell lines. Serum CA 19-9 is a momentous marker for advanced cancer, and is valuable for envisaging the prognosis of the disease. CA19-9 is now a well-known marker for pancreatic carcinoma and has also been reported to be positive in gastrointestinal cancers, papillary carcinoma of thyroid, and endometrial adenocarcinomas. In the recent years, cases of urothelial carcinoma demonstrates high serum CA19-9 level in various studies (Bastos et al., 2008). It comes into view that the role of CA19-9 as a serum marker in urothelial cancers has not yet been defined. Thus, the present study was undertaken to find out correlation of elevated levels of CA19-9 with tumor stage or grade of urothelial carcinoma.

Materials and Methods

It was a hospital based study carried out in the department of biochemistry of Nepalese Army Institute of Health Sciences between 1st July 2012 and 31st December 2012. The variable collected was CA19-9. Approval for the study was obtained from the institutional research ethical

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committee. CA19-9 was assayed with ELISA reader for all cases (Herberman et al., 1977). The value of CA19-9 was expressed in U/ml and 37U/ml was taken as cut-off upper value of normal. Fifteen patients with histologically proven urothelial carcinoma were included in this study as cases and 5 healthy volunteers as control. Staging and grading were done according to tumor, node, metastases (TNM) classification system and WHO/International Society of Urological Pathology consensus classification of urothelial neoplasms of the urinary bladder (Bladder Consensus Conference Committee, 1998). G1 and G2 were taken as low grade and G3 and G4 as high grade tumors (Epstein et al., 1998). For nonparametric values, 't' test was used and for qualitative results, Chi square test and ANOVA were used for statistical analysis. Cross tabulation was done. A p value of <0.05 was considered statistically significant. The data was analyzed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version.

Results

Out of 20 cases enrolled, 15 were of urothelial carcinoma and rest 5 were controls.

Table 1 illustrates that there was marked difference between the mean values of CA19-9 in cases 40.23±19.28U/ml of urothelial carcinoma and controls 7.98±7.34U/ml. The number of cases suffering from Ta, T1, T2, T3, T4 stages of urothelial carcinoma were 2, 6, 3, 3, 1 respectively.

Table 2 depicts that the percentage of rise in CA19-9 was very less low grade tumor (22.2%) when compared to the percentage of high grade tumor (66.6%) and it was found statistically significant (p value 0.001*). The percentage of rise in CA19-9 for muscle invasive tumors were very high when compared to the percentage of superficial tumors. Similarly, the percentage of rise in CA19-9 for metastatic disease was very high when compared to non metastatic disease and it was found

Table 1. CA 19-9 Level in Different T Stages, Grades, Depth of Invasion, and in Metastatic Urothelial Tumors

		No. of patients	CA-19-9 U/ml (mean±SD)	p value
Staging and Grading of Cases				
Cases		15	40.23±19.28	0.001*
Control		5	7.98±7.34	
T stages:				
	Ta	2	12.24±7.15	0.001*
	T1	6	19.34±8.26	0.001*
	T2	3	30.12±21.56	0.41
	T3	3	46.23±17.67	0.256
	T4	1	67.04±11.78	0.001*
Tumor grades:				
	Low	9	20.34±23.22	0.308
	High	6	33.56±34.23	
Tumor invasion				
	Superficial tumors	10	16.53±20.13	0.001*
	Muscle invasive tumors	5	47.17±34.83	
Tumor spread				
	Metastatic disease	4	61.23±22.41	0.001*
	Non-metastatic disease	11	22.65±26.39	

Table 2. Frequency of Cases with CA 19-9 >37U/ml in Different Tumor Grades, Depth of Invasion and in Metastatic Urothelial Tumors

		No. of Patients with CA-19-9>37 U/ml	%	p value
Staging and Grading of Cases with CA 19-9>37U/ml				
Tumor grades	Low grade	2	22.20	0.001*
	High grade	4	66.60	
Tumor invasion	Superficial tumors	2	20.00	0.001*
	Muscle invasive tumors	3	60.00	
Tumor spread	Metastatic disease	3	75.00	0.001*
	Non-metastatic disease	2	18.10	

statistically significant (p value 0.001*).

Discussion

Transitional cell carcinoma is primarily invasive or can subsequently progress, leading to a grave prognosis. 5-year survival patient with invasive bladder carcinoma is merely 36 to 48% still subsequent to radical cystectomy as there is succession to also regional (lymph nodes) or distant metastasis (Supit et al., 2011). The clinical usefulness of monitoring CA19-9 in urothelial carcinoma is less commonly described. The reports so far published have provided different opinions about serum CA 19-9 level in urothelial carcinoma. The present study revealed that the serum level of CA19-9 was significantly correlated with tumor size, depth of invasion, and degree of differentiation. The percentage of rise in CA 19-9 level in cases with invasive tumor 60.0% had significantly higher in comparison to cases with superficial tumors (20.0%) (p value 0.001*). Our findings concurred with the results of Pall et al. (2012). This result revealed that there was noteworthy rise in serum CA19-9 in invasive disease in comparison with superficial disease (47.17±34.43 vs 16.53±20.13) (p<0.001). The percentage of rise in CA 19-9 level in patients with metastatic disease (75.0%) was significantly higher than in patients without metastasis (18.1%) (p value 0.001*) (Hegele et al., 2010). CA 19-9 level was also found to be increased in high-grade tumors (66.6%) as compared with low-grade tumors (22.2%) (p value 0.001*) (Washino et al., 2011). Therefore, even though no serological tumor marker has so far been amply sensitive and specific to be used in screening for transitional cell carcinoma, elevated pre-operative levels of carbohydrate antigen (CA) 19-9 correlate with advanced stages of disease and a poorer clinical outcome. Conclusion: Serum CA19-9 levels predicts the prognosis of urothelial carcinoma as it is almost invariably raised in tumors having metastatic spread.

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