Some Hematological Changes in Patients with Bladder Cancer

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Abstract

Objective: To estimate some hematological changes in patients with bladder cancer.

Patients: One hundred patients admitted to Al-Hilla General Teaching Hospital and to the Radiation Oncology and Nuclear Medicine Hospital in Baghdad, and 30 healthy persons (control group) were enrolled in this study which lasted from February to June 2011. The patients included 72 males and 28 females, their ages ranged from 41-84 years, with a mean age of 62.82±9.52 years. Those patients were divided into male and female subgroups.

As well, the healthy controls were matched in age and sex with them.

Results: The study demonstrated that red blood corpuscular (RBCs) count, hemoglobin (Hb), packed corpuscular volume (PCV), mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) were significantly decreased in both male and female bladder cancer patients compared to the control group while the values of mean corpuscular hemoglobin concentration (MCHC) were insignificantly decreased in both male and female patients compared to the control group. The white blood cells (WBCs) and platelets counts were insignificantly changed in both male and female patients in comparison with the control group; on the other hand, erythrocyte sedimentation rate (ESR) was found to be significantly increased in both male and female patients compared to the control group.

Conclusion: The changes in all previously mentioned markers in bladder cancer patients might be potentially important findings as hematological tools for the disease.

Key words: Hematological changes, bladder cancer.

بعض التغيرات الدموية لدى المرضى المصابين بسرطان المثانة

الخلاصة:

الهدف: هدفت هذه الدراسة إلى معرفة التغيرات الحاصلة لبعض المعايير الدموية لدى المرضى المصابين بسرطان المثانة.

المرضى: تضمنت الدراسة مئة مريض مصاب بسرطان المثانة ممن أدخلوا إلى مستشفى الحلة التعليمي العام ومستشفى الإشعاع والطب النووي في بغداد، بالإضافة إلى ثلاثين شخصاً من غير المصابين بالمرض (مجموعة السيطرة)؛ وقد استمرت من شباط لغاية حزيران ٢٠١١ م. ضمن مجموعة المرضى كان هنالك ٧٢ ذكراً و٢٨ أنثى تراوحت أعمارهم بين٤١–٨٤ سنة، وبمعدل عمري هو ٦٢,٨٢±٩,٥٢ سنة. قسم المرضى إلى مجاميع ذكور وإناث وتمت مطابقة مجموعة السيطرة معهم من حيث العمر والجنس.

النتائج: أظهرت الدراسة أن هنالك انخفاضاً معنوياً لكل من العدد الكلي لكريات الدم الحمراء، خضاب الدم، حجم الكرية المضغوط، معدل حجم الكرية ومعدل خضاب الكرية بالمقارنة مع مجموعة السيطرة. فيما شهد معدل تركيز خضاب الكرية انخفاضاً غير معنوي لدى المرضى مقارنة مع مجموعة السيطرة. فيما يتعلق بالعدد الكلي لخلايا الدم البيضاء والصفيحات الدموية فلا توجد فروق معنوية لدى المرضى مقارنة بمجموعة السيطرة؛ من جانب آخر، شهد معدل الترسيب لخلايا الدم الحمراء زيادة معنوية لدى مرضى سرطان المثانة بالمقارنة مع مجموعة السيطرة.

الاستنتاج: إن جميع ما ذكر من متغيرات لدى مرضى سرطان المثانة قد تكون نتائج مهمة كمعايير دموية لهذا المرض.

Introduction

Bladder cancer is one of the most commonly diagnosed malignancies worldwide. It is the most common urological cancer; it comprises a significant part of urologists' work [1]. The term bladder cancer is used to describe collectively tumors of urinary bladder urothelial origin which exhibit diverse biological behavior, ranging from relatively benign to highly malignant. Thus, bladder cancer can be without serious clinical consequences for the patient who has an isolated superficial bladder tumor, or it can be a lethal disease. Eighty per cent of bladder cancers are superficial at presentation in that they have not invaded into the muscle. The remaining 20% are muscle-invasive, which carry a much worse prognosis [2].

Two main types of bladder cancer are identified: the transitional cell carcinomas (TCC), related to cigarette smoking and most prevalent in Western and industrialized countries, and the squamous cell carcinomas (SCC), which are more frequently seen in some Middle Eastern and African countries, where urinary schistosomiasis is an endemic disease. Rare types of bladder cancer include small cell carcinoma, carcinosarcoma, primary lymphoma, and sarcoma [3].

Bladder cancer occurs more frequently in men than in women (sex ratio 3:1). The incidence of bladder cancer is highest in industrialized countries. It has been associated mainly with smoking, but also with occupational exposure to carcinogens from aniline dyes, paints, rubber, and chronic irritation of the bladder mucosa due to bladder stones, or schistosomiasis [4].

