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## CONNECTIVE TISSUE STROMA IN MALIGNANT BLADDER AND BENIGN DENUDING CYSTITIS

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# CONNECTIVE TISSUE STROMA IN MALIGNANT BLADDER AND BENIGN DENUDING CYSTITIS

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## INTRODUCTION

Non papillary insitu carcinoma of urothelium denudes unusually easily. This uncovering produces a characteristic, syndrome of intractable antibiotic-resistant bacterial cystitis with a granular and velvet appearance on cystoscopy. the exposed stroma histologically demonstrate vasodilatation, oedema and leucocytic infiltration resulting in clinical symptoms which are the same as those of benign cystitis due to other causes (Riddle et al., 1979; Ooms et al., 1986 and Boob et al., 1986).

The aim of this work is to differentiate between denuded areas of carcinoma insitu and those in benign cystitis by examination of the superficial stroma. Also to determine if there are significant differences in stromal features seen in papillary carcinoma and carcinoma insitu, in an attempt to im-

prove histological differentiation between folded fragments of bladder mucosa with a lining of carcinoma insitu and real papillary tumour fragments as it is may be difficult in biopsy material and because of the different therapeutic measure for the two lesions.

## MATERIAL AND METHODS

- a- 50 patients underwent cystectomy for infiltrating carcinomas originating from insitu lesions. in all specimens there was histological evidence of both insitu and invasive tumour. from each specimen histological slides were selected with typical characteristics of carcinoma insitu and denuding cystitis.
- b- 20 patients with papillary transitional cell carcinoma obtained

by trans-urethral resected biopsy. 50 patients with benign cystitis, of diverse aetiology a biopsy material was also obtained in all these patients. carcinoma insitu was excluded cytologically as a possible cause of denudation and inflammation.

Specimens were fixed, embedded in paraffin then 5m thick histological sections were cut. the slides were stained by :

- 1 - Hx. & Eosin.
- 2 - Giemsa.
- 3 - Periodic acid-Schiff (PAS) and PAS diastase.
- 4 - Alcian blue (AB).
- 5 - Gomori's silver stain.

## RESULTS

The stroma of each case was analysed for the following morphological features: oedema, vascularity, vasodilation, endothelial proliferation and or swelling, presence of polymorphnuclear granulocytes eosinophiles, mast cells, lymphocytes. histiocytes, plasma cells, lymph follicles and density of reticulin network.

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After semiquantitative assessment of the above morphological features of the subepithelial connective tissue, three features only appeared to be significant :

- 1 - The density of reticulin fibres.
- 2 - The pattern of its distribution.
- 3 - The reaction of the intercellular substance with AB stain.

In the stroma of the papillary carcinomas the reticulin stains showed scanty fibres without a specific pattern of distribution, (Fig. 1, 2).

Carcinoma insitu on the other hand showed dense network of fibres in the stroma (Fig. 3, 4). In denuding cystitis the density of fibres was slightly diminished but the reticular pattern was retained, (Table 1).

The important results were obtained on the Alcian blue stain. The superficial stroma of papillary transitional cell carcinoma appeared to be strongly positive in non invasive as well as in invasive papillary tumour (Fig. 5). on the other hand the subepithelial stroma in carcinoma insitu, denuding cystitis and benign cystitis was AB negative (Table 1).

It was very difficult, however to differentiate with any of the above histo-

logical features between the denuded areas in benign cystitis and in carcinoma in situ.

## DISCUSSION

It is a major problem for the pathologist to differentiate between denuding cystitis in carcinoma in situ and benign cystitis with denudation of the urothelium. with semi-quantitative examination of the morphological features in the stroma, denuding cystitis in carcinoma in situ appeared to be indistinguishable from benign cystitis with denudation. this was in agreement with the work of Brawn (1982) and Oomas et al. (1986) in such cases cytological examination of the urine would be more helpful (Boon et al., 1986).

Another problem from the practical point of view both for the clinician and pathologist is to discriminate between papillary tran. c. c. and flat intraepithelial carcinoma because of the different biological behaviour and therapeutic approach to these lesions. the distinction between papillary carcinoma and folding of the bladder mucosa lined with carcinoma in situ may be very difficult, especially in transurethral resected biopsy material. the AB stain

clearly demonstrates the different nature of these structures.

The stroma of papillary tumours is stained blue, while the pseudopapillary stroma is negative. the reticulin stains also show morphological differences, with scanty fibres in papillary tumours, in contrast to the dense reticular pattern in pseudopapillary structures. Elliot et al., 1973 and Melamed et al. (1986) stated that examination of the stroma with AB and reticulin stains makes discrimination possible between papillary tumours and fragments of bladder mucosa lined with carcinoma in situ.

Foci of tumour invasion were accentuated by AB staining of the surrounding stroma. This finding corresponds with the findings of Maltoni and Prodi (1986) who demonstrated similar stromal alterations in experimental carcinogenesis of the skin in rabbits. on the basis of autoradiography and biochemical analysis they postulated an active turnover of mucopolysaccharides at the site of carcinogenic evolution.

It can be concluded that additional criteria from examination of the stroma can be useful, and the classification of bladder tumours, besides employing the WHO (1973) criteria which ex-



sively concern features of anaplasia of the urothelium, it is also very important to consider the morphological properties of the subepithelial stroma of the bladder wall of the tumour. the use of alcian blue in combination with reticulin stains makes recognition of papillary carcinoma and its distinction from carcinoma insitu possible. this allows a more appropriate therapy of these two lesions.

