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Cancer of the Bilharzial Bladder

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Summary. Based on the experience from 3212 patients with Bilharzial bladder carcinoma a review is given of the pathology, clinical course, treatment and prognosis of the disease.

Key words: Bilharzia - Schistosomiasis - Urinary bladder cancer.

INCIDENCE

Cancer of the Bilharzial bladder is the most common cancer in Egypt, accounting for about 20-25% of all cases in both sexes and approximately 38% in males. 3212 cases were reported to the Cairo Cancer Institute over a period of 5 years (1970-1974), representing 27.6% of all cases. It is also found in certain districts of Iraq, Yemen, Saudi Arabia, Sudan and several other African countries, though the incidence is less than in Egypt. This could be attributed to the lower degree of endemicity, intensity and persistence of bilharziasis in these regions.

Cancer of the bilharzial bladder affects males five times more frequently than females, primarily because males are exposed to bilharziasis as they work in the fields. The usual age at diagnosis is the fifth decade, followed by the sixth, fourth, third and seventh. This younger age incidence is remarkable compared to the usual age at diagnosis of non-bilharzial bladder cancer.

PATHOLOGY

Cancer of the bilharzial bladder differs from non-bilharzial bladder cancer in many significant areas: age at diagnosis, site, tumour type, degree of lymph node involvement and clinical manifestations.

Metaplastic, hyperplastic and dysplastic epithelial changes may occur in the bladder mucosa. Squamous cell metaplasia is particularly common. Columnar cell metaplasia, frequently associated with mucus formation, in less common. All grades of dysplasia, including carcinoma-in-situ and ultimately invasive cancer, may develop.

These epithelial changes appear many years before malignant transformation and are generally well manifested in the surrounding mucosa of most established lesions, especially those of the squamous cell variety.

Tumours may arise in the vault, anterior, lateral or posterior walls of the bladder. A nodular, fungating, infiltrating tumour, which may attain considerable size, is the most common type of bilharzial bladder cancer, accounting for 80 percent of lesions. A verrucous variety that may present as a fibrillary, filamentous or mammilated growth or as a mixed lesion, comprises another five percent of cancers. Tumours of the trigone are rare (2%), but the area may be involved by direct spread of advanced disease. Papillary lesions are also rare (2%), in contradistinction to non-bilharzial cancer. Malignant penetrating ulcer and diffuse, infiltrating growths account for the remainder of lesions. Multiple tumours are present in about 25% of patients.

Squamous cell tumours predominate (75%), a characteristic feature of bilharzial bladder cancer. The transitional cell variety comprises about 20% of cancers and adenocarcinoma approximately 5%. Leiomyosarcoma and other sarcomas are rarely encountered. The grade of malignancy is usually low (80%). Cellular differentiation and excessive keratinization are very marked.

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Most patients present with advanced disease, T3 and T4 clinically, and P3 and P4 pathologically. At the time of surgery, deep muscle invasion is almost always present and extravesical infiltration is common. Lymph node involvement, generally confined to the pelvis, is found in 27% of patients. Blood stream dissemination is unusual. Compared to non-bilharzial bladder cancer, the degree of lymphatic and blood stream involvement is relatively limited, despite the depth of invasion and size of the lesion at presentation. The low grade of malignancy, the associated vesical, perivesical and perivascular fibrosis and, probably, an as yet unknown immunological mechanism, may explain this phenomenon.

CLINICAL ASPECTS

Various manifestations of cystitis are the main clinical feature in all stages of bilharzial bladder cancer, unlike the classic picture of gross haematuria encountered with non-bilharzial bladder cancer. This may be attributed to the solid nature and keratinized surface of most tumours, compared to the soft, friable, vascular, papillary lesions that characterize non-bilharzial neoplasms. Microscopic haematuria is always present, however, and macroscopic haematuria is an occasional complaint. The passage of whitish shreds of keratinized, fibrinous and necrotic tissue is common. Clot retention may sometimes occur. A white clot, formed of keratin, fibrin and necrotic tissue, is frequently the result of a verrucous, low-grade squamous cell carcinoma. A red clot, on the other hand, is usually a complication of a highly malignant anaplastic lesion. Most patients present with a palpable mass, which is easily felt without anaesthesia.

