Eur J Med Res (2007) 12: 212-215

PROSTATE CANCER TISSUE IS MASKED BY BICALUTAMIDE: A CASE REPORT

J. Ellinger[1], P. J. Bastian[1], K. Biermann[2], M. E. Schmidt[3], J. Textor[4], D. Bollmann[5], H. Zhou[2], S. C. Müller[1]

[1]Klinik und Poliklinik für Urologie, Universitätsklinikum Bonn, Germany
[2]Institut für Pathologie, Universitätsklinikum Bonn, Germany
[3]Medizinisches Zentrum Bonn, Bonn, Germany
[4]Abteilung für Radiologie, Gemeinschaftskrankenhaus Bonn, Bonn, Germany
[5]Institut für Pathologie Bonn-Duisdorf, Bonn, Germany

Abstract
Prostate cancer is the most common malignant tumor in men. Recently, a slightly decreased frequency of margin positivity following neoadjuvant bicalutamide treatment due to tumor shrinkage was reported. Trials investigating other anti-androgens in the past also reported lower frequencies of surgical margin positivity, but patients outcome has not improved.

In this case, local recurrence was confirmed by needle biopsy in a patient five years following radical prostatectomy for prostate adenocarcinoma. After therapy with 50 mg bicalutamide for a month, the tumour was resected. Despite of detailed histological work-up and immunohistochemistry cancer suspicious lesions were not found. We think that bicalutamide may be capable of masking prostate cancer cells.

Key words: Prostate cancer; bicalutamide

INTRODUCTION

Prostate cancer (PCA) is the most common malignancy in western countries [1]. A standard curative therapy is radical prostatectomy and achieves long-term cancer control in approximately 75% of patients. In case of recurrence, recommended treatment includes hormonal manipulation and/or radiation [2]; a common drug in non-steroidal anti-androgen hormonal ablation is bicalutamide. Herein, we describe a case of disappeared cancerous lesion following the treatment with 50mg bicalutamide daily for one month.

CASE REPORT

A 60-year-old man presented with histological confirmed, cT3 staged prostate cancer in the left lobe. The prostate specific antigen (PSA) was 25.04 ng/ml. Scintigraphy and lung x-ray were without evidence of metastasis. He underwent radical retropubic prostatectomy. A small glandular, in part cribriform prostate adenocarcinoma was seen with capsular penetration and infiltration of the left seminal vesicle; bilateral resection of the seminal vesicles was described in the surgical report (pT3b N0 R0 G2b, Gleason Score 3 + 3 = 6).

Serum PSA was 0.03 ng/ml two months postoperatively, but started to increase (0.13 ng/ml) six months postoperatively. PSA levels were continuously increasing but the patient refused additional treatment (0.23 ng/ml, 12 months; 0.39 ng/ml, 21 months; 0.85 ng/ml, 34 months; 2.15 ng/ml, 47 months, 3.85 ng/ml, 60 months postoperatively). Serum PSA was 6.36 ng/ml 62 months postoperatively and abdominal sonography showed a suspicious mass behind the urinary bladder. Magnetic resonance imaging (MRI) confirmed a 14 mm x 10 mm x 10 mm tumour at the posterior wall of the urinary bladder, 3 cm cranial the bladder neck. No additional suspicious lesions in the lower pelvic cavity were seen. A needle biopsy was performed, and a small glandular, in part cribriform tumour was detected (Gleason Score 4 + 3 = 7). Immunhistochemical staining was positive for alpha-methylacyl-CoA racemase and negative for p53 (see Fig. 1a/b). The patient started with daily intake of 50 mg bicalutamide.

One month later, he was admitted to our hospital for the resection of this suspicious lesion. With a transvesical approach a solid mass was removed in the left paramedian region behind the urinary bladder. Macroscopically, the mass resembled seminal vesicle tissue, and this astonishing finding following radical prostatectomy was confirmed by histology. Despite of serial sections, there were no signs of cancerous tissue (see Fig. 1c/d). Additionally, there were no characteristics of previous antiandrogen treatment. PSA and pancytokeratin staining were negative.

Nevertheless, we assume that the preoperative identified tumour mass was removed as serum PSA decreased (0.29 ng/ml within a period of 6 days). Serum PSA was decreasing under bicalutamide therapy (3.01 ng/ml, 2.85 ng/ml, 2.50 ng/ml, 2.23 ng/ml, 2.02 ng/ml, 2.35 ng/ml: one, two, four, six, 12 and 18 months postoperatively). 18 month following the resection of the local recurrence, the patient does not suffer from signs of metastatic disease, and MRI of the pelvis did not show any recurrent tumor.

DISCUSSION

The effect of bicalutamide on prostate histology was investigated in two studies [3, 4]: Treatment with 50