## SUMMARY

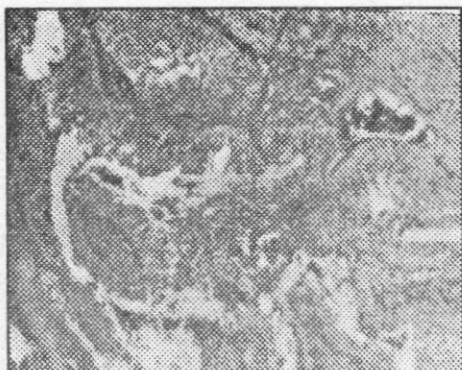
120 patients were the material of this study. 50 patients with carcinoma of the stroma of the bladder tumours

by carcinoma insitu accompanied by denuding cystitis and cystitis due to other aetiological factors. it is concluded that histopathological examination of the stroma of the bladder tumours improves diagnostic accuracy.

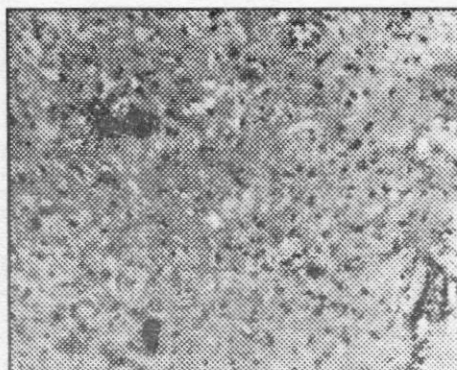
**Table (1) : Density and pattern of reticulin fibres and Alcian blue staining of the stroma.**

	Reticulin Fibres				
	Dense	Scanty	Dense net work	Negative	Positive
Papillary carcinoma	18 / 20	2 / 50	46 / 50	50 / 50	0 / 50
Carcinoma insitu	2 / 50	48 / 50	30 / 30	4 / 20	16 / 20
Benign cystitis	4 / 50	2 / 50	46 / 50	50 / 50	0 / 50

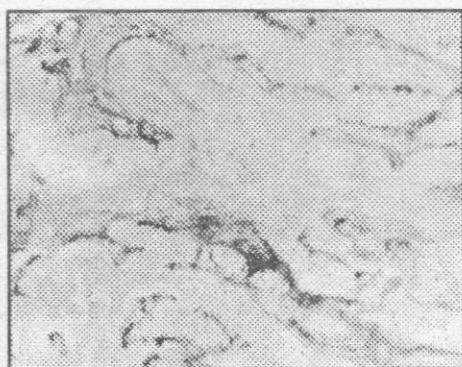
30 cases of carcinoma insitu were stained with (AB).



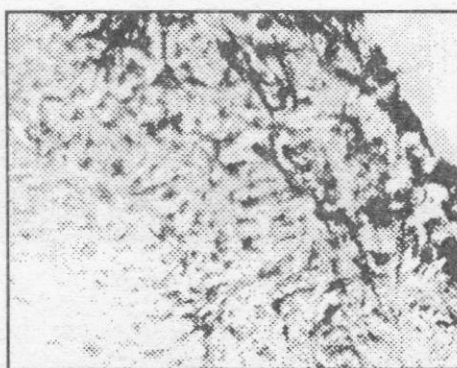
**Fig . 1 :** Papillary transitional cell carcinoma with dilated vessels in the stroma (Hx. and E. X 40).



**Fig. 3 :** Carcinoma insitu of bladder mucosa with partial denudation. (Hx. & E. x 40).



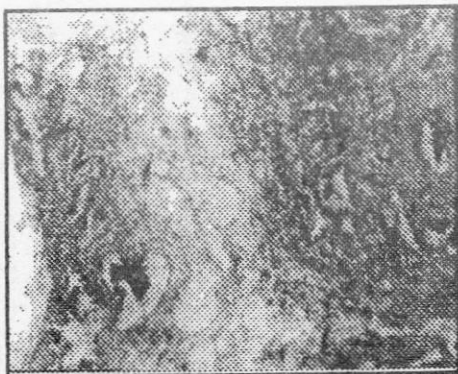
**Fig. 2 :** Scanty fibres in the papillary stroma of the same case (Gomori's stain x 40).



**Fig. 4 :** Dense reticular pattern of fibres in the subepithelial stroma of the same case (Gomori's stain x 40).

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Fig. 5 : Papillary carcinoma with positive Alcian blue stain of the stroma x 100).



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## الملخص العربى

### دراسة لخصائص النسيج الضام فى حالات الأورام الخبيثة والالتهابات التقرحية للمثانة

أجريت هذه الدراسة على ١٢٠ حالة منها ٥٠ حالة سرطان غير نافذ، ٢٠ حالة سرطان حلمى نافذ بالإضافة إلى ٥٠ حالة التهاب تقرحى لأسباب مختلفة، وكان هدف هذه الدراسة بحث امكانية استخدام خصائص النسيج الضام فى التفرقة بين حالات الالتهاب التقرحى وحالات السرطان وكذلك التفرقة بين السرطان الحلمى والتعلم الكاذب فى حالات السرطان الغير نافذ.

وقد تبين من البحث أنه لاتوجد خصائص مميزة لكل من السرطان الغير نافذ والالتهاب التفرجى، فى حين وجدت خصائص مميزة ممكن بها التفرقة بين السرطان الحلمى والتعلم الكاذب للسرطان الغير نافذ مما يزيد من كفاءة التشخيص الباثولوجى. وبالتالي اعطاء فرصة أفضل لاختيار نوع العلاج المناسب فى كل من الحالتين.



