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Galectin 3 for the diagnosis of bladder cancer

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KEYWORDS

Galectin 3;
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Transitional cell carcinoma;
Squamous cell carcinoma

ABBREVIATIONS

G-3, galectin-3, SCC, squamous cell carcinoma, (N)MI, (non-) muscle-invasive, ROC, receiver operating characteristic

Abstract ***Objective:*** To evaluate serum levels of galectin-3 (G-3) in patients with bladder cancer and a control group, as a potential diagnostic and prognostic serum tumour marker.

Patients and methods: Between November 2012 and January 2013, 55 patients (median age 58 years) were enrolled into three groups, i.e., a control, those with transitional cell carcinoma (TCC) or those with squamous cell carcinoma (SCC). The serum G-3 level was measured the night before cystoscopy. The levels of G-3 levels were correlated with tumour type, stage and grade, and in relation to levels in normal urothelium. The results were analysed statistically using the Mann–Whitney *U*-test, the Kruskal–Wallis test and the receiver operating characteristic curve, as appropriate.

Results: The median serum G-3 level was 100, 720 and 920 pg/mL in the control, TCC and SCC groups, respectively, with very significantly greater G-3 levels in both the TCC and SCC groups than in the control group. Patients with high-grade TCC had a statistically significantly greater serum G-3 level than those with low-grade tumours, as did those with muscle-invasive TCC than those with Ta tumours.

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Conclusions: The level of G-3 can aid as a diagnostic marker in patients with either TCC or SCC of the bladder, but the prognostic significance of G-3 remains to be confirmed.

Introduction

Carcinoma of the bladder is still a worldwide health problem, and is ranked ninth in cancer incidence [1]. Several urine and serum tumour markers have been studied for diagnosing this cancer, but a histopathological examination of transurethrally resected bladder tumour is the cornerstone of the diagnosis of bladder cancer, allowing both a histological diagnosis and tumour staging [2]. The management of non-muscle-invasive (NMI) TCC of the bladder is based on frequent endoscopic examinations, together with urinary cytology, which has stood the test of time as a diagnostic and prognostic marker [3].

The galectins are a group of proteins that regulate various biological cycles, including cell growth, cell differentiation, cell adhesion and apoptosis [4]. Galectin-3 (G-3) shows pathological expression in many tumours, e.g., in human pancreas, colon and bladder cancer [5,6]. The intensity of expression depends on tumour progression, invasiveness and metastatic potential [7]. High circulating levels of G-3 were also found to correlate with its anti-apoptotic activity as a possible cause for carcinogenesis [8].

Thus we measured the levels of serum G-3 in patients with bladder cancer, both TCC and squamous cell carcinoma (SCC), and in control patients, to evaluate its role in the diagnosis of bladder cancer, and to correlate these levels with different tumour stages and grades.

Patients and methods

This prospective non-randomised study followed the tenets of the Declaration of Helsinki (1975) and had the approval of the ethics committee of the Theodor Bilharz Research Institute. The study initially included 75 patients (58 men and 17 women, median age 58 years, range 30–84) admitted to the urology department between November 2012 and January 2013. Fifty-four patients had a primary radiological diagnosis of bladder tumour for investigation, while 21 were enrolled as controls. After providing informed consent, a blood sample was taken from all patients the night before cystoscopy. The bladder tumour was resected transurethrally in all patients with apparent tumour, while cold-cup biopsies were taken from the control group, who were having a cystoscopy as part of another endourological procedure.

The samples were evaluated histopathologically by a uropathologist in the pathology department of the institute, according to the international histological classification of urinary bladder tumours proposed by the WHO in 2004.

About 2 mL of blood was collected under aseptic conditions the night before surgery, and the samples were delivered into a plain tube and allowed to clot. Serum was then removed, aliquoted into clean vials and stored frozen at −20 °C. An enzyme immunoassay technique was used to measure the serum level of G-3 (eBioscience, Vienna, Austria) [9].

The results were expressed as the median (range). The variables were compared statistically between the two groups using the Mann–Whitney *U*-test, and among the three groups compared using the Kruskal–Wallis test followed by the Mann–Whitney *U*-test. A receiver operating characteristic (ROC) curve was used to determine the sensitivity and specificity of serum G-3 for detecting cancer. In all tests $P < 0.05$ was considered to indicate significance and $P < 0.01$ was considered highly significant.

Results

From the 54 patients with a radiologically diagnosed bladder growth, seven had normal findings on cystoscopy and two had bilharzial granulomas, so all nine were excluded. The histopathological evaluation of the control arm showed cystitis in 11 of the 21 patients and they were also excluded. The final results were obtained from 55 patients, divided into three groups, i.e., those with normal urothelium, those with SCC and those with TCC. The clinicopathological distribution is shown in Table 1.

For an accurate evaluation of the serum G-3 level, patients with NMI TCC were classified according to the depth of invasion into those with Ta tumours (six) and those with T1 tumours (11).

The serum G-3 levels in the various groups are shown in Table 2. The level was significantly higher in both the TCC and SCC groups than in the controls, with no significant difference between the TCC and SCC groups ($P > 0.05$; Table 2).

The serum G-3 level was significantly higher in MI tumours than in papillary noninvasive tumours (Ta; $P < 0.05$). There was no significant difference between MI tumours and tumours invading the subepithelial connective tissue (T1), nor between papillary noninvasive tumours (Ta) and T1 tumours ($P > 0.05$; Fig. 1). There was a significantly higher G-3