Overexpression of IL-8 in patients with abdominal tumor after radiotherapy leads to ureteral obstructive renal dysfunction: a case-control study

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Research article

Keywords: interleukin-8, radiotherapy, renal insufficiency

Posted Date: May 29th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-31208/v1

Abstract

Purpose: To analyze the expression of interleukin-8 in patients with post-renal insufficiency after radiotherapy of abdominal tumors.

Methods: 60 patients (experimental group) with post-renal insufficiency and 30 patients (control group) without renal insufficiency after the radiotherapy for abdominal tumors were collected for case-control study. Serum interleukin-8 levels were measured before and after the cystoscopy from September 2017 to March 2019, and the relationship between interleukin-8 levels and serum creatinine, and urea nitrogen, and hydronephrosis was analyzed.

Results: The level of serum interleukin-8 levels were significantly increased in patients with post-renal insufficiency after radiotherapy for abdominal tumors($P<0.05$).After treatment, the level of interleukin-8 in the experimental group was significantly lower than that before the treatment ($P<0.05$). The expression of interleukin-8 was positively correlated with serum creatinine ($r=0.297$, $P=0.004$), but not with urea nitrogen level and hydronephrosis ($r1=-0.055$, $P1=0.605$; $r2=0.116$, $P2=0.277$). Cox proportional risk regression model showed that interleukin-8 was a high risk factor for the occurrence of post-renal insufficiency ($R2=0.826$, $P<0.05$).

Conclusion: Interleukin-8 is helpful to judge the renal function of patients with abdominal tumors after radiotherapy, In the early stage of renal insufficiency, it will overexpresses, and its evaluation is better than urea nitrogen.

1. Introduction

Most of the effects of radiotherapy on urinary system are not caused by direct infiltration of tumors, especially on renal function. Most of them are a gradual process. The incidence of renal insufficiency caused by moderate or severe injury of ureter is 2%-6%[1]. Some studies believe that ureteritis and cystitis after pelvic radiotherapy can cause ureteral stricture, fibrosis and ureteral obstruction[2-3], but how to detect the tendency of ureteritis after radiotherapy at an early stage has not been reported. Therefore, timely detection of the possibility of ureteritis and correction of the reversible factors of renal function damage are the key to ensure the timely recovery of renal function.

Interleukin-8 (IL-8) can promote inflammatory response and stimulate capillary proliferation, which is closely related to the occurrence of inflammation. We think that interleukin-8 may be one of the important factors for early prediction of ureteral inflammation. So we conducted a case-control study of 60 patients with renal insufficiency after radiotherapy for abdominal tumors.

The aim of this study is to found that whether the interleukin-8 will overexpresse in patients with radiation-induced injury of urinary capillaries after radiotherapy for abdominal tumors? What is the relationship between the interleukin-8 and serum creatinine, and urea nitrogen, and hydronephrosis.

2. Materials And Methods

2.1 General information

From September 2017 to March 2019, all the 60 patients in the experimental group were treated by radiotherapy for abdominal tumors with post-renal insufficiency in the Department of Urology, First Affiliated Hospital of Guangdong Pharmaceutical University. There were 24 males and 36 females in the experimental group, which aged 46~57 years, with an average age of 48.97±1.70 years, and was with a course of 0.5~2 years, with an average of 1.33±0.56 years. Between them there were 16 cases of rectal cancer, 20 cases of colon cancer, 13 cases of cervical cancer and 11 cases of ovarian cancer. The control group contained 30 patients without renal insufficiency who underwent the radiotherapy for abdominal tumors at the same time. There was no difference in the age, sex, course of disease and type of disease between the two groups.

2.2 Ethical approval

The ethical approval was The First Affiliated Hospital/School of Clinical Medicine of Guangdong Pharmaceutical University Ethics Committee: Medical Aaron no.(70) [2016].

2.3 Radiotherapy

All patients were treated with three-dimensional conformal radiotherapy (3-D conformal radiotherapy) with a dose of 220 cGy per time, 5 times a week, totaling 2000~3000 cGy.

