RETROSPECTIVE STUDY OF CARCINOMA OF THE URINARY BLADDER

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INTRODUCTION

Carcinoma of the urinary bladder is not an uncommon tumour and is the 10th commonest tumour among males in Singapore.

It is an intriguing and challenging disease and up to this day, controversies still exist regarding its early diagnosis and management.

The purpose of this paper is to study the clinical presentation of the disease and its histopathology in the local population as well as to review the wide range of methods of treatment used over the years in the University Department with the hope of making recommendations for the future policy in the management of carcinoma of the bladder.

MATERIAL AND METHOD

A retrospective study of carcinoma of the urinary bladder seen at the University Department of Surgery from the period 1973 to 1978 was undertaken.

73 cases were reviewed with respect to their clinical presentations, pathology of tumours (with special attention to the grade according to WHO Classification), and methods of treatment. The cases were obtained from the Cancer Registry and clinical data derived from case records. Follow-up of these patients has been a problem. Patients lost to follow up have been called for an interview. The assistance of the Registry of Births and Deaths, Singapore, has been sought to establish the present status of some of the patients.

RESULTS

Patient Population

Of the 73 cases reviewed, 60 were males and 13 females thereby giving a male to female ratio of 4.6 to 1. This compares with most of the reported series where the male to female ratio varied from 2.3 : 1 (Anderson 1973) to 5 : 1 (Westcott 1966). The higher incidence in males have been variously attributed to environmental exposure to carcinogens such as cigarette smoking and other occupational hazard and social habits.

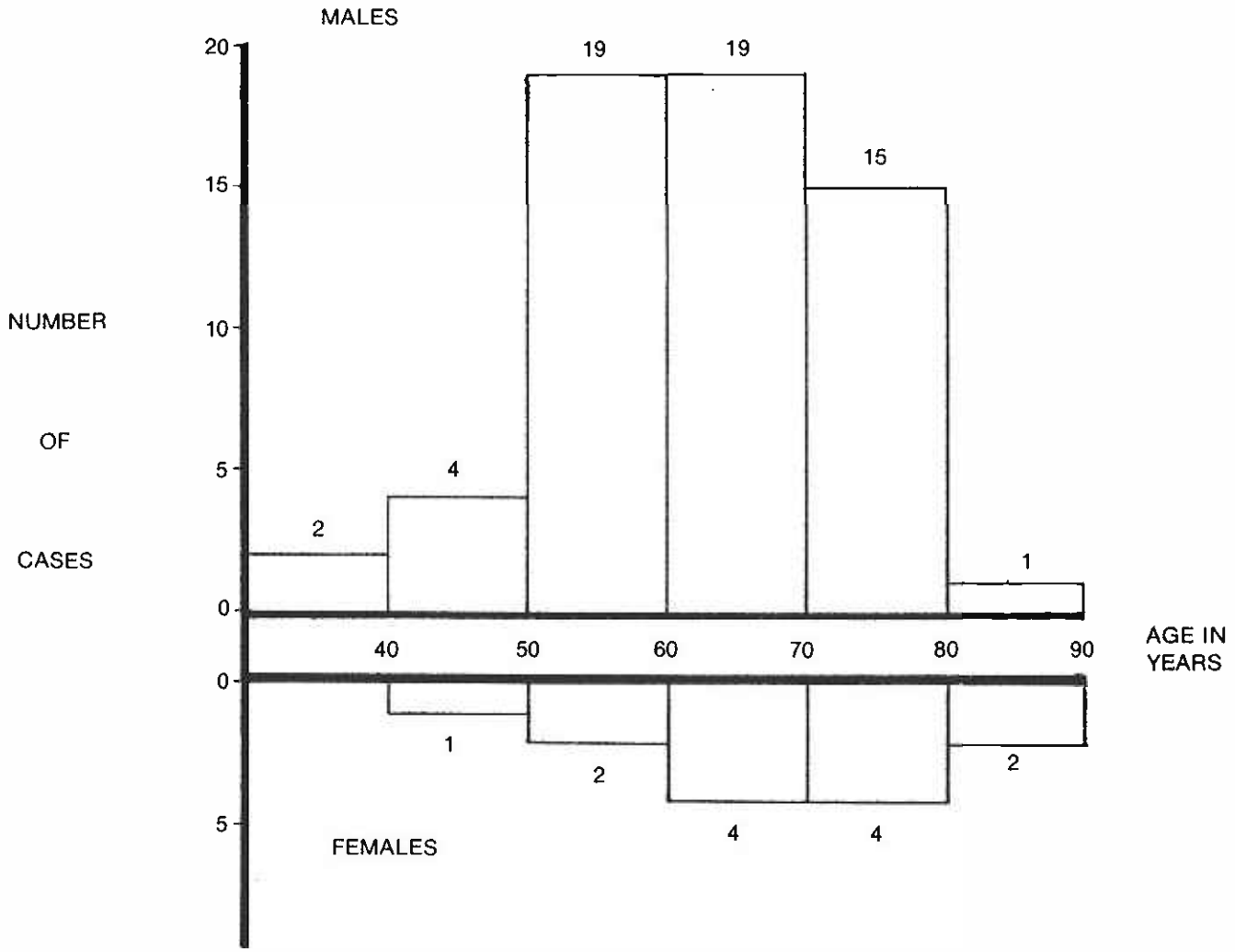
87.7% of the cases were Chinese. There were noticeably few Indians seen with this tumour.

