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# Serum Beta 2 Microglobulin Levels in Patients with Renal Cell Carcinoma

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**Summary.** Serum $B_2m$ concentrations were evaluated preoperatively in 40 patients with renal cell carcinoma and normal renal function, as assessed by serum creatinine < 1.4 mg/dl, and compared with those of 23 age-matched controls. Mean value ± SD was 3,088 ± 966 ng/ml for renal cancer patients, while controls had a value of 1,800 ± 240 ng/ml. Statistical analysis, performed by Student t test, revealed a very high degree of significance ($p < 0.0005$). No statistically significant differences were found between groups of patients classified according to tumor stage and cell type. Seventy percent of renal cell carcinoma cases had preoperatively elevated serum levels of $B_2m$.

**Key words**: Beta 2 microglobulin, Renal cell carcinoma.

## Introduction

Beta 2 microglobulin ($B_2m$) is a low molecular weight protein consisting of a single chain of 100 aminoacids which is part of the HLA antigen molecule, where it represents the invariant light chain [1, 2]. It is found on the membrane of all nucleated cells, and is detectable in all body fluids as a shedding product of cell membranes [3]. Its serum and urine concentrations are used to monitor glomerular and tubular nephropathies [4].

Serum $B_2m$ levels may increase because of greater production related to accelerated cell turnover in chronic inflammatory disorders [5–9] and in neoplasms [10–15]. In the more specific field of urological oncology the results published so far are scarce and partially conflicting [16–18].

For this reason we investigated the preoperative serum levels of $B_2m$ in a large series of patients with renal cell carcinoma. In fact, although this solid tumor may attain considerable size, renal insufficiency is unlikely to occur, unlike high stage prostate and bladder cancers; this eliminates changes caused by reduced glomerular filtration rate.

## Patients and Methods

Serum $B_2m$ concentrations were evaluated in a group of 40 patients (27 male, 13 female) presenting with renal cell carcinoma. Ages ranged between 33 and 79 years, with a mean of 54.8. Blood samples were drawn preoperatively to exclude false positives due to impaired renal function, and for the same reason patients presenting with serum creatinine greater than 1.4 mg/dl were excluded from the study (3/43 = 7%).

Patient distribution according to tumor stage was: 4 $T_1$, 7 $T_2$, 8 $T_3$, 4 $T_4$, 4 $V_+$ and 13 $M_+$. Two patients with widespread metastases did not undergo surgery, while the cell type of the remaining 38 cases was: 28 clear cells, 6 dark and 4 mixed.

Concentrations of $B_2m$ were assayed in duplicate by radiommunoassay (Phadebas Beta 2 Microtest, Pharmacia, Uppsala, Sweden). Sera were stored at −20 °C until analyses were performed. Results are expressed in nanograms per milliliter. Statistical analysis of the results was performed using Student t test.

## Results

Mean serum concentration (± SD) in the 40 patients with renal cell carcinoma was 3,088 ± 966 ng/ml, while controls showed a value of 1,800 ± 240 ng/ml. The difference between these two populations is statistically highly significant ($P < 0.0005$, $T = 6.32$).

We compared the serum $B_2m$ concentrations of renal cancer patients stratified according to tumor stage with controls, and they were significantly higher, even for low stage tumors (Fig. 1). The means and the standard deviations and the significance levels of each group versus normals are shown in Table 1.

On the other hand, there was no statistically significant difference when tumors of different stages were compared, nor was the comparison of tumors of different cell type significant.

In order to evaluate the test sensitivity, we chose to consider the mean $B_2m$ concentration in the control group plus two standard deviations (2,228 ng/ml). With this arbitrary limit, 28 out of 40 patients with renal cell carcinoma (70%) presented pathologically high levels.

