Thrombocytosis as a Significant Indicator of Prognosis of Renal Cell Carcinoma

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Abstract

Background: Various prognostic factors have been studied to predict the survival of renal cell carcinoma (RCC) during last decades. In many types of malignancies, thrombocytosis has been reported and studied as a prognostic factor. The objective of present study was to evaluate the significance of thrombocytosis in determining prognosis in patients with localised RCC who underwent radical nephrectomy. **Material and methods:** The study included 100 consecutive patients. Patients were divided into a normal platelet count group (group A) and a thrombocytosis group (group B) according to the preoperative platelet count. Thrombocytosis was defined as a platelet count greater than 450,000/mm^3. The data about stage distribution, grade, tumor size, histological subtype, hemoglobin level, Body Mass Index (BMI), age, gender, and survival rate of tumors between these two groups were compared. **Results:** The mean age of the patients was 58.9 years and the mean follow-up period was 52.7 months. Of these 100 patients, 19 had a preoperative platelet count greater than 450,000/mm^3 (group B). The mean age of the patients with thrombocytosis was 56.4 ±7.79 years compared with 61.5±8.29 years in patients with normal platelet counts (p<0.05). Thrombocytosis was noted in 7 (10.93%) of 64 patients with stage pT1-T2 disease and in 12 (30%) of 36 patients with stage pT3-T4 disease. Patients with thrombocytosis had a worse prognosis than patients without thrombocytosis. **Conclusion:** The platelet count can be considered a useful prognostic factor in patients with RCC who undergo radical nephrectomy.
Keywords: Thrombocytosis, Renal cell carcinoma, Radical nephrectomy, prognosis.

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INTRODUCTION

Renal cell carcinoma (RCC) accounts for 3% of all adult malignancies and it is the most common primary malignancy among all urological cancers with continuous increase in the incidence in last few decades.[1] RCC is radio-resistant, refractory to known chemotherapeutic agents, and poorly responsive to hormonal therapy. Although, Surgery remains the most effective form of therapy for localized or localized advanced RCC about 20-30% of patients develop metastasis post-operatively.[2,3] Most of the patients with new diagnosis of RCC have metastatic presentation due to it's wide range of biological behavior.

Determining the prognostic factors would help in directing further therapy and follow-up. Various prognostic factors have been studied in RCC for diagnosis, follow-up and predicting survival. After radical nephrectomy, several prognostic factors have been established including pathological findings, clinical symptoms and laboratory findings.[4,5,6,7]

Pathological findings like tumor proliferation, microvascular invasion, tumor stage and tumor grade have not been accepted widely, whereas, clinical symptoms and laboratory parameters like erythropoietin, haptoglobulin, interleukin-6 (IL-6), carcinoembryogenic antigen (CEA), lipid-associated sialic acid, and acute phase reactant proteins proved to have poor predictive value and low specificity.[8-12]

Platelet count can increase in a variety of conditions, such as anemia, reduced iron stores, inflammation and primary proliferative disorders. Of all these conditions, malignant neoplasms are one of the most frequent causes of thrombocytosis. Thrombocytosis has been studied as a prognostic factor in various kinds of malignancies. Recently, the role of the platelet count has been studied in RCC and the association between thrombocytosis and decreased survival has been revealed in patients with early-stage or metastatic RCC.[13,14]

In the present study, we retrospectively evaluated the effect of thrombocytosis on survival and prognosis in patients with renal cell carcinoma.

MATERIAL AND METHODS

A total of 100 consecutive patients treated by radical nephrectomy for RCC at New Hope Hospital, India were enrolled in the study. Thrombocytosis was defined as a at least one platelet counts greater than $4,50,000/mm^3$. Patients were divided into two groups: Group A included 90 patients whose platelet counts remained at $\leq 4,50,000/mm^3$ at the time of nephrectomy; Group B included 22 patients with platelet count of $> 4,50,000/mm^3$. Patients with renal tumors other than RCC, metastatic RCC, and had received radiotherapy, systemic chemotherapy or medication at presentation that might cause thrombocytosis were excluded from the study. In the preoperative period, at least one platelet count was obtained. Preoperatively, all patients were evaluated with physical examination, routine hematologic and biochemical analysis, and radiologic studies, including abdominal computed tomography, chest X-ray, renal Doppler ultrasonography if necessary and, in selected cases, magnetic resonance imaging. Patient height and weight was used to calculate the BMI, which categorized patients into obese (BMI 30 or greater), overweight (BMI 25–30), and normal (BMI 25 or less) groups. Pathologic staging was performed according to the 1997 TNM classification.[15] Fuhrman grading system was used for tumor grading. In each case, regional lymphadenectomy was performed. All patients were evaluated postoperatively every 3–6 months for the first 2 years and every 6 months thereafter. Follow-up consisted of physical examination, chest radiography, abdominal and thoracic CT, ultrasonography, bio- chemical and hematologic analysis.

The two groups were compared according to age, sex, Body Mass Index (BMI), hemoglobin level, pathologic T stage, Fuhrman grade and survival rates.

