

Intravesical instillation therapy with Adriamycin for bladder cancer in the Korean study group

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Summary. Eighteen cases of bladder cancer were treated with intravesical instillation therapy with 60 mg Adriamycin daily.

Overall, the treatment was markedly effective in two cases, effective in nine cases, and ineffective in seven cases.

Bladder irritation was noted in four cases. Postinstillation therapy was required in most cases.

Introduction

We have evaluated the effectiveness of Adriamycin for the treatment of bladder cancer by intravesical instillation in Korean patients. We now present our findings, based primarily on the results of cystoscopic examination and cystographic findings.

Materials and methods

From June 1980 to June 1982, a total of 18 cases diagnosed histologically as bladder cancer were studied (Table 1). There

Table 1. Intravesical instillation of Adriamycin for the treatment of bladder cancer

1. Number of cases		18 cases
2. Sex distribution	Male	16 cases
	Female	2 cases
3. Age distribution	Range	39–77 years
	Median age	57.5 years
4. Stage distribution	A (T ₁)	9 cases
	B1 (T ₂)	7 cases
	B2 (T ₃)	1 case
	C (T ₃)	1 case
5. Grade distribution	Grade I	5 cases
	II	10 cases
	III	3 cases
6. Number of tumors	Solitary	4 cases
	Multiple	14 cases
7. Shape of tumor	Papillary	14 cases
	Nonpapillary	4 cases

Table 2. Results of intravesical instillation of Adriamycin for bladder cancer treatment

Case no.	Patients initials	Age	Sex	No. of tumors ^a	Shape of tumors ^b	Size (cm)	Stage	Grade	Previous treatment ^c	Result ^d	Side-effects
1	A. J.	42	M	M.	P.	1.0	A	I	TUC	G.	—
2	P. Y.	53	M	S.	P.	1–3	B1	II	TUC	P.	—
3	L. S.	64	M	M.	N.P.	1–0	B1	II	TUC	P.	—
4	H. M.	64	M	M.	N.P.	1–3	B1	II	TUC	P.	Local Sx. (+)
5	M. C.	59	M	M.	N.P.	1–3	B1	II	TUC	P.	Local Sx. (+)
6	L. I.	46	F	M.	P.	1–0	A	I	TUC	G.	Local Sx. (+)
7	K. C.	63	M	S.	P.	5 <	C	III	TUR	P.	Local Sx. (+)
8	L. B.	41	M	M.	P.	1–3	B1	III	TUR + rad.	G.	—
9	L. Y.	39	M	S.	P.	1.0	A	II	TUR	G.	—
10	K. K.	57	M	M.	N.P.	1–2	A	I	TUC	G.	—
11	S. K.	70	M	M.	P.	3–5	B1	III	TUR	P.	—
12	I. W.	77	M	M.	P.	5 <	B1	II	P. Ex.	G.	—
13	C. J.	64	M	S.	P.	3–5	A	I	P. Ex.	G.	—
14	B. S.	64	F	M.	P.	2–3	A	I	P. Ex.	G.	—
15	K. J.	70	M	M.	P.	1–0 <	A	II	P. Ex.	Excellent	—
16	K. Y.	48	M	M.	P.	1–3	A	II	TUC	Excellent	—
17	I. Y.	64	M	M.	P.	3–5	B2	II	TUC	P.	—
18	K. Y.	50	M	M.	P.	1–3	A	II	TUC	G.	—

^a M., multiple; S., single

^b P., papillary; N.P., non-papillary

^c P. Ex., partial excision

^d G., good; P., poor

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Week	Days						
	1	2	3	4	5	6	7
1st	↑	↑	↑				
2nd	↑	↑	↑				
3rd	↑	↑	↑				
4th							
5th							
6th	Cystoscopy						
7th							

Fig. 1. Schedule for Adriamycin instillation

Table 3. Results of intravesical instillation of Adriamycin for the treatment of bladder cancer

	Number of cases		
	Markedly effective	Effective	Ineffective
Sex			
Male	2	7	7
Female	0	2	0
Solitary	0	2	2
Multiple	2	7	5
Papillary	2	8	4
Non-papillary	0	1	3
Papillary			
Grade I–II	2	7	2
Grade III–IV	0	1	2
Non-papillary			
Grade I–II	0	1	3
Grade III–IV	0	0	0