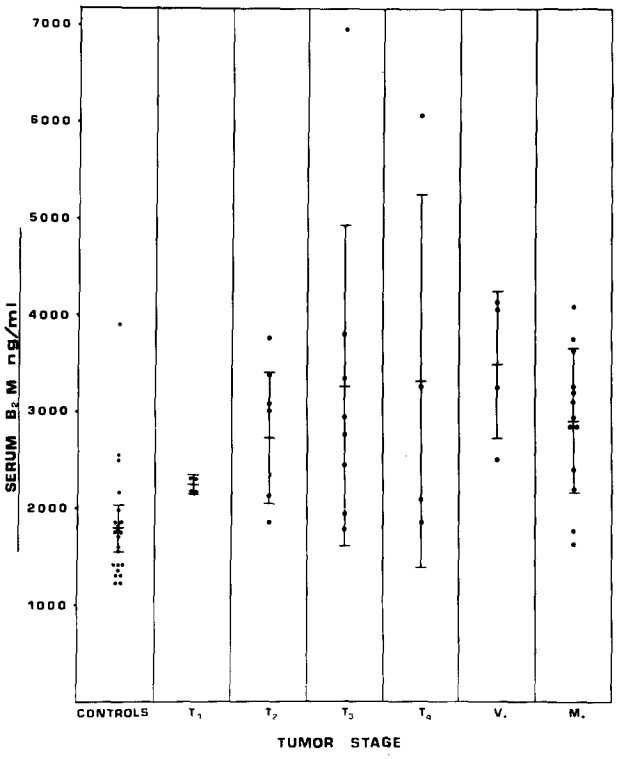


Fig. 1. Serum $B_2m$ concentrations in controls and renal cancer patients stratified according to tumor stage

In two cases selective blood samples from both renal veins were obtained at the time of angiography, but we failed to find a net lateralization of $B_2m$ concentrations from the tumor side.

## Discussion

Reliable markers for renal cell carcinoma are still lacking [19]. Sufrin et al. [20] found that renin was elevated in 21 of 57 patients (37%) who presented with high stage renal cancer, while erythropoietin was elevated in 36 of 57 (63%), but its levels failed to correlate with tumor stage and grade. Renal tumors were not identified as the source of proteins, and it is possible that elevated levels are due to stimulation of the contralateral kidney or decreased degradation rate.

Vickers [21] considered the levels of haptoglobin, which is an alpha-2 globulin, and found high levels in 14/16 patients with low stage tumors, and in all six patients who presented with metastatic cancer.

Richards et al. [18] considered the "acute phase reactant proteins" together with $B_2m$, and concluded that all those substances can provide a warning of the likelihood of extensive tumor spread at presentation.

It has also been found that tissue concentrations of $B_2m$ are four times greater in renal carcinoma when compared to normal renal tissue [22].

The remaining published data about the clinical value of $B_2m$ as a marker for renal cell carcinoma concerns small numbers of patients within large series of different tumors [16, 17].

The present study demonstrates that serum $B_2m$ values are preoperatively elevated in 70% of renal cell carcinoma cases, and that the rise is statistically significant even for low stage tumors. On the other hand we found that there was no relationship between tumor stage and cell type and serum $B_2m$ concentrations. In other words, it would not be possible to utilize this protein to determine the extent of the neoplasm.

Since we have selected a patient population on the basis of normal renal function, we can correctly assume that the raised serum concentrations of $B_2m$ are due to its increased production by neoplastic cells.

Even a small tumor load causes an increase in serum $B_2m$, and we intend to follow in time the non-metastatic patients in order to evaluate if $B_2m$ can be useful as an early marker of tumor recurrence, obviously within the limits posed by reduced renal function after unilateral nephrectomy. However, slight serum creatinine elevations do not seem to represent a major factor in the interpretation of the results [18].

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**Table 1.** Means and standard deviations of serum $B_2m$ levels in controls and renal cell carcinoma patients

| | Controls | Stage | | | | | |
|---|---|---|---|---|---|---|---|
| | | $T_1$ | $T_2$ | $T_3$ | $T_4$ | $V_+$ | $M_+$ |
| Number | 23 | 4 | 8 | 8 | 4 | 4 | 13 |
| Mean | 1,800 | 2,231[a] | 2,712[b] | 3,268[b] | 3,366[b] | 3,491[b] | 2,896[b] |
| ± SD | 240 | 91 | 682 | 1,662 | 1,853 | 777 | 743 |

[a] $p < 0.0025$ compared to controls
[b] $p < 0.0005$ compared to controls

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