

VERRUCOSE SQUAMOUS CARCINOMA OF BLADDER

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ABSTRACT—The clinical and pathologic features of 22 cases of verrucose squamous carcinoma of the bladder are presented. This tumor is a rare but distinct variant of squamous carcinoma and on gross examination has a warty keratotic appearance with a pushing rather than infiltrative deep margin. Pathologically it is a low-grade, low-stage tumor, with no tendency for invasion or metastasis. Radical cystectomy is the treatment of choice, since a firm preoperative pathologic diagnosis is difficult to establish.

Verrucose carcinoma is a well-distinct variant of squamous cell carcinoma. It was first described by Ackerman in 1948.¹ He emphasized the predilection of this tumor for the oral cavity, its warty appearance, slow-growing rate, and low incidence of lymph node metastasis.

In a series of 105 cases reviewed by Kraus and Perez-Mesa in 1966,² 77 occurred in the oral cavity, 12 in the larynx, 4 in the nasal fossa, 8 in the penis, 1 each in the vagina, vulva, scrotum, and perineum.

In 1961 El Sebai³ first reported this tumor in the bladder of bilharzial patients. He described it grossly as a "fibrillary" tumor because of its peculiar filiform keratotic appearance almost resembling a tuft of white hair.

We present the particular clinical and pathologic features of verrucose carcinoma of the bilharzial bladder and compare it with other squamous carcinoma.

Material

The clinical and pathologic records of 655 cases treated with radical cystectomy for bladder carcinoma between 1968 and 1973 at the Cancer Institute of Cairo, and at the department of urology, Mansoura University Hospital, were reviewed. All these patients gave a history of previous bilharzial cystitis.

In our review of the pathologic material we adhered to the diagnostic criteria of verrucose carcinoma as established by Ackerman,¹ and later emphasized by Krauss and Perez-Mesa.² These criteria include the following: (1) the tumor should be exophytic with multiple filiform or warty surface projections; (2) it should be composed of thick folds of well-differentiated squamous epithelium both in its superficial and deep parts; (3) it should lack the histologic features of anaplasia; and (4) the advancing margin should be expanding rather than infiltrating.

Results

Squamous carcinoma accounted for 483 tumors (73.7 per cent) of the total 655 cases studied. Twenty-two instances of verrucose carcinoma were observed. A relative frequency of 3.4 per cent of the total series and 4.6 per cent of the squamous carcinoma cases.

The mean age of patients with verrucose carcinoma was 45.2 years and ranged between thirty to sixty-eight years. In other cases of squamous carcinoma, the mean age was 46.1 years and ranged from twenty-two to seventy-three years. In verrucose carcinoma 19 patients were men and three women, a ratio of 6 to 1, as compared with a sex ratio of 4 to 1 in other cases of squamous carcinoma.

TABLE I. Comparison of grade, stage, and lymph node metastases in verrucose and other squamous carcinoma*

	Verrucose Carcinoma		Other Squamous Carcinoma		Total Number†
	Number	Per Cent	Number	Per Cent	
Grade					
1	18	94.7	177	38.1	195
2	1	5.3	173	37.3	174
3	114	24.6	114
TOTAL	19		464		483
Stage					
P1	2	10.5	9	1.9	11
P2	7	36.8	52	11.2	59
P3	9	47.4	345	74.4	354
P4	1	5.3	58	12.5	69
TOTAL	19		464		483
Lymph node metastases					
Positive	89	19.2	89 (19.2)
Negative	19	100	375	80.8	394 (8.16)
TOTAL	19		464		483

*Three cases with focal verrucose changes were excluded.

†Numbers in parentheses represent per cent.

