Synchronous primary malignancies of the male urogenital tract

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Abstract

The finding of prostate cancer after a cystoprostatectomy for a bladder tumour can occur in up to 70% of cases. The incidence of prostate cancer in patients with a bladder tumour is 18 times higher than in the general population; moreover, the incidence of bladder cancer in patients with prostate cancer is 19 times higher than in the general population. This association can be explained by the common embryological origin of these organs, with molecular similarities. Other similarities between these two cancers are noted. They are multifocal and may be secondary to urinary stasis. However, this association does not seem responsible for an increased risk of progression of both diseases. The prognosis is related to the extension of each cancer. The stage and grade of bladder cancer are, in terms of prognosis, greater than those of prostate cancer. Most often, this is insignificant prostate cancer. Despite this, the prostate-specific antigen test should be administered to monitor patients after cystoprostatectomy.

Introduction

Bladder cancer is the second most prevalent urologic cancer after prostate cancer.¹ It may occur alone or associated with other cancers of the urogenital tract, particularly the prostate. Several authors report a surprisingly close association between bladder and prostate cancer. Prostate cancer is incidentally found during the pathological test after a radical cystoprostatectomy (RCP) in patients without any symptoms or in patients for whom this disease was not suspected during the digital rectal examination (DRE) or the estimating laboratorial (PSA) and instrumental (prostate biopsy) tests.¹⁻³ We evaluate the frequency of incidentally found prostate cancer after RCP, its histopathological characteristics and its impact on overall survival.

Discussion

Billroth was the first to describe the phenomenon of multiple primary malignant neoplasms in the same individual.⁴ Since then, there have been several cases of double and even triple synchronous primary malignant neoplasms. Prostate and bladder cancers occur more often in elderly patients, as the incidence of malignancies increases with age.⁵ For bladder cancer, RCP is the standard and effective treatment for patients with invasive tumour. It is commonly related to a sexual and urinary dysfunction, which is why the new prostate-sparing techniques have been described, including procedures that spare the apex, the prostatic capsule, the seminal vesicle, and even the total prostate with a neurovascular bundle.⁶⁻⁸ These sparing techniques can improve urination and potency results, but are also associated with non-radical elimination if prostate cancer was not diagnosed before the operation.^{9,10} After RCP, incidental prostate cancer is diagnosed in 23% to 54% of patients.^{11,12}

Indeed, the incidence of prostate cancer in patients with bladder tumour is 18 times higher than in the general population; moreover, the incidence of bladder cancer in patients with prostate cancer is 19 times higher than in the general population.¹³ This risk varies from 2.8% to 70%.¹³⁻¹⁶ This variability can be explained by several factors, including histological techniques. The Stanford technique, with 3-mm cuts from the base to the apex of the prostate is usually performed during the radical prostatectomy (RP). The Stanford technique is highly efficient in discovering prostate cancer.¹⁷ Ruffion and colleagues found 51% of prostate cancer by making 2.5-mm cuts.¹¹ Similar results were reported by Abbas and colleagues; they made 3-mm cuts in 39 RCP patients.¹⁸ Moutzouris and colleagues identified 16 cases of prostate cancer (27%) using 5-mm slices.¹⁹ This rate increased to 42% in the series by Montironi and colleagues.²⁰ However, the rate is down to 4% in a Taiwanese study. This can be explained by the influence of the study population and the low-risk of prostate cancer in Asia.²¹

The combination of prostate and bladder cancer can be due to their common embryological origin with similarities at the molecular level.^{18,22} Indeed, Fradet has shown the involvement of three oncogenes and deletion of 3 genes suppressors (Rb, p53 and 23 nm) as possible causes for this association.²³ Also, the prostate stem cell antigen is over-expressed in the most transitional cell carcinomas and there are more genotypes of rapid N-Acetyltransferase in patients with these 2 cancers. This enzyme, known for its activation of carcinogenic amines, is higher in patients with double cancers than controls.^{23,24} Prostate and bladder cancer are also multifocal and may be secondary to urinary stasis.²⁵ The incidence of bladder cancer in a diverticulum is estimated at 10%.²⁶ Kirby and colleagues observed a reflux of urine with prostatic intra-urinary stasis in the peripheral zone of the prostate.²⁵ They concluded that carcinogens identified in the bladder may be responsible for the development of prostate cancer. Chronic inflammation and a common carcinogen in the bladder and prostate may be responsible for the concurrent cancers.²⁵⁻²⁸

Incidentally found prostate cancer is classified into 2 groups: clinically significant and clinically insignificant cancer. Prostate cancer is clinically significant when there are positive tumour margins, extraprostatic extension, a Gleason score of more than 6 or when the tumour volume is ≥ 0.5 cc. Perineural invasion is a clinically significant sign of biological malignancy and recurrence risk.²⁹⁻³¹ Most prostate cancers are considered insignificant.³² Thompson and colleagues found a 24.4% incidence of prostate cancer in patients via biopsy, despite normal digital rectal exams and prostate-specific antigen levels.³³ Revelo and colleagues found that 41% of prostate cancers are found as part of an RCP, but only 48% of these cancer are clinically significant.⁹ Montironi and colleagues studied the expression of some markers, such as size of the nucleus and nucleolus, proliferation measured by Ki67, HER2 gene amplification, HER2 protein expression, endotheline 1 and racemase in incidentally found prostate cancer and compared these results to clinically found cancer. They found that these markers are less expressed in insignificant cancers.

However, this association does not seem responsible for the increased risk of progression of both diseases.²⁰ The prognosis is related to the extension of each cancer. Konski and colleagues found that the stage and grade of bladder cancer are, in terms of prognosis, greater than those of prostate cancer.³⁴ Moutzouris and colleagues followed 16 patients with prostate cancer. They found prostate cancer recurrence in 1 patient with apical prostate cancer who recurred at the anastomosis between the neobladder and the urethra. After a mean follow-up of 39 months, 7 patients died of metastatic bladder cancer, while the patient with prostate cancer recurrence was still alive.¹⁹

Conclusion

Synchronous primary malignancies of the prostate and bladder are very common. Most often, this is insignificant prostate cancer and the prognosis is related to the extension of bladder cancer. Despite this, a prostate-specific antigen test should be administered to monitor patients after an RCP, especially in patients treated with prostate-sparing techniques.

Competing interests: Dr. Qarro, Dr. Bazine, Dr. Asseban, Dr. Najoui, Dr. Samir, Dr. Ouhibi, Dr. Beddouch, Dr. Lezrek and Dr. Alamim all declare no competing financial or personal interests.

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