The majority of patients were in the 5th to the 7th decade of life.

Only 2 patients, both males, were below the age of 40 years, the younger being 29 years. The oldest patient was a female aged 83 years (Fig. 1).

BLADDER CARCINOMA (Fig. 1)

Age — Sex Distribution



Clinical Presentation (Table 1)

Haematuria was by far the most common presenting symptom and almost 85% of patients in this study had haematuria, either as the sole complaint or together with symptoms of cystitis and outflow obstruction. 85 to 90% of patients with urothelial malignancy present with haematuria with 15% having dysuria and frequency as well (Hendry, Bloom 1976). In our series, 31.5% had frequency and dysuria and another 17.8% had symptoms of outflow obstruction.

12 patients presented with other symptoms which consisted mainly of backache and loin pain. Only 1 patient had a palpable suprapubic mass on clinical examination.

TABLE 1

BLADDER CARCINOMA

Presentation

	NUMBER	% OF 73 CASES
HAEMATURIA	62	84.9
CYSTITIS	23	31.5
OUTFLOW OBSTRUCTION	13	17.8
SUPRAPUBIC MASS	1	1.4
OTHERS	12	16.4

Duration of Haematuria (Table 2)

32 patients (51.6%) sought medical advice within 1 month of the onset of bleeding and 46 patients (74.2%) within 6 months. Wallace (1965) has pointed out that most tumours are curable when the first symptoms appear and has shown that the 3 year survival rate for infiltrative tumours fell drastically from 60% to 25% when treatment was delayed for more than 1 month from the time of bleeding.

TABLE 2

BLADDER CARCINOMA

Duration of Haematuria

1. Within 1 week	:	13 patients (21.0%)
2. Within 1 month	:	32 patients (51.6%)
3. Within 6 months	:	46 patients (74.2%)

Duration of Haematuria & Stage of Disease (Table 3)

We next correlated the duration of haematuria with the clinical stage of the disease and found that T_3 and T_4 tumour presented with a long history of haematuria, 10 out of 14 patients with T_3 tumours had bleeding for months to years while all 4 cases of T_4 tumours presented late. Patients with T_1 tumours may present either early or late.