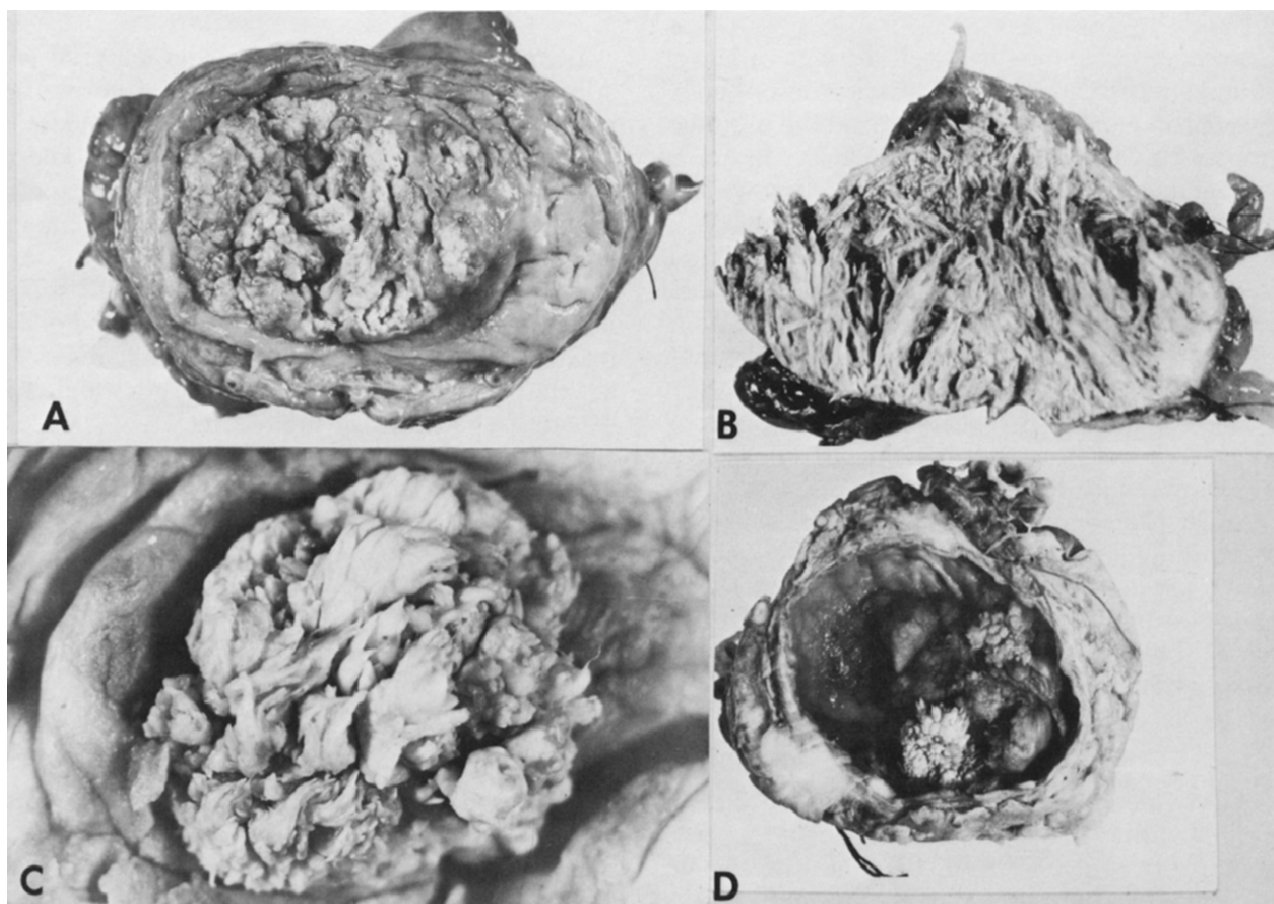


FIGURE 1. (A) Multiple mammillated verrucose carcinoma; (B) advanced filiform verrucose carcinoma filling bladder; (C) mixed verrucose carcinoma showing both mammillated and filiform appearance; (D) fibrillary tumor associated with ulcerative carcinoma.

The clinical presentation of patients with verrucose carcinoma was essentially similar to those of other patients with carcinoma of the bilharzial bladder, namely, exaggerated cystitis symptoms with painful micturition and frequency.⁴ Hematuria was an unusual symptom. All patients gave a history of passing white encrusted fragments of tissue during urination. Three patients had acute retention of urine; the internal urinary meatus was obstructed by loose keratotic fragments of tumor.

Grossly, verrucose carcinoma appeared as an exophytic warty tumor, white in color, and firm in consistency. The surface projections had various morphologic characteristics. Some were mammillated with short broad surface projections (Fig. 1A). Others were filiform with thin, elongated needle-like appearance (Fig. 1B). Tumors showing both patterns were also encountered (Fig. 1C). In 3 cases the verrucose tumor presented as a focal change in an otherwise ordinary nodular infiltrating squamous carcinoma (Fig. 1D).

Histopathologically, verrucose tumors were extremely well-differentiated hyperkeratotic squamous carcinoma with elongated surface projections and downgrowths of club-shaped finger-like processes (Figs. 2A and B). The deep advancing margin had a pushing rather than an infiltrating border. In this area the tumor was arranged in large bulbous masses of tightly coherent squamous cells, with abundant cytoplasm and uniform nuclei, lacking the cytologic features of anaplasia (Fig. 2C). The stroma at the deep margin showed marked chronic inflammatory reaction, as well as bilharzia ova.

The various pathologic features of the verrucose tumors (grade, stage, and frequency of lymph node involvement) were compared with those of other squamous carcinoma (Table I). The 3 cases of focal verrucose changes were excluded since the biologic behavior was probably determined by the anaplastic component of the tumor. Verrucose carcinoma was an essentially low-grade, low-stage tumor. Moreover, all 19 cases of true verrucose carcinoma were not associated with regional lymph node metastasis.

