



## A Study of The Biopsy of The Normal Appearing Urothelium in Muscle Non Invasive Bladder Tumours

### KEYWORDS

Biopsy , Papillary Urothelium , Random

#### \* Dr Aseema Das

Associate Professor, Dept. of Pathology, Assam Medical College and Hospital. \* corresponding author

#### Dr Bandita Das

Associate Professor, Dept. of Pathology, Assam Medical College and Hospital

#### Dr Simanta Jyoti Nath

Assistant Professor Dept. of Urology Assam Medical College and Hospital

### ABSTRACT

*Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide. After trans-urethral resection of the tumour (TUR) upto 60% -70% of patients develop recurrent disease after the operation and the most common cause of recurrence is the presence of residual tumour mass or presence of any dysplastic urothelium. Our study included 30 random mucosal biopsy specimen of the urothelium adjacent to the tumour mass from patients with previous diagnosis of non invasive papillary urothelial carcinoma. Positive biopsy finding was found in 80% of cases with high grade muscle non invasive bladder cancer while 20 % cases showed normal results. Thus, random mucosal biopsy of normal appearing urothelium that surrounds the tumour can provide a valuable insight into the status of the urothelium and help in preventing recurrences.*

### Introduction

Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females with a ratio of about 3.5:1. Although bladder cancer can occur at any age, it is generally a disease of the elderly with a median age of diagnosis being approximately 60-70 years. About 95% of bladder tumours are of epithelial origin, the remainder being mesenchymal tumors<sup>1</sup>. Epithelial tumours comprise a broad spectrum of tumours including urothelial carcinoma, squamous cell carcinoma, adenocarcinoma, small cell carcinoma and miscellaneous sub types. Among these urothelial carcinomas are the most common subtypes. Urothelial carcinomas can again be classified into infiltrating urothelial carcinoma and non invasive urothelial neoplasm. Non invasive urothelial neoplasms can again be further classified as urothelial carcinoma in situ, non invasive papillary urothelial carcinoma high grade, non invasive papillary urothelial carcinoma low grade and non invasive papillary urothelial neoplasm of low malignant potential<sup>1</sup>. Urothelial carcinoma of the bladder presents as a non- invasive disease in the majority of patients. These muscle non invasive tumors are mucosa-confined tumors (Ta), tumors which affect lamina propria (T1), and tumor in situ (Tis). After trans urethral resection of the tumour (TUR) upto 60% -70% of patients develop recurrent disease, most frequently within the first year after the operation. The basic causes of tumor recurrence are implantation during primary resection (large and multiple tumors), undiscovered residual tumor (later manifested as a recurrence), and the existence of macroscopically invisible pre-malignant and malignant lesions of urothelium during the primary resection<sup>2</sup>. For the prediction of tumor behaviour, many parameters can be studied like tumour grade, stage, multiplicity, size and localization, primary or recurrent disease and the reaction to intravesical instillation of drugs. Concomitant abnormalities of the apparent normal looking mucosa by taking random mucosal biopsy also seem to have a prognostic value<sup>3</sup>. The existence of these lesions can be detected by taking biopsy from apparently normal mucosa in the vicinity of the tumor by trans urethral resection (TUR). The purpose of taking random mucosal biopsies is to identify the distribution and frequency of lesions that are not otherwise visible to the naked eye which can be the harbinger of recurrent urothelial carcinoma.

### AIMS AND OBJECTIVE:

Although various studies have been done in different parts of the country regarding the biology and behaviour of bladder tumours, very few studies have been done in this part of the country regarding random mucosal biopsy of normal appearing urothelium in patients of urothelial carcinoma. So, the present study was done to study the biopsy pattern of the normal-appearing urothelium which surrounds the tumor in relation to the tumour grade.

### Materials and Methods:

Place of study: - The study was undertaken in the Department of Pathology, Assam Medical College and Hospital, Dibrugarh (Assam) for a period of one year

The study group consisted of 30 patients who were initially diagnosed as muscle non invasive bladder cancer. The urologist took random mucosal biopsy from the normal appearing urothelium at the edge of the resected tumour. These biopsy specimens were then sent to the Department of pathology for histopathological examination. The biopsy findings were categorized as normal finding or abnormal finding such as hyperplasia, dysplasia and carcinoma in-situ. Normal urothelium is three to six layers thick without cytological atypia and minimal crowding and nuclear overlap while marked thickening of the urothelial mucosa without cytological atypia was considered as hyperplasia and thickening and architectural changes in the urothelial mucosa with cytological atypia was considered as dysplasia. Marked nuclear pleomorphism, prominent nucleoli throughout the urothelium and presence of mitotic figures and intact basement membrane was considered as carcinoma in situ.

### Results and observation

A total number of 30 random mucosal biopsy specimens were obtained during the period of one year. All the patients were previously diagnosed as non invasive papillary urothelial carcinoma. In our study the age group of the patients ranged from 31-70 years and maximum number of cases were found in the age group of 51- 60 years with a total of 12 cases. The incidence in male is more than in female showing a male to female ratio of 6:1. In our study highest number of cases were of non invasive papillary

urothelial carcinoma low grade followed by non invasive papillary urothelial carcinoma high grade and the distribution of the different histologic types is shown in Table -1. In the present study random mucosal biopsy results were interpreted as normal, epithelial hyperplasia, dysplasia and carcinoma –in- situ .The distribution of the different patterns are shown in Table-2. Correlation of the results of random mucosal biopsy with non invasive papillary urothelial carcinoma of different grades as shown in Table -3 ,showed maximum abnormal findings in high grade urothelial carcinomas and only two cases showed normal findings. Papillary urothelial neoplasm of low malignant potential showed highest normal result with the exception of one case which was interpreted as hyperplasia. Thus ,twenty percent of the cases of non invasive bladder carcinoma showed normal random mucosal biopsy findings and eighty percent cases showed abnormal random mucosal biopsy findings.