TABLE 3

BLADDER CARCINOMA

Duration of Hamaturia & Stage of Disease (62 cases)

	T_1	T_2	T_3	T_4	Unknown
Days/ Wks	13 (44.8)	5 (45.5)	4 (28.6)	0 (0.0)	0 (0.0)
Mths/ Yrs	15 (48.3)	3 (27.25)	10 (71.4)	4 (100)	3 (100)
Un-known	2 (6.9)	3 (27.25)	0 (0.0)	0 (0.0)	0 (0.0)
TOTAL	30 (100%)	11 (100%)	14 (100%)	4 (100%)	3 (100%)

Intravenous Urogram Findings (Table 4)

A few interesting points were noted on analysis of 61 cases with IVU available. It was found that almost 1/4 of the cases had a normal IVU. 16 cases (26.2%) had evidence of ureteric obstruction and in 15 of these, 1 or both of the ureteric orifices were occluded by bladder tumours. 1 patient had a ureteric tumour which resulted in a left hydronephrosis.

In only 35 cases (57.4%) was a filling defect demonstrated on the IVU leaving 42.6% of cases in which the tumour was not outlined. Thus a normal bladder outline does not exclude a bladder tumour.

TABLE 4

BLADDER CARCINOMA

IVP Findings (61 cases)

	No		%	
Normal IVP	15		24.5	
Dilated Upper Tract	16		26.2	
Non-Function	2)	4	3.3)	6.6
Poor-Function	2)		3.3)	
Filling Defect	35		57.4	
Associated Bladder stones	2		3.2	

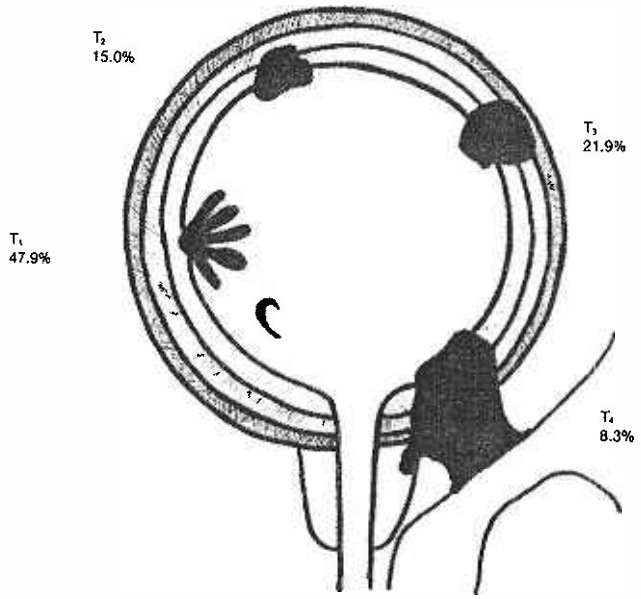
Clinical Stage of Tumour (Figure 2)

47.9% of tumours were clinically staged as T_1. This incidence of T_1 tumours was much lower than results quoted elsewhere which is in the region of about 80% (Hendry 1976). In this series there was quite a large number of T_3 tumours which accounted for 21.9% of cases.

Clinical staging of bladder tumours is notoriously inadequate and difficulties in clinical staging has been repeatedly emphasized by various workers. Riches (1975) in an evaluation of 134 patients found that clinical and pathological staging agreed in only 46 patients (34%).

This being a retrospective study, we have derived the clinical staging as best we could from information obtainable from the case records.

BLADDER CARCINOMA (Fig. 2)



Clinical Stage of Tumours

Clinical Stage and Pathological Grade of Transitional Cell Carcinoma (Table 5)

A correlation was noted between clinical stage of the disease and the pathological grade of tumours. T_1 tumours were usually well differentiated or moderately differentiated, whereas T_3 and T_4 tumours were poorly differentiated.

Williams et al in a review of 167 T_1 transitional cell tumours found that 68.7% were well differentiated, 24.4% moderately differentiated and 6.8% poorly differentiated. In this series of 36 T_1 transitional cell tumours, only 38.2% were well differentiated while 35.3% were moderately differentiated and 14.7% poorly differentiated.