Table 4. Relationships between efficacy of Adriamycin instillation and post-instillation treatment

Efficacy	Post-instillation				
	No. treatment required	TUC, TUR	Partial Cyst-ectomy	Radi-ation Tx.	Other operation
Markedly effective	1	1	0	1	0
Effective	0	6	2	0	1
Ineffective	0	4	3	2	0
Total	1	11	5	3	1

were 16 males and two females. The average age was 57.5 years, ranging from 39 to 77. All these patients had transitional cell carcinoma: there were five with grade I, nine with grade II, and four with grade III tumors.

The disease was classified as stage T1 in nine cases and stage T2 in seven, according to the UICC classification [1]; there were 14 cases of papillary-type tumors among them. Four patients had solitary tumors and the remaining 14 cases had multiple lesions (Table 2).

Table 5. Adverse effects of Adriamycin instillation for bladder cancer

	Cases
1. G-I tract	
Nausea, vomiting	0
Diarrhea, melena	0
Stomatitis	0
2. Hematologic	
Leukopenia 3,000	0
Thrombocytopenia	0
Anemia	0
3. Cardiac	
Arrhythmia	0
ECG changes	0
Heart failure	0
4. Dermatologic	
5. Allergic reaction	0
6. Pulmonary	0
7. Local (bladder irritation)	4
8. Others	0
Total	4
Cases without side-effects	14
Discontinuation	0

Adriamycin 60 mg dissolved in 30 ml physiological saline was instilled through a Nelaton catheter transurethrally.

After instillation, the patients were positioned so that the tumor was below the instilled fluid to ensure maximum contact. The drug was retained for more than 2 h and the treatment was repeated daily on 3 consecutive days followed by a 4-day interval, for 3 weeks (Fig. 1).

Evaluation of efficacy and side-effects. In all cases cystoscopy and biopsy were carried out prior to therapy, and cystography and polycystography were also performed.

CBC and hepatic and renal function tests were also carried out in all cases, and ECG in most cases. Immediately after completion of the therapy the same tests were repeated. Follow-up cystoscopy, however, was performed 3–4 weeks later. Therapeutic effectiveness was analysed as follows.

In the event of a reduction of 90% or more in tumor size the therapy was evaluated as markedly effective; with a reduction of 50% or more, as effective, and in all other cases, as ineffective.

Results

The therapy was markedly effective in two cases and effective in nine, while in seven it was ineffective (Table 3).

Treatment of bladder tumors persisting after cessation of Adriamycin instillation was needed in most cases. TUC or TUR was performed in 11 cases including one in which the therapy was markedly effective and six in which it was effective. Segmental resection of bladder was performed in five cases, including two in the 'effective' and three in the 'ineffective' group (Table 4).

Adverse effects were checked routinely, and no systemic side-effects were noted in any of our cases. Local adverse effects such as bladder irritability were encountered in four cases, but interruption of the therapy was not necessary (Table 5).

Discussion

Many investigators have proved that Adriamycin is active in transitional cell carcinoma and has strong affinity for cancer tissues [6, 10], while its transfer from the body cavity into the bloodstream is negligible [3].

To ascertain a suitable dose for instillation, Niiijima [9] and Matsumura [7, 8] conducted studies with three doses, 1,000 µg/ml, 1,600 µg/ml, and 2,000 µg/ml; of these 1,600 µg/ml gave good results with tolerable side-effects.

These authors also decided that administration of three instillations in a week, on consecutive days was adequate and avoided severe irritation of the bladder.

Edsmyr et al. [2] reported complete disappearance of T1 tumors in 11 of 19 cases after Adriamycin instillation.

Kai et al. [5] reported a therapeutic effective rate of 53.3% in his 15 cases.

Hayashida et al. [4] reported good results with administration of 20 ml of 2,000–3,000 µg/ml of Adriamycin on each of 5 consecutive days. However, bladder irritation and hematuria seemed to be problems in this study.

In our series most cases required surgery or radiation after instillation treatment; surgery was easily performed because the tumor sizes had been reduced.

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