The calcified outline of the urinary bladder, the lower ends of the ureters and occasionally the seminal vesicles may be demonstrated on plain radiography. Interruption of the calcified outline of the urinary bladder and the presence of irregular finger-print opacities due to calcific deposits on the tumour surface may also be shown on plain X-ray films.

Extensive cytological studies of the urine of patients with bilharzial cystitis and established cancer have been carried on at the Cairo Cancer Institute for the last five years. Cytology has not yet been used for mass screening of the population in endemic areas, but some projects have recently been started.

TREATMENT

Radiotherapy

Many modalities and techniques of radiotherapy have been attempted in the past 40 years, but the results so far are generally disappointing. Because of the tumour's advanced stage at diagnosis, the presence of extensive fibrosis and resistant pyogenic infection, long-term survival with radiotherapy as the sole therapeutic modality has not been achieved, although limited palliation is sometimes obtained.

Postoperative irradiation after limited resection is almost always followed by local and/or metastatic recurrence, as well as the typical complications of bladder fibrosis, contracture and telangiectasia. Preoperative cobalt irradiation using limited fractionated dosages (2500-4000 rads) is now under trial at the Cairo Cancer Institute. Available data suggest that this method may be of some value in patients with anaplastic lesions, T4 disease, or when conservative surgery has been recently attempted. Preoperative radiotherapy with a haemostatic limited dosage is usually beneficial in patients with persistent, severe haematuria.

Surgery

Endoscopy and conservative surgery have little or no place in the management of bilharzial bladder cancer, because of its advanced stage, large size, multiplicity of tumours and the frequency of associated, generalised precancerous lesions involving the bladder mucosa.

Segmental resection has been, and still is, practised by some urologists. However, only limited palliation is offered and local and lymphatic recurrences usually follow.

Radical cystectomy (anterior pelvic exenteration) is still the only modality that can provide long-term survival. Pelvic lymph nodes are widely and thoroughly dissected, and removed with the excised organs. Total destruction of one kidney, limited invasion of the small intestine, colon, uterus, vagina or muscles of the abdominal wall, and superficial adhesion to the back of the pubic bone are not contraindications to radical surgery. Wider resections are then carried out. Invasion of the lower part of the rectum is usually associated with diffuse infiltration of the pelvic cellular tissue, and the results of total pelvic exenteration have been extremely disappointing.

The ureters are implanted into an isolated ileal or colonic segment to form a conduit. This technique has proven to be the most satisfactory, provided that the patient is able to manage the conduit. Some patients, especially those who come from outlying districts and whose social and economic conditions are very low, are faced with considerable inconveniences and difficulties, such as regularly obtaining collecting bags. Under these circumstances a rectal bladder with a terminal colostomy, or rectal

bladder combined with a perineal, transanal colostomy have proven, over the last 10 years, to be convenient. The mobilised terminal segment of the colon is brought out through a space dissected between the internal and external anal sphincters, and fixed to the perianal skin. Provided that little damage is done to the anal musculature and that the blood supply of the mobilised colonic segment is adequate, satisfactory control of both urine and stools is obtained, especially in younger men who represent the vast majority of patients.

Our experience with more reconstructive techniques, such as subtotal cystectomy, ileo-or colocystoplasty, total cystectomy, cystoprostatectomy and uretero-ileo or colo-urethral anastomoses has been less favourable. Late renal damage is a common complication, generally resulting from stricture formation at one or some of the multiple anastomotic sites or from persistent reflux.

However, radical cystectomy is associated with high morbidity and mortality, which may be prohibitive especially in the elderly, and should be confined to highly specialised centres; our experience during the last 30 years clearly demonstrates this fact. In the Cairo Cancer Institute the average operative mortality rate is about 10%. The figure is below five percent when patients with similar stages and conditions are operated on by the more senior staff. This represents a great improvement as 25 years ago the figure was about 20%. Postoperative peritonitis and intestinal obstruction, primarily from leakage at anastomotic sites and spreading infection from the pelvis are the main causes of mortality. Cardiovascular and pulmonary complications are rather uncommon, since most patients are younger than those suffering from non-bilharzial bladder cancer.