TABLE 5

BLADDER CARCINOMA

Clinical Stage & Pathological Grade of transitional cell carcinoma (69 cases)

CLINICAL STAGE	GRADE				
	0	1	2	3	Unknown
T_1	2	13	12	5	2
T_2	—	2	5	4	—
T_3	—	1	6	7	—
T_4	—	—	3	3	—
Unknown	—	—	2	2	—

Number of Tumours

The majority of cases (71.3%) were found to have single tumours. 15 cases (20.5%) had multiple tumours (less than 6) and there were 3 patients with papillomatosis.

Site of Tumours (Figure 3)

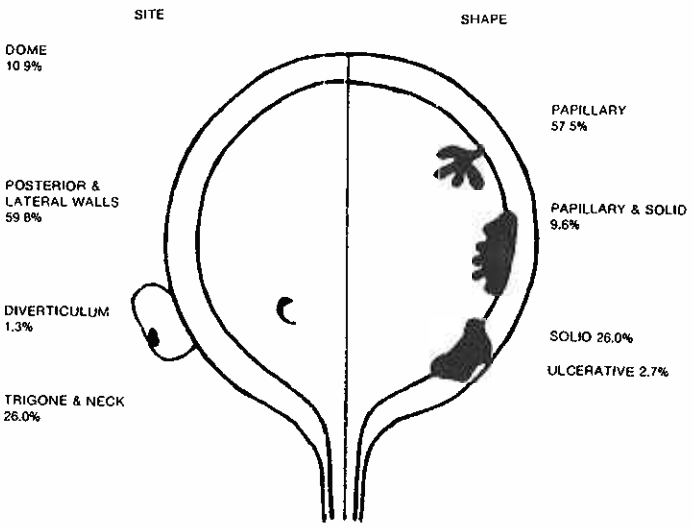
The lateral walls were the most common sites of tumours where 69.8% of the tumours were found. Both the right and left lateral walls were affected almost equally. Tumours were less common on the dome, trigone and bladder neck.

Morphology of Tumours (Figure 3)

There were only 42 cases (57.5%) with a papillary appearance of the tumour. This finding is unlike those of other workers where most of the tumours were papillary. (Melicow 1974).

19 patients had solid tumours and 2 patients had ulcerative lesions. These usually represented a late stage of the disease.

BLADDER CARCINOMA (Fig. 3)



Incidence of sites and shapes of 73 bladder tumours

Morphology & Clinical Stage (Table 6)

33 patients with T_1 disease had papillary tumours and there were few T_1 tumours with other morphological appearances. On the other hand, tumours in late stage disease were more often solid. 50% of T_3 tumours were solid and 5 out of 6 cases of T_4 tumours had this appearance. Hence papillary tumours are most likely to be early stage whereas solid tumours are more often invasive lesions.

As expected most of the tumours were transitional cell carcinoma (94.5%). There were 2 cases of adenocarcinoma (2.7%), one occurring in a 61 year old female and one in a 64 year old male.

2 patients had squamous cell carcinoma (2.7%), one occurring in a bladder diverticulum and one on the trigone and right lateral wall. Both cases were inoperable and were dead within 2 months.

TABLE 6
BLADDER CARCINOMA
Morphology & Clinical Stage

	T_1	T_2	T_3	T_4	Unknown
Papillary	33 (91.4)	4 (36.4)	4 (25.0)	0	1
Papillary + Solid	0	3 (27.3)	3 (18.7)	0	1
Solid	2 (5.7)	3 (27.3)	8 (50.0)	5 (83.3)	1
Ulcerative	1 (2.8)	0	1 (6.3)	0	0
Unknown	0	1 (9.0)	0	1 (16.7)	1
	36	11	16	6	4

Extravesical Sites of Tumour (Table 7)

5 cases of extravesical urothelial tumours were seen in this series. 1 patient had a lesion in the left ureter. 4 patients had lesions in the renal pelvis. In all 5 patients, bladder carcinoma was found after treatment of the extravesical lesion.