Table -1 (Frequency of different histological types of non invasive urothelial tumours)

| Frequency of different histological types of non invasive urothelial tumours | number of cases |
|--|-----------------|
| PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL                     | 4               |
| NON INVASIVE PAILLARY UROTHELIAL CARCINOMA LOW GRADE                         | 15              |
| NON INVASIVE PAILLARY UROTHELIAL CARCINOMA HIGH GRADE                        | 11              |

Table -2 (Results of the different patterns of random mucosal biopsy )

| Results of the patterns of random mucosal biopsy | Number |
|--|--------|
| Normal   | 6      |
| Epithelial hyperplasia                           | 12     |
| Dysplasia  | 10     |
| Carcinoma in situ                                | 2      |

Table -3 (Correlation of the results of random mucosal biopsy with non invasive papillary urothelial carcinoma of different grades)

| Correlation of the results of random mucosal biopsy with non invasive papillary urothelial carcinoma of different grades |                                  |                        |           |                   |
|--|----------------------------------|------------------------|-----------|-------------------|
| Type of papillary urothelial carcinoma   | Results of random mucosal biopsy |                        |           |                   |
|  | normal                           | epithelial hyperplasia | dysplasia | carcinoma in situ |
| PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL   | 3                                | 1                      |           |                   |
| NON INVASIVE PAILLARY UROTHELIAL CARCINOMA LOW GRADE   | 1                                | 8                      | 6         |                   |
| NON INVASIVE PAILLARY UROTHELIAL CARCINOMA HIGH GRADE  | 2                                | 3                      | 4         | 2                 |

**Discussion**

The muscle noninvasive bladder cancer has a great tendency for recurrence and progression. The most important cause of recurrence is the character of the disease and presence of macroscopically invisible premalignant and malignant lesions of urothelium that later manifest as re-

currence. In our study the biopsy material was taken from the normal appearing urothelium in the close vicinity of resected tumors. Abnormal biopsy finding was found in 80 % of cases with muscle noninvasive bladder cancer and most of these cases were diagnosed earlier as non invasive papillary urothelial carcinoma high grade while 20 % cases showed normal results which correlates with the study of Herr et.al who found residual tumour tissue in 75% of cases who did a routine secondary resection of the tumor 2-6 weeks after the initial resection<sup>4</sup>. Another study by Vogeli et al. found positive random mucosal biopsy results in 43% of cases of non invasive bladder cancer<sup>5</sup>. We propose that the higher percentage of abnormal findings in our biopsies of the normal-appearing urothelium in comparison with the above study may be due to the fact that we took biopsies from the lining that closely surrounds the resected tumor base. A study done by J.A.Witjes et al. showed abnormal findings in 78.8% of cases and maximum number of these cases were of high grade papillary urothelial carcinoma (56.8%)<sup>6</sup>. In our study the random mucosal finding of non invasive papillary urothelial neoplasm of low malignant potential showed maximum number of normal results which correlated with the study of Davor Librenjak et al. who found normal findings in 78% of cases of non invasive urothelial carcinoma<sup>7</sup>. Thus from our study we can suggest that random mucosal biopsies in patients with initial diagnosis of non invasive papillary urothelial neoplasm of low malignant potential may be avoided provided other prognostic factors are normal.

**Conclusion :**

Based on the results of our study, we can conclude that the routine random biopsy of normal-appearing mucosa that closely surrounds tumors contributes to a more precise insight into the status of urothelium. Patients with high grade non invasive papillary urothelial neoplasms needs to be followed up clinically to prevent their recurrence and progression as in this study we have found high percentage of abnormal finding in the normal appearing urothelium which may be one of the many causes of recurrences besides other factors like tumour stage and size and random mucosal biopsy can be avoided in non invasive papillaru urothelial neoplasm of low malignant potential . Taking the biopsy material from the normal-appearing mucosa near the resection edge is a safe procedure which allows a change in the therapeutic approach for a significant number of patients based on biopsy findings and thereby preventing morbidity and mortality of the patients.

**References :**

1. John N.Eble, Guido Sauter et al. WHO classification of Tumours of the Urinary System and Male Genital organs
- 2.. Kumano M, Miyake H, Nakano Y, Fujisawa Significance of random bladder biopsies in non-muscle invasive bladder cancer. M.Curr Urol. 2013 Nov; 7(2):57-61. Epub 2013 Oct 30.
3. Fernández Gómez JM, Rodríguez Martínez JJ et al Significance of random biopsies of healthy mucosa in superficial bladder tumor]. J. Arch Esp Urol. 2000 Nov; 53(9):785-97.
4. Herr HW. The value of 1a second transurethral resection in evaluating patients with bladder tumors. J Urol. 1999;162:74-6
5. Vogeli TA, Grimm M, Ackermann R. Prospective study for quality control of TUR of bladder tumors by routine second TUR (reTUR) J Urol. 1998;159:143.
- 6.. J.A.Witjes et al Random bladder biopsies and the risk of recurrent superficial bladder cancer: a prospective study in 1026 patients world J Urol(1992)10.231-234
7. Davor Librenjak et al. Biopsies of the normal-appearing urothelium in primary bladder cancer. Urol Ann. 2010 May; 2(2):71-5.