Long-term follow-up of advanced bladder adenocarcinoma

Seguimento a longo prazo do adenocarcinoma avançado da bexiga

Karen Korkes[1], Marcela Presti[2], Fernando Korkes[3], Marilia Germanos Castro[4]

ABSTRACT

Objective: to evaluate patients treated with primary bladder adenocarcinoma at our institution. **Methods:** A review of 30 patients diagnosed with bladder adenocarcinoma at a single institution from 1994 of 2005 was undertaken. Cases of primary bladder adenocarcinoma were retrospectively evaluated. **Results:** Out of 490 patients with bladder carcinoma, 30 had bladder adenocarcinoma: 22 metastatic tumors, eight (1.6%) primary adenocarcinoma. Of these, three (0.6%) were primary non-urachal and five (1.0%) were urachal adenocarcinoma. All patients were men with mean age of 55.8 years (range 37-83). Dysuria and hematuria were the main symptoms reported. Of the total, four patients had cancer-related mortality. **Conclusion:** Primary bladder adenocarcinoma is a rare neoplasm, observed in 1.6% patients with bladder malignancies. Late diagnosis limits therapeutic possibilities. Partial cystectomy seems to have unsatisfactory results and radical cystectomy, although remains as the gold standard, have no proven efficacy. New methods of adjuvant treatment must be studied to improve treatment outcomes, as high mortality is observed despite treatment.

Keywords: Urinary bladder; Urinary bladder neoplasms; Adenocarcinoma/therapy; Adenocarcinoma/mortality

RESUMO

Objetivo: avaliar pacientes com adenocarcinoma primário da bexiga tratados em uma instituição. **Métodos:** foi realizada uma revisão em 30 pacientes diagnosticados com adenocarcinoma da bexiga, em uma única instituição, no período de 1994 a 2005. Os casos de adenocarcinoma primário da bexiga foram avaliados retrospectivamente. **Resultados:** dos 490 pacientes tratados com carcinoma da bexiga, 30 tinham adenocarcinoma da bexiga: 22 eram tumores metastáticos, oito (1,6%) tinham adenocarcinoma primário. Destes, três (0,6%) eram não-úraco primários e cinco (1,0%) do úraco. Todos os pacientes eram homens com média de idade de 55,8 anos (entre 37-83). Disúria e hematúria foram os sintomas predominantes. Do total, quatro pacientes tiveram mortalidade relacionada ao câncer. **Conclusões:** adenocarcinoma da bexiga é um tumor raro, observado em 1,6% dos pacientes com neoplasias da bexiga. O diagnóstico tardio limita as possibilidades terapêuticas. A cistectomia parcial parece ter resultados pouco satisfatórios e a cistectomia radical, embora permaneça o padrão ouro, não provou eficácia. Novos métodos de tratamentos adjuvantes devem ser estudados para melhorar os resultados terapêuticos, pois alta mortalidade é observada mesmo após o tratamento.

Descritores: Bexiga urinária; Neoplasias da bexiga urinária; Adenocarcinoma/terapia; Adenocarcinoma/mortalidade

INTRODUCTION

Urothelial carcinoma represents approximately 90% of all vesical neoplasms. Other neoplasms, such as squamous cell carcinoma, adenocarcinoma and small cells carcinoma are less frequent[1-6].

Primary bladder adenocarcinoma is an uncommon vesical neoplasm presenting itself histologically as a pure glandular phenotype[7] and accounts for 0.5 to 2% of bladder malignancies[7-9]. It can be originated from the bladder urothelium or from an urachal remnant[8-9]. Since the histological subtypes are identical to adenocarcinomas originated in other organs, it is often difficult to distinguish between primary or secondary bladder adenocarcinomas.

There are only a few small series or case reports of bladder adenocarcinoma described in the literature, and no Brazilian series to the best of our knowledge.

OBJECTIVE

The aim of the present study was to report our experience treating eight additional cases of bladder adenocarcinoma in Brazil.