TABLE 7
BLADDER CARCINOMA
Extravesical Sites of Tumour

5 cases of urothelial tumours were seen in this series.

1 patient had a lesion in the left mid ureter.

4 patients had lesions in the renal pelvis on one side.

In all 5 patients Ca bladder was found after treatment of the extravesical urothelial lesions.

Modes of Initial Therapy (Table 8)

It is quite evident from this table that a wide range of methods of treatment had been employed in the management of bladder carcinoma. Treatment varied from cystodiathermy alone to total cystectomy and there was apparently a lack of a unified policy for management of this tumour.

Treatment of T_1 Tumours (Table 9)

Before 1976 when transurethral resection was not available, most T_1 tumours whether single or multiple were treated by biopsy and cystodiathermy.

After 1976, the majority of T_1 tumours were treated by transurethral resection. This is now a widely accepted mode of therapy for early stage tumours and is the treatment of choice in the Department for this tumour.

TABLE 8
BLADDER CARCINOMA
Modes of Initial Therapy

	No	%
TUR only	19	26.0
TUR + DXT	11	15.0
Biopsy + DXT	12	16.4
Open excision	3	4.2
Partial cystectomy	3	4.2
Total cystectomy	4	5.4
Preop. DXT + cystectomy	1	1.4
Cytotoxic	1	1.4
Cystodiathermy	11	15.0
Others	8	11.0
	73	100%

TABLE 9
BLADDER CARCINOMA
Treatment of T_1 Tumours

Treatment	Before 1976		After 1976	
	T_1	T_1 (m)	T_1	T_1 (m)
TUR only	—	—	11	6
TUR + DXT	—	—	—	1
Biopsy + DXT	2	1	1	—
Open Excision	1	—	—	—
Partial Cystectomy	1	—	—	—
Cystodiathermy	6	2	1	1
Others	—	—	2	—

TABLE 10
BLADDER CARCINOMA
Treatment of T_2 Tumours

Treatment	Before 1976		After 1976	
	T_2	T_2 (m)	T_2	T_2 (m)
TUR + DXT	—	—	4	—
Biopsy + DXT	—	2	—	—
Partial Cystectomy	1	—	—	—
Total Cystectomy	1	—	—	1
Cytotoxics	—	—	—	1
Cystodiathermy	—	1	—	—

Treatment of T_2 Tumours (Table 10)

Here again, transurethral resection followed by radiotherapy is the mode of therapy adopted for most patients since the introduction of transurethral resection locally.

Treatment of T_3 Tumours (Table 11)

Various forms of treatment have been used over the years and results are generally poor whatever the treatment prescribed. However reports of preoperative irradiation followed by cystectomy have been encouraging and Whitmore and others have shown that preoperative radiotherapy can greatly improve the survival of patients with T_3 tumours. We would recommend a course of radiotherapy followed by cystoscopy at 4 to 6 weeks after completion of radiotherapy and proceed to total cystectomy only if there is no response. For treatment of T_4 tumours only palliative radiotherapy is recommended.

TABLE 11
BLADDER CARCINOMA
Treatment of T_3 T_4 Tumours

Treatment	Before 1976		After 1976	
	T_3 T_4	T_3(m) T_4(m)	T_3 T_4	T_3(m) T_4(m)
TUR only	—	—	1	—
TUR + DXT	—	—	1	—
Biopsy + DXT	4	1	1	—
Open Excision	1	—	1	—
Total Cystectomy + DXT	1	—	1	—
Preop. DXT + Cystectomy	—	—	—	1
Others	1	1	—	—

Recurrences in low stage, low grade disease (Table 12)

28 cases of low stage, low grade tumours were found in the series. Out of 15 cases of single T_1 tumours, 8(53.3%) developed recurrence after treatment. T_1 multiple tumours had a higher incidence of recurrence (75%). The overall recurrence rate for T_1T_2 tumours in grades 1 and 2 was 58.3%.