The classic presentation of bladder cancer is painless gross hematuria, which is seen in approximately 80-90% of patients. Physical examination results are often unremarkable. Cystoscopy, cytology, and biopsy when necessary are the principal diagnostic tests [5].

Bladder cancer has the highest recurrence rate of any malignancy. Although most patients with bladder cancer can be treated with organ-sparing therapy, most experience either recurrence or progression, creating a great need for accurate and careful surveillance [6].

The aim of this study was the estimation of some hematological changes in patients with bladder cancer because this will help the medical staff for proper management with less morbidity and mortality.

Patients and Methods

One hundred patients admitted to Al-Hilla General Teaching Hospital and to the Radiation Oncology and Nuclear Medicine Hospital in Baghdad, and 30 healthy persons (control group) were enrolled in this study which lasted from February to June 2011. The patients included 72 males and 28 females, their ages ranged from 41-84 years, with a mean age of 62.82±9.52 years. Those patients were divided into male and female subgroups. As well, the healthy controls were matched in age and sex with them.

All of them were sent for the hematological investigations. A blood sample was drawn from both patients and controls for the estimation of those investigations.

* The RBCs count was done by the use of Neubaur hemocytometer counting chamber [7].

*The Hb was estimated photometrically using the cyanomethemoglobin method [8].

* The microhematocrit method was used to determine PCV [7].

* The red corpuscular indices were measured by applying special equations to estimate them [7].
* The total WBCs count was also done by the use of Neubaur hemocytometer counting chamber [7].
* Neubaur hemocytometer was used also in platelets count [7].
* Measurement of ESR was done using Westergren tube [7].

Results

* Table (1) showed the values of RBCs, Hb and PCV for male and female bladder cancer patients and control group.

Table 1 Values of red blood corpuscular count, hemoglobin and packed corpuscular volume for bladder cancer patients and control group.

Gender	RBCs count millions/mm^3		Hb g/dl		PCV %	
	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE
Male	* 4.093±0.488	5.169±0.842	*** 12.670±0.275	14.514±0.149	** 0.392±0.827	0.446±0.439
Female	* 3.627±0.215	4.204±0.705	** 11.196±0.349	12.400±0.196	* 0.346±1.055	0.379±0.637

- *** (P<0.001). - ** (P<0.01). - * (P<0.05). - SE: Standard error.

The values of RBCs count showed a significant decrement (P<0.05) in both male and female bladder cancer patients compared to the control group. Regarding the values of Hb they showed a highly significant decrement (P<0.001) for male patients compared to the control group and a significant decrement (P<0.01) for female patients compared to the control group; while PCV values showed a significant decrement (P<0.01) for male patients compared to the control group and a significant decrement (P<0.05) for female patients compared to the control group.

* Table (2) showed the values of MCV, MCH and MCHC for male and female bladder cancer patients and control group.

Table 2 Values of mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration for bladder cancer patients and control group.

Gender	MCV fl		MCH pg		MCHC %	
	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE
Male	* 80.28±2.023	86.29±1.295	* 25.78±0.666	27.76±0.462	0.319±0.003	0.339±0.004
Female	* 84.00±2.488	90.00±1.384	* 27.10±1.112	29.11±0.455	0.319±0.005	0.337±0.001

- * (P<0.05). - Values without (*) are insignificant (P>0.05). - SE: Standard error.

The values of both MCV and MCH for male and female patients with bladder cancer had showed a significant decrement (P<0.05) compared to the control group. Regarding the values of MCHC they were insignificantly decreased (P>0.05) in both male and female patients compared to the control group.

* Table (3) showed the values of WBCs, platelets and ESR for male and female bladder cancer patients and control group.

Table 3 Values of total white blood cells count, platelets count and erythrocyte sedimentation rate for bladder cancer patients and control group.

Gender	WBCs count $\times 10^3/mm^3$		Platelets count $\times 10^3/mm^3$		ESR mm/hr	
	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE	Patients Mean ± SE	Controls Mean ± SE
Male	6.029±1.068	6.271±0.283	254.864±8.749	260.857±9.384	*** 42.46±3.717	12.00±0.483
Female	6.215±0.738	6.455±0.239	248.000±1.548	253.111±1.573	*** 59.05±6.763	11.56±0.603

- *** (P<0.001). - Values without (*) are insignificant (P>0.05). - SE: Standard error.

In regard for the values of WBCs and platelets counts, they were all insignificantly changed (P>0.05) in both male and female patients compared to the control group. On the other hand; the values of ESR showed a highly significant increment (P<0.001) in both male and female patients compared to the control group.

Discussion

Table (1) and (2) demonstrated that the values of RBCs count, Hb, PCV, MCV and MCH were significantly decreased in both male and female bladder cancer patients compared to the control group; on the other hand, the values of MCHC were insignificantly decreased in both male and female patients compared to the control group.