2.4 Examination Method

1.3.1 The experimental group was treated with local anesthesia and bilateral ureteral catheter by cystoscopy. Zebra catheter was inserted, F_6 double J catheter was inserted through catheter, one end of bladder was about 5 cm, and double J catheter was placed for 3 months. After catheterization, abdominal plain film was performed to determine the location of double J catheter.

1.3.2 The control group underwent cystoscopy under local anesthesia, but did not retain stents.

2.5 Detection Method

2.5.1 Serum interleukin-8:

All patients received venous blood 3 mL in the morning on an empty stomach, and then place at room temperature for 20 minutes and solidify naturally. Serum was collected and centrifuged on a centrifuge of 3000 R. min for 20 min. The supernatant 500 uL after centrifugation was subdivided and numbered, and then transferred to the refrigerator at -80℃ for storage, so as to unify the detection. Blood samples were collected before and 3 days after bladder examination in both groups.

The Serum interleukin-8 (IL-8) was detected by enzyme-linked immunosorbent assay (ELISA) with the Human IL-8/CXCL8 Quantikine ELISA Kit(Bio-Techne, Solid Phase Sandwich ELISA, 96T,50uL) after melting at the room temperature by the specialized testing technicians.

2.5.2 Serum creatinine and urea nitrogen:

Serum creatinine and urea nitrogen were detected by urease method.

2.5.3 Degree of hydronephrosis:

The degree of hydronephrosis was detected by urinary color Doppler ultrasonography.

2.6 Evaluation Criteria

2.6.1 Serum creatinine: male: 44-133 mmol/L; female: 70-106 mmol/L

2.6.2 urea nitrogen: 3.2-7.1 mmol/L for adults

2.6.3 Degree of hydronephrosis: Urinary color Doppler ultrasonography was used to observe and evaluate the degree of hydronephrosis (mild, moderate and severe).

2.7 Statistical Method

The *t* test was used to measure the data, χ^2 test was used to count the data, Spearman correlation analysis was used to analyze the correlation between the various indicators; Cox proportional risk regression model was used to assess the level of interleukin-8 and the risk ratio of renal insufficiency, $P<0.05$ was statistically significant.

3. Results

3.1 Comparison of general data between two groups

There was no difference in gender, age, course of disease and type of disease between the two groups ($P>0.05$), the results were shown in Table 1.

3.2 The serum interleukin-8 levels between two groups

Before cystoscopy, the average level of serum interleukin-8 in the experimental group was significantly higher than control group ($P<0.05$). After the cystoscopy, the level of interleukin-8 in the experimental group was significantly lower than that before the treatment ($P<0.05$), but there was no difference between the experimental group and the control group ($P>0.05$). The results are shown in Fig 1.

3.3 the correlation between serum interleukin-8 and renal function

Serum interleukin-8 level was highly expressed in patients with post-renal insufficiency after radiotherapy for abdominal tumors, and its expression was positively correlated with serum creatinine (r=0.297, p=0.004), but not with urea nitrogen level and hydronephrosis (r_1=-0.055, P_1=0.605;r_2=0.116, P_2=0.277). Cox proportional hazard regression model showed that interleukin-8 was a high risk factor (R^2= 0.826, P<0.05) indicating the occurrence of post-renal insufficiency. The results were shown in Fig 2.

4. Discussion

Some studies have shown that post-renal insufficiency after radiotherapy for abdominal tumors is mostly caused by ureteral stricture or obstruction. The pathology of ureteral obstruction can be divided into three categories [4-5]: Firstly, there are fibrous spots in the ureter tissue and external pressure ureteral stricture. Second, the ureteral wall fibrosis, rigidity, poor peristalsis, or abnormal dysfunction can cause the obstruction. Third, the parametrial cellulitis and triangular ulceration after radiotherapy also a important factor. One study has found that the effect of radiotherapy on the urinary system of dogs was the smaller the area of radiotherapy, the slighter the damage to the ureter. In the same area, the damage to the ureter was negatively correlated with the dose of radiotherapy[6]. It is suggested that under the premise of not affecting the effect of radiotherapy, the area and dose of radiotherapy should be reduced as much as possible, so as to reduce the ureteral injury and the incidence of postrenal renal insufficiency.