Recurrences

Recurrence after surgery usually occurs locally in the pelvis, and is frequently manifested during the first or second postoperative years. Metastases in the pelvic bones, lungs and liver, respectively, may develop. Irradiation may offer marked palliation for bony lesions. In our experience, postoperative irradiation to reduce the incidence of local recurrence has been disappointing. Nevertheless, trials are now underway employing preoperative irradiation and radical surgery, followed by external or interstitial irradiation to localized fields of suspected residual tumour tissue. It is still too early to assess the results.

The value of various chemotherapeutic agents is also very limited, although short periods of palliation are occasionally obtained.

Table 1. Cancer of the bilharzial bladder treated by Anterior Pelvic Exenteration 5 year survival rates

	Cases	5 yr survival	%
1949-1958	376	98	26%
1959-1969	631	177	28%
1949-1969	1007	275	27.3%

Long-Term Survival

The overall five-year survival rate for different groups of patients subjected to radical surgery between 1949 and 1969 (1,007 patients) was 27.3% (Table 1). The five-year survival rate was 35% when the lymph nodes were clear, and 18% when pelvic lymph nodes were involved but involvement was limited to the obturator and/or the external iliac nodes on one side. When other groups were involved, there was no long-term survival.

The five year survival rate was 10-15% when loops of small intestine and/or colon were locally invaded and resected, and when the lesion was superficially adherent to the back of the pubic bone, which was partly removed.

There was no long-term survival after extensive surgery when muscles of the pelvic floor were invaded and the prostate and/or the lower part of rectum were deeply infiltrated.

REFERENCES

1. Abdel-Tawab, G. A., Kelada, F. S., Kelada, N. L., Abdel-Daim, H., Makhyoun, N.: Studies on the aetiology of bilharzial carcinoma of the urinary bladder. V. Excretion of tryptophan metabolites in the urine. International Journal of Cancer 1, 377 (1966)
2. Aboul Nasr, A. L., Gazayerli, M. E., Fawzi, R. M., Elsebai, I.: Epidemiology and pathology of cancer of the bladder in Egypt. Acta Universitatis International Cancer 18, 528 (1962)
3. Anthony, P. P.: Carcinoma of the urinary tract and urinary retention in Uganda. British Journal of Urology 46, 201 (1974)
4. El-Boulkany, M. N., Ghoneim, M. A., El-Morsey, B. A., Nasr, S. M.: Carcinoma of the bilharzial bladder. Diagnostic value of urine cytology. Urology 3, 319 (1974)

5. El-Boulkany, M. N., Ghoneim, M. A., Mansour, M. A.: Carcinoma of the bilharzial bladder in Egypt. Clinical and Pathological features. British Journal of Urology 44, 561 (1972)
6. El Sebai, L.: Abstracts. Tenth International Cancer Congress, Houston, Texas 1970
7. El Sebai, I.: Gynecological Urology. Springfield, Illinois: Charles C. Thomas 1960
8. El Sebai, I.: Proceeding of the First Symposium on Bilharziasis 1962
9. El Sebai, I., Sherif, M., El Bolkainy, M. N, Mansour, M. A., Ghoneim, M. A.: Verrucous squamous carcinoma of the bladder. Urology 4, 407 (1974)
10. Gelfand, M., Weinberg, R. W., Castle, W. M.: Relation between carcinoma of the bladder and infestation with Schistosoma Haematobium. Lancet I, 1249 (1967)
11. Ishak, L. G., Le Golvan, P. C., Elsebai, I.: Malignant bladder tumours associated with bilharziasis. A. gross and microscopic study. In: Mostofi, F. K. (ed): Bilharziasis Monograph of the International academy of Pathology. Berlin, Heidelberg, New York: Springer 1967
12. Khafagy, M. M. et al.: Carcinoma of the urinary bladder. A study of the associated mucosal lesions in 86 cases. Cancer 30, 150 (1972)
13. Makar, N.: Urological aspects of bilharziasis in Egypt Cairo. S. Op. Press 1955
14. Mansour, M. A., el-Boulkany, M. N.: Radical cystectomy for carcinoma of the bilharzial bladder. British Journal of Urology 44, 461 (1972)

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