RESULTS

The clinical and demographic characteristics of the patients are seen in table 1. The mean age of the patients was 58.9 years (range 28 to 76), and the mean follow-up period was 52.7 ± 19.6 months (range 9–96). Of these 100 patients, 19 had a preoperative platelet count greater than $450,000/mm^3$ (group B). The mean age of the patients with thrombocytosis was 56.4 ± 7.79 years compared with 61.5 ± 8.29 years in patients with normal platelet counts ($p < 0.05$). Thrombocytosis was present in 5 (16.66%) of 30 female patients and 14 (20%) of 70 male patients ($p < 0.05$).

Thrombocytosis was noted in 7 (10.93%) of 64 patients with stage pT1-T2 disease and in 12 (30%) of 36 patients with stage pT3-T4 disease. Patients with thrombocytosis had a worse prognosis than patients without thrombocytosis. Eleven (57.89%) of 19 patients with thrombocytosis died of disease progression. This rate was found as 21.06% in patients with normal platelet counts ($p < 0.05$).

Table 1: Demographic characteristics of patients

	Group A (n=81)	Group B (n=19)	Test of Significance	P value
Age	61.5±8.19	56.4±7.79	t = 2.43	< 0.05
Sex				
Male	56	14	χ^2 = 0.1516	< 0.05
Female	25	05		
BMI	22.84 ±2.95	21.95±2.89	t = 1.24	<0.05
Hemoglobin	13.38±2.42	10.93±2.18	t = 4.04	<0.05

Table 2: Clinical characteristics of patients

	Group A (n=81)	Group B (n=19)	Test of Significance	P value
T stage				
1-2	57	07	χ^2 = 7.50	< 0.05
3-4	24	12		
Grade				
1	09	01		
2	54	09	χ^2 = 5.04	>0.05
3	14	07		
4	04	02		

Survival rates were found to be 63 in group A without thrombocytopenia, whereas, it was 07 in group B with thrombocytosis. (Fisher <0.001; p>0.05). Thrombocytosis was significantly associated with tumor size, pathologic T stage, lymph positivity, hemoglobin level, and cancer specific survival. Thrombocytosis were not related to histological subtype, grade, gender, and BMI. Only the stage, platelet count, lymph positivity and tumor size of renal cell carcinoma were observed to be independent prognostic predictors of disease-specific survival.

DISCUSSION

The incidence of RCC is increasing due to the incidental detection of small tumors and environmental factors. RCC remains a major cause of mortality with approximately 40% of patients dying of cancer progression. Important prognostic factors have been established including tumor related factors (tumor size, grade and stage), clinical symptoms and laboratory findings. Pathological stage is recognized to be the most important prognostic factor in RCC. Nuclear grade, mostly represented by the Fuhrman grade, also has an important prognostic value with 5-year survival decreasing from 64% to 10% in grade 1 and 4 tumors, respectively. Presenting symptoms, suboptimal performance status or significant weight loss have an adverse effect on prognosis in all stages of RCC. In terms of laboratory values, an increased erythrocyte sedimentation rate, anemia, hypercalcemia and increased alkaline phosphatase are the strongest parameters recognized to have a prognostic value in retrospective studies. Thrombocytosis has been recently suggested to indicate a poor prognosis in patients with various malignancies.

The exact mechanism of thrombocytosis in patients with RCC is unknown. Several theories have been proposed on how thrombocytosis may relate to the metastatic potential and worse survival in malignancy.

In majority of previous studies, the incidence of thrombocytosis in patients with RCC vary between 8.1 and 13.90%.[1,4,6,16,17] In our study this ratio was found as 19%. Our results were higher than the ones in the literature. In the present study patients were more advanced cases than the ones in the literature that could explain the high ratio in our study. The relationship between platelet count and survival in patients with RCC who underwent radical nephrectomy or a variety of adjuvant therapies after radical nephrectomy have been evaluated in various studies.[1,4,13,16,17,18] Generally, most authors have found a statistically significant difference regarding survival rates in patients with or without thrombocytosis.[1,4,7,13,16] Authors reported that the cancer-specific death rate was five times greater in patients with thrombocytosis. According to their results, they concluded that the platelet count was a powerful independent prognostic factor in patients with localized RCC.

The correlation between thrombocytosis and histologic grade and tumor stage are other important points in patients with RCC. Many prior reports retrospectively evaluated the relationship between thrombocytosis and histologic grade in patients with RCC.[4,7,13] In general, malignancy-associated thrombocytosis tends to present in high stage renal cancers and is related to a poor prognosis. In the present study, thrombocytosis was found more frequently in patients with advanced stage RCC, and patients with preoperative thrombocytosis had a worse survival compared to those with normal platelet counts. The platelet count may be considered as a useful prognostic factor in patients with RCC who undergo radical nephrectomy.

In conclusion, the present study shows a clear association of thrombocytosis with decreased survival in patients with RCC. While it is difficult to determine the precise reason for this association, it is possible that the thrombocytosis is causally linked to increased tumour cell survival or enhanced metastatic capability. Even when tumour stage, grade and cell type are controlled for, thrombocytosis remains an important independent prognostic indicator. The clinical utility of this powerful independent prognosticator is in the counselling of individual patients, and in selecting patients for experimental or adjuvant therapies. The analysis of new therapies must take platelet counts into consideration, as those patients with thrombocytosis will have a poorer survival independent of the treatment that is being evaluated.

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