Comment

Verrucose carcinoma of the bilharzial bladder is a relatively unusual special variant of squamous cell carcinoma. Its recognition is important for therapeutic and prognostic reasons.

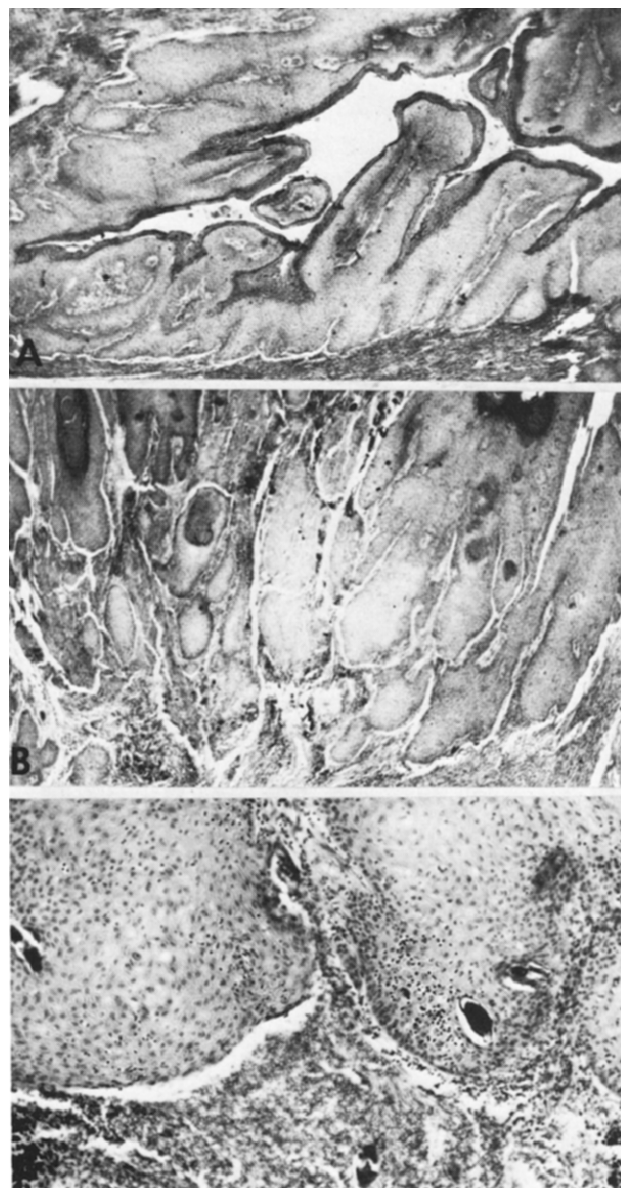


FIGURE 2. Verrucose carcinoma showing (A) hyperkeratotic surface projections, (B) downgrowths of squamous epithelium with bulbous ends, and (C) well-differentiated squamous cells, pushing rather than infiltrating stroma which contain ova and inflammatory cells.

Chronic irritation appears to be an important etiologic factor. There is an extremely high association between tobacco chewing and lesions in the oral cavity.² Penile lesions occur more frequently on the uncircumcised penis.⁵ In the bladder verrucose carcinoma arises from areas of squamous metaplasia of the urothelium. Such metaplastic changes often occur following prolonged chronic irritation secondary to bilharzial cystitis.^{3,6}

This type of tumor constituted 3.4 per cent of all carcinoma of the bladder, and 4.6 per cent of

the squamous variety in this series. Its biologic behavior is characteristic, being a low-grade tumor, without a tendency for infiltration or metastasis. In this respect, it is similar to verrucose tumors reported in other locations.^{1,2,5,7,8}

Verrucose carcinoma of the bladder should be distinguished pathologically from other bladder tumors with warty surfaces, namely, papillary transitional carcinoma and other types of squamous carcinoma. This is easily accomplished by adhering to the criteria established by Ackerman¹ and Kraus *et al.*² Verrucose carcinoma is composed of well-differentiated keratinizing squamous epithelium throughout the neoplasm. The base of the tumor shows club-shaped, avascular downgrowths, with an expanding rather than infiltrating border. Papillary carcinoma of the bladder is a transitional-cell tumor with well-developed villous structure and vascular central core. Ordinary squamous carcinoma of the bladder may show a warty surface, but careful examination of the base of the tumor will reveal areas of cytologic anaplasia as well as stromal infiltration by small groups of malignant cells.

The treatment of verrucose carcinoma of the bladder is essentially surgical. The use of radiation therapy is not recommended, since it is ineffective and may lead to rapid anaplastic transformation of some verrucose tumors.^{2,9} In spite of the very low incidence of lymph node involvement, radical cystectomy is the procedure of choice because of the difficulty in establishing a

firm preoperative diagnosis. The only way to confirm diagnosis is to obtain a biopsy specimen from the deep margin of the tumor at several sites, a procedure which carries the risk of bladder perforation.

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