TABLE 12
BLADDER CARCINOMA
Recurrences in Low Stage, Low Grade Disease
(T_1 T_2) (G_1 G_2)
(28 cases)

	No Recurrence	Recurrence	Recurrence (%)
T_1	7	8	53.3
T_1 (m)	2	6	75.0
T_2	0	0	0.0
T_2 (m)	1	0	0.0
Unknown 4			
Overall recurrence rate: 58.3%			

Results of Treatment

The overall mortality was 46.6% with 22 out of 34 deaths (64.7%) attributed directly to carcinoma of the bladder. The majority of deaths occurred within the first 2 years. 8 patients with T_1 tumours died. Of these 6 patients died of causes other than bladder tumour. These included senile debility (1 case), corrosive poisoning (1), congestive cardiac failure (1), emphysema with respiratory failure (1), cerebrovascular accident (1) and cholangio carcinoma (1). One patient developed invasive carcinoma and another was staged wrongly.

The majority of patients with invasive carcinoma died of the tumour.

COMMENTS

The problems met with in carcinoma of the bladder are many. First the concept of the "urothelium" as a single continuous membrane lining the urinary drainage tract implies that eradication of a tumour in the bladder does not mean eradication of the disease, for urothelial tumours may still develop in other parts of the urinary tract as long as the aetiological agent exists.

Another important problem is the question of preservation of the bladder. Late tumours of the bladder are generally treated more radically than early tumours. However, is there a place for total cystectomy in low stage, low grade disease and if so at what point in treatment should one consider this mode of therapy, especially when one realises that about 15% of T_1 tumours become invasive later on.

Tumours of the bladder may be multiple not only in space but also in time and it is particularly in patients with asynchronous tumours that treatment policy must be carefully designed. Unlike late stage disease where prognosis is poor whatever the treatment prescribed, in early disease, tumours tend to recur in 50% to as high as 75% of cases. Patients would therefore, have to be checked regularly for recurrences. One problem that arises is that after a while, most patients abscond from check cystoscopies. They do not understand the necessity of regular follow-up when they are asymptomatic. Even if they do, some patients called up for interview attributed abscondment to painful regional anaesthetic techniques which at times do not work. It is therefore important to educate our patients and to provide adequate anaesthesia for check cystoscopies.

CONCLUSION

The clinical presentation of carcinoma of the bladder is similar in many respects to most of the reported series. The male to female ratio is 4.6 to 1. The majority of patients were in the 5th to 7th decades of life. 85% of patients presented with gross haematuria, and only about ½ (51.6%) sought treatment within one month of the onset of symptoms. In 42.6% of cases the tumour was not outlined by intravenous urogram. Thus a negative IVU does not exclude a bladder tumour, and all patients with

symptoms suggestive of the disease should have a cystoscopy as a minimum investigation.

There was a much lower incidence of low stage, low grade papillary tumours (57.5%) compared to other series of about 80% (Melicow 1974).

For low stage tumours, our present policy is to resect these tumours endoscopically and to start on radiotherapy if there is evidence of superficial muscle involvement on histology. Papillomatosis of the bladder would need total cystectomy. Multiple small superficial low grade tumour may be controlled by intravesical cytotoxic agents. Localised high grade tumours especially near the vault of the bladder may be treated with partial cystectomy.

For T_3 tumours which have invaded the whole thickness of the bladder wall or perivesical fat, reports have shown that preoperative irradiation followed by cystectomy has improved the 5-year survival rate from about 20% to 40% (Whitmore 1978). However, we feel that in view of the attending mortality and morbidity following cystectomy and that some patients respond very well to radiotherapy, we should be more selective in doing total cystectomy, reserving it for patients who do not respond to the initial radiotherapy.

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