Scher and Motzer [9]; Eble *et al.* [10]; Millikan *et al.* [11] and many other researchers stated that the most common primary symptom of bladder cancer is painless hematuria (80-90% of patients) and gross hematuria more commonly predicts bladder cancer than does microscopic hematuria. In conclusion, all the above results of RBCs count and indices, Hb and PCV could be attributed to hematuria which consequently causes anemia that the study patients were suffering from.

Blood loss is the most common cause of acute anemia seen. Anemia in this situation is caused by chronic slow bleeding and nutritional deficits [12].

Another probable explanation for the study results is what's called anemia of chronic disease. Anemia of chronic disease is a blood disorder that refers to anemia found in people with certain long-term medical conditions, such as cancers. It is a common problem for cancer patients and sometimes results from the therapies used to suppress or control tumors. Approximately one-third of cancers have anemia [13].

The anemia of cancers is caused by stimulation of the cellular immune system and inflammatory changes, which stimulate the production of chemicals called cytokines and affect both red cell production and survival. Several cytokines, including tumor necrosis factor (TNF), Interferon Gamma and Interleukin-1 (IL-1), can suppress bone marrow production (erythropoiesis) by affecting red cell production [14].

The MCV is an extremely useful value in classification of anemia [15], but the MCH and MCHC often do not add significant, clinically relevant information. However, the MCH and MCHC play an important role in laboratory quality control because these values will remain stable for a given specimen over time [16].

Microcytosis and hypochromia are also present in some cases of anemia of chronic disease [17].

For WBCs and platelets counts; Table (3) showed that they were all insignificantly changed in both male and female bladder cancer patients compared to the control group. These results may be

attributed to that the majority of the study patients may not be presented with an advanced stage of the disease, and thus they were devoid of distant cancer metastasis especially to the bone marrow, because in that situation the cancerous cells may suppress the production of WBCs and platelets from the bone marrow.

Though not very frequent, bone marrow is one of the important sites of metastasis of solid tumors. The involvement of the bone marrow is not only a sign of diffuse hematogenous spread of the tumor; it also results in cytopenias that increase the risk of bleeding and infection [18].

In contrast, there was an inconsistency between the above results of the study and what was stated by Stav *et al.* [19] about a rare condition called paraneoplastic syndrome of bladder cancer. Paraneoplastic syndromes are defined as nonmetastatic systemic effects that accompany malignant disease. These syndromes may occur in up to 10-15% of malignancies.

A few paraneoplastic syndromes have been reported in metastatic transitional cell carcinoma including hypercalcemia, thrombocytosis, eosinophilia, and leukemoid reaction. Leukemoid reaction has rarely been reported in patients with primary bladder carcinomas.

Additionally, there was also a disagreement of the results with what was mentioned by Gontero *et al.* [20], who stated that cancer invasion and metastasis develop through a sequence of processes involving loss of cell-cell and cell matrix adhesions, proteolysis and induction of angiogenesis.

Blood coagulation and fibrinolysis has been shown to play an important role in these metastatic processes. During haematogenous metastasis, cancer cells migrate to the vasculature and interact with platelets resulting in tumor cell-induced platelet aggregation.

The risk of venous thrombosis during cancer is largely increased especially in case of chemotherapy, surgery and advanced stage of the disease [21].

The values of ESR as was shown in Table (3) reflected a significant increment in both male and female patients compared to the control group.

The erythrocyte sedimentation rate (ESR) is a simple and inexpensive laboratory test for assessing the inflammatory or acute response. Unfortunately, the ESR is neither sensitive nor specific when used as a general screening test [22].

As with any other malignancy, bladder cancer can raise ESR to high levels as was declared by the study result.

In oncology, a high ESR has been found to correlate with overall poor prognosis for various types of cancers [23]. In patients with solid tumors, a sedimentation rate greater than 100 mm per hour usually indicates metastatic disease, but for most tumors this relatively nonspecific finding has been supplanted by more precise diagnostic tests. Any condition that elevates fibrinogen (e.g., malignancy) may also elevate the ESR [24].

In the present study, it's probable that in addition to the malignancy itself, anemia that the patients were suffering from could also raise ESR; this is well-matched to what was stated by Smith and Samadian [22] that ESR is always raised with anemia.

In contrast to what was stated above that raised ESR is one of the indicators of malignancy; Mönig *et al.* [25] declared that in hospitalized patients with elevated ESR, malignancies were found in 25% of all cases, which was not significantly different from the incidence of malignancies in patients with normal ESR. This clearly demonstrates that measuring ESR is of no value as a screening procedure for malignant diseases.

Conclusion

Anemia is a common finding among bladder cancer patients and nearly all patients with gross hematuria may present with anemia. ESR is an essential acute phase reactant and a critical marker of inflammation and bladder malignancy. Absence of distant cancer metastases could possibly be reflected through normal WBCs and platelets counts.

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