Study carried out at Faculdade de Ciências Médicas da Santa Casa de São Paulo – FCMSCSP, São Paulo (SP), Brazil.

[1] Medical student of Faculdade de Ciências Médicas da Santa Casa de São Paulo – FCMSCSP, São Paulo (SP), Brazil.

[2] Medical student of Faculdade de Ciências Médicas da Santa Casa de São Paulo – FCMSCSP, São Paulo (SP), Brazil.

[3] Assistant professor of the Department of Urology of Faculdade de Medicina do ABC – FMABC, Santo André (SP), Brazil.

[4] Pathologist; Assistant professor of Pathology, Faculdade de Ciências Médicas da Santa Casa de São Paulo – FCMSCSP, São Paulo (SP), Brazil.

Corresponding author: Fernando Korkes – Rua Pirapora, 167 – Vila Mariana – CEP 04008-060 – São Paulo (SP), Brasil – Tel.: 11 3884-2233 – e-mail: fkorkes@terra.com.br

Received on: June 6, 2009 – Accepted on: Oct 14, 2009

METHODS

We have retrospectively evaluated 30 patients treated with bladder adenocarcinoma between 1994 and 2005 at our institution. All files were reviewed, and patients with primary bladder adenocarcinoma were included in the present study. All slides were reviewed by the same uropathologist, and additional immunohistochemical studies were performed as needed.

RESULTS

During the studied period, 490 patients with bladder carcinoma were treated at our institution, 6.1% (n = 30) of which with adenocarcinoma. Among patients with bladder adenocarcinoma, 22 (4.5%) had metastatic bladder adenocarcinoma and 8 (1.6%) had primary bladder adenocarcinoma; 3 (0.6%) being non-urachal and 5 (1.0%) urachal (Table 1). All patients with primary bladder adenocarcinoma were male (mean age = 55.8 years, Table 2). The most frequent symptoms were dysuria and hematuria (Figure 1).

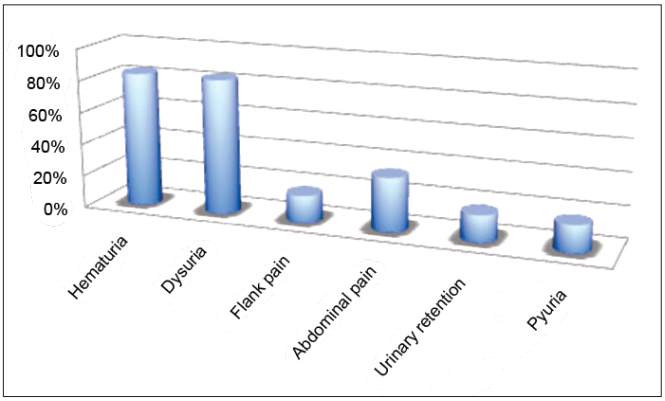

Figure 1. Main symptoms of patients with primary bladder adenocarcinoma (n = 8)

Fifty percent of patients underwent radical cystectomy with heterotopic diversion or ileal conduit. One patient required an abdominal wall reconstruction. Three patients underwent partial cystectomy (Figure 2). Pelvic lymphadenectomy was performed in all cases.