Interleukin-8 is a neutrophil chemokine discovered in the 1980s. It can act on T lymphocyte, mast cell, monocyte, eosinophil and so on. It can promote inflammatory reaction, mitosis and capillary formation. It is also associated with the occurrence and development of many inflammatory diseases[7]. Some scholars believe that after radiotherapy for abdominal tumors, radioactive substances can lead to injury of urinary capillaries, endothelial cells of blood vessels can produce a large number of interleukin-8, so that neutrophils can aggregate and activate around small blood vessels, and have a variety of morphological changes. They swim to inflammatory reaction sites and release cell surface adhesion molecules, lysosomal enzymes and so on, finally. They can form perivascular polymorphonuclear leukocytes (PMN), which can cause severe inflammatory damage to blood vessels [8]. In our study, we also found that interleukin-8 levels increased significantly in patients with post-renal insufficiency after radiotherapy, which may be a sign of early inflammation. We found the level of serum interleukin-8 levels in patients with post-renal insufficiency after radiotherapy for abdominal tumors can reach to (0.615±0.096) umol/L which was significantly higher than the patients without renal insufficiency(0.482±0.112) (P<0.05).

Some studies have shown that: The interleukin-8 has important value for predicting inflammation in chronic kidney disease or acute kidney injury after pediatric cardiac surgery[9.10]. The animal experimental studies have shown that: The interleukin-8 receptors are renoprotective in rats with acute kidney injury[11]. Some scholars found IL-8 levels have an important diagnostic power in acute kidney injury in newborns with perinatal asphyxia.and IL-8 level may be an independent risk factor in non-small cell lung cancer patients[12-13], However, whether interleukin-8 can cause ureteritis and renal insufficiency after

radiotherapy has not been reported too much.In our study, we also found that the serum interleukin-8 expression was positively correlated with serum creatinine (r=0.297, p=0.004), but not with urea nitrogen level and hydronephrosis (r_1=-0.055, P_1=0.605, r_2=0.116, P_2=0.277). Meanwhile we use the cox proportional risk regression model to analysis its value, the results showed that interleukin-8 was a high risk factor for the occurrence of post-renal insufficiency (R^2=0.826, P<0.05). Therefore, we believe that interleukin-8 is helpful in judging the renal function of patients with abdominal tumors after radiotherapy, and its evaluation of renal function is better than urea nitrogen, which is worthy of clinical application.

Inconclusion our study confirms that interleukin-8 is helpful to judge the renal function of patients with abdominal tumors after radiotherapy, In the early stage of renal insufficiency, it will overexpress, and its evaluation is better than urea nitrogen.

Declarations

Author Contributions

Liang Bai is in charge of the overall work, Jun Li is in charge of the design and guidance of the subject, Li Luo is in charge of the operation, Weicheng Gao is in charge of data collection, and Chengfeng Bu is in charge of follow-up observation. Huang Liu guides the writing.

Statement of Ethics

The study was approved by the Ethics Committee of the First Affiliated Hospital/School of Clinical Medicine of Guangdong Pharmaceutical University. All patients provided written informed consent.

Conflicts of Interest

There was no conflicts of interest

Funding Sources

Fund projects：Guangdong Medical Science and Technology Research Fund Project(B2017041); the Medical Research Fund project of Guangdong Province (NO.B2018250).