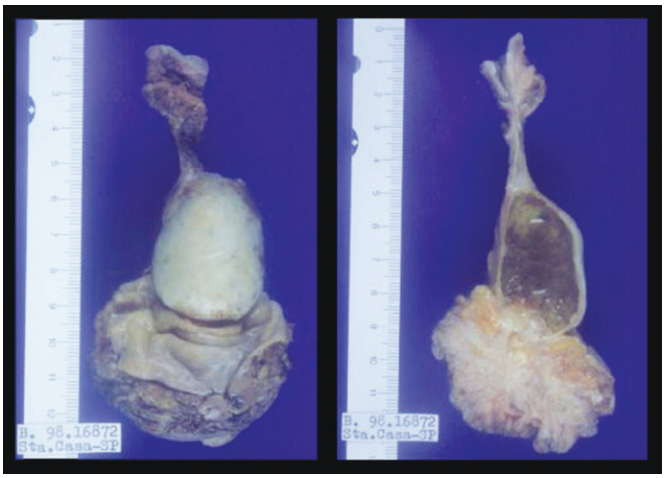

Figure 2. Macroscopic view of urachal adenocarcinoma

One man had a conservative management as advanced tumor stage and poor clinical condition deferred surgical treatment. He died 30 days after the

Table 1. Distribution of bladder carcinoma according to pathological diagnosis and body region

Pathological diagnosis and body region	n	(%)	Mean age (mean ± SD)
Primary bladder adenocarcinoma		1.2	55.8 ± 15.7
Urachal	5	1.0	49.4 ± 11.1
Non-urachal	3	0.6	66.7 ± 18.6
Secondary bladder adenocarcinoma		4.4	60.9 ± 12.3
Prostate	3	0.6	70.0 ± 7.2
Uterus	4	0.8	60.5 ± 15.0
Colon	9	1.8	61.0 ± 14.4
Vagina	1	0.2	55.7 ± 0.0
Undiferentiated	5	1.0	56.6 ± 7.1
Other bladder carcinomas (urothelial and epidermoid)	460	94.2	68.7 ± 12.4

Table 2. Characteristics of patients with primary bladder adenocarcinoma

Histological subtypes	Gender	Age (years)	Stage T / N / M	Surgery	Postoperative survivel (months)	Outcome
NU	M	47	4b / 0 / 0	Radical cystectomy	70.2	Death
NU	M	70	X / X / X	Radical cystectomy	71.7	Alive
NU	M	83	3b / 1 / X	Radical cystectomy	2.0	Death
U	M	48	3 / 0 / X	Partial cystectomy	49.0	Death
U	M	51	3b / 0 / X	Partial cystectomy	2.6	Death
U	M	44	3 / X / X	Partial cystectomy	7.3	Death
U	M	37	2 / 0 / 0	Radical cystectomy	96.0	Alive
U	M	67	4 / x / 1	-	0.9	Death

NU: Non-urachal; U: Urachal.

initial diagnosis. Follow-up information was available for seven patients. The overall 3-year survival was of 25.0% (n = 2) and disease-specific mortality rate was 50.0% (n = 4) (Table 2).

DISCUSSION

Primary bladder adenocarcinoma is a rare disease, with little information about risk factors, early diagnosis and treatment. Distinguishing primary and metastatic disease is also difficult sometimes, as the immunophenotype of these tumours is identical to that of other adenocarcinomas. The presence of adenocarcinoma *in situ* adjacent to the invasive areas helps diagnosing primary bladder neoplasm[6].

Our study has some important findings. For instance, we could establish the prevalence of bladder adenocarcinoma in our population of patients, indeed quite large. Primary bladder adenocarcinomas represented 1.6% of all vesical neoplasms (non-urachal: 0.6%; urachal: 1.0%). These results are similar to previously reported prevalences varying from 0.5 to 2.0%[8-9]. Mean patient age at diagnosis was also similar to previous reports (55.8 years) occurring at younger ages than urothelial neoplasms[5,10-11]. These findings suggest that no particular or environmental risk factors might be associated with development of these neoplasms in the population studied.

Second, hematuria and dysuria were the most frequent symptoms. Previous studies described hematuria as one of the most important symptoms[8-9]. However, dysuria was not previously reported as a common symptom, occurring in less than 7.0% of the cases described in the literature[8-9]. In the present series, all patients had locally advanced disease, hypothesizing that these symptoms might occur lately in disease progression.