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Tables

Table 1: Comparison of general data between the two groups

Groups	Sample Size(n)	Age (Y)	Course of disease(Y)	Gender(n)		Type of disease(n)			
				Male	Female	Rectal cancer	Colon cancer	Cervical cancer	Ovarian cancer
Experience group	60	48.97±1.70	1.33±0.56	24	36	16	20	13	11
Control group	30	48.20±1.79	1.30±0.48	14	16	8	9	7	6
t/χ^2	-	1.984	0.279	2.178*			3.600*		
P	-	0.050	0.781	0.140			0.308		

Remarks* was χ^2 value

Figures

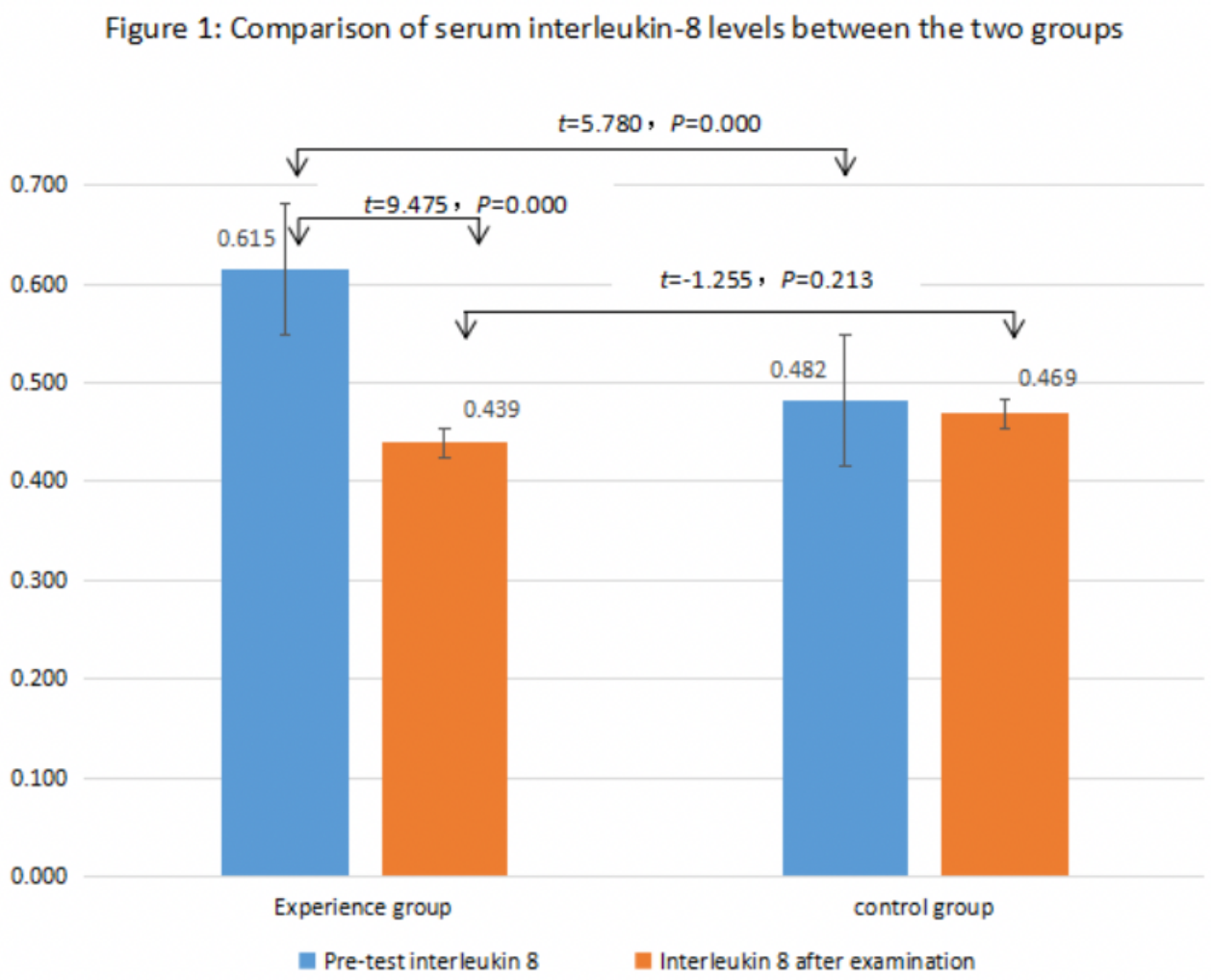

Figure 1

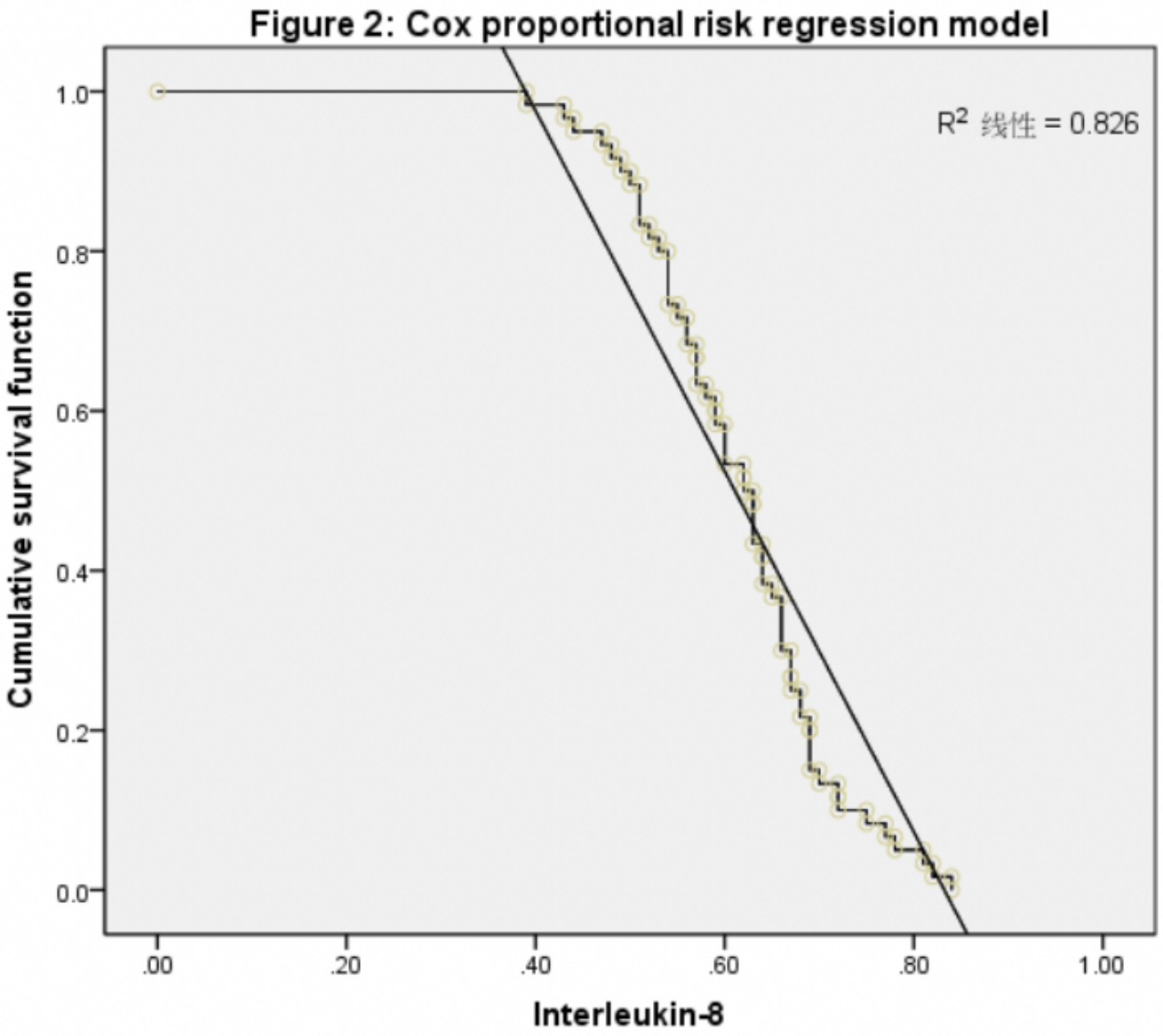

Figure 2