Third, many treatment modalities have been applied to patients with primary bladder adenocarcinoma. However, since much information is based on case reports, therapeutic strategies are still uncertain[10]. Some authors advocated partial cystectomy for patients with disease in movable parts of the bladder. However, safety and oncological outcomes of partial *versus* radical cystectomy is not consensual yet. A five-year survival following radical cystectomy was reported varying from zero to 80%[8-9]. In our series, partial *versus* radical cystectomy was performed selectively. The five-year disease specific mortality was of 50.0%. Although we have treated a limited number of patients, these results suggest low efficacy of surgery as a single treatment for advanced stage patients. Also, patients who were cured had been treated with radical cistectomy. Nevertheless, these patients had been diagnosed at an earlier disease stage than the others. Additional neoadjuvant or adjuvant treatments are expected to improve patient survival rates[9]. As recently postulated, adjuvant treatments such as radiotherapy might bring additional survival benefits[8], and should be further evaluated.

Our study has some limitations. First, the limited number of patients precludes more consistent conclusions about treatment modalities. Second, adjuvant therapies were not performed in these patients, due to institutional limitations by the time they were treated. However, the retrospective evaluation of these patients allowed us to assess the results of a single modality-based treatment for patients with primary bladder adenocarcinoma, in a period of reasonable preoperative care.

CONCLUSION

Bladder adenocarcinoma is a rare neoplasm, which is lethal for most patients diagnosed at advanced stages and surgically treated. Earlier diagnosis and efficient adjuvant treatment modalities might bring some benefit, and there are expectations regarding these strategies.

REFERENCES

1. Wilson RT, Richardson LC, Kelly JJ, Kaur J, Jim MA, Lanier AP. Cancers of the urinary tract among American Indians and Alaska Natives in the United States, 1999-2004. Cancer. 2008;113(5 Suppl):1213-24.
2. Murta-Nascimento C, Schmitz-Drager BJ, Zeegers MP, Steineck G, Kogevinas M, Real FX, et al. Epidemiology of urinary bladder cancer: from tumor development to patient's death. World J Urol. 2007;25(3):285-95.
3. Korkes F, Silveira TS, Castro MG, Cuck G, Fernandes RC, Perez MD. Carcinoma of the renal pelvis and ureter. Int Braz J Urol 2006;32(6):648-53; discussion 653-5.
4. Altwein JE. [Primary prevention of bladder cancer. What's new?]. Urologe A. 2007;46(6):616-21.
5. Nieder AM, Mackinnon JA, Huang Y, Fleming LE, Koniaris LG, Lee DJ. Florida bladder cancer trends 1981 to 2004: minimal progress in decreasing advanced disease. J Urol. 2008;179(2):491-5; discussion 495.
6. Reuter VE. The pathology of bladder cancer. Urology. 2006;67(3 Suppl 1):11-7; discussion 17-8.
7. Eble J, Sauter G, Epstein J, Sesterhenn I. World Health Organization classification of tumours: pathology and genetics of tumours of the urinary system and male genital organs. Lyon: IARC Press; 2004.
8. Zaghloul MS, Nouh A, Nazmy M, Ramzy S, Zaghloul AS, Sedira MA, et al. Long-term results of primary adenocarcinoma of the urinary bladder: a report on 192 patients. Urol Oncol. 2006;24(1):13-20.
9. el-Mekresh MM, el-Baz MA, Abol-Enein H, Ghoneim MA. Primary adenocarcinoma of the urinary bladder: a report of 185 cases. Br J Urol. 1998;82(2):206-12.
10. Thomas AA, Stephenson AJ, Campbell SC, Jones JS, Hansel DE. Clinicopathologic features and utility of immunohistochemical markers in signet-ring cell adenocarcinoma of the bladder. Hum Pathol. 2008.
11. Cheng CW, Chan SF, Chan LW, Chan CK, Ng CF, Cheung HY, et al. 15-year experience on intravesical therapy of T1G3 urinary bladder cancer: a conservative approach. Jpn J Clin Oncol. 2004;34(4):202-5.