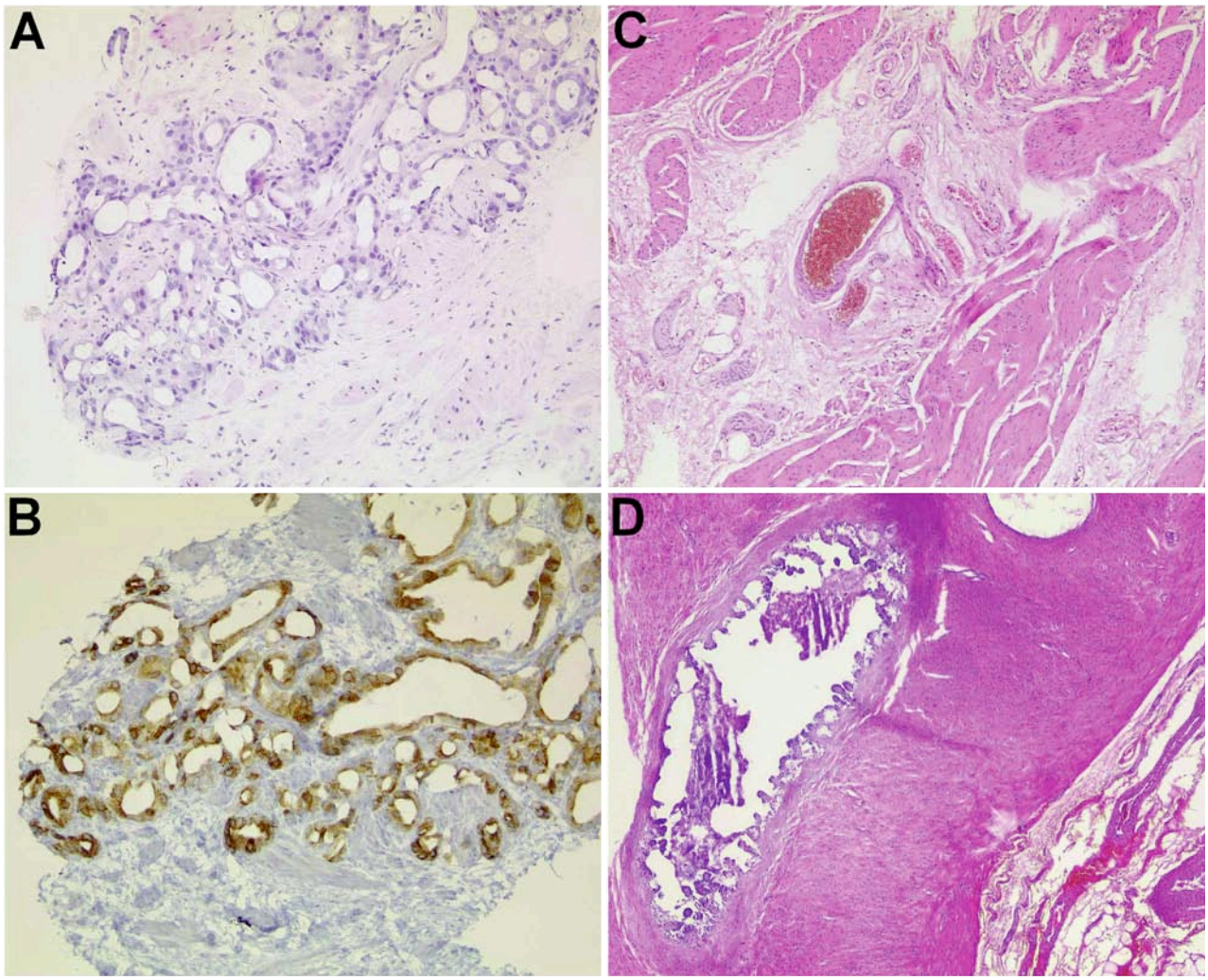

Fig. 1. A and B, needle biopsy of the suspicious mass posterior the urinary bladder. Haematoxylin and eosin (A) and immunhistochemical staining (positive for alpha-methylacyl-CoA racemase, B) shows the local recurrence of an moderately differentiated adenocarcinoma of the prostate. C and D, the surgical specimen does not show any suspicious tumor cells in haematoxylin and eosin staining. Histology demonstrates the presence of unstriated tissue from the urinary bladder and residual seminal vesicle tissue (D).

mg bicalutamide per day for 24 weeks did not induce characteristic changes in prostate histomorphology [3]. A higher dosage (150 mg daily for 3 months) induced basal cell hyperplasia, transitional cell metaplasia and atrophic epithelium [4]. Total prostate volume [3, 4], and cancer and high-grade prostate intraepithelial neoplasia volume were reduced [3]. The frequency of positive surgical margins was numerical reduced in the bicalutamide treated group [3]. It was therefore suggested that bicalutamide could be a worthwhile neoadjuvant drug. In the presented case, cancer cells were undetectable using routine (haematoxylin and eosin) or immunhistochemical (pancytokeratin, PSA) staining techniques following one month of daily 50 mg bicalutamide intake. Nevertheless, serum PSA was decreasing following surgery, implicating that cancer cells were removed.

In the past it was observed that steroidal anti-androgens such as cyproterone acetate induce distinct changes of prostate cancer morphology that make an accurate pathological diagnosis difficult [5]. Furthermore, it was suggested that clandestine tumor cells could be missed in routine haematoxylin and eosin staining, and therefore immunohistochemistry would be necessary for accurate diagnosis after hormonal blockade [6]. Additionally, tumor shrinkage following hormonal blockade complicates histological assessment [5]. Nevertheless in the study of Kollermann et al., a third of pT0 prostatectomy specimens following neoadjuvant hormonal blockade did not show any cancer cells despite of very detailed histological analysis [7]. Importantly, pT0 tumors failed to show significant prognostic differences in the risk of biochemical recurrence [8]. In general, the incidence of margin positivity following neoadjuvant hormone ablation is decreased, but disease free survival was not improved (reviewed in [9]).

This is what we believe the first report of prostate cancer tissue masked by bicalutamide treatment. The reduced observation of margin positivity following neoadjuvant bicalutamide therapy could be at least partially caused by this phenomena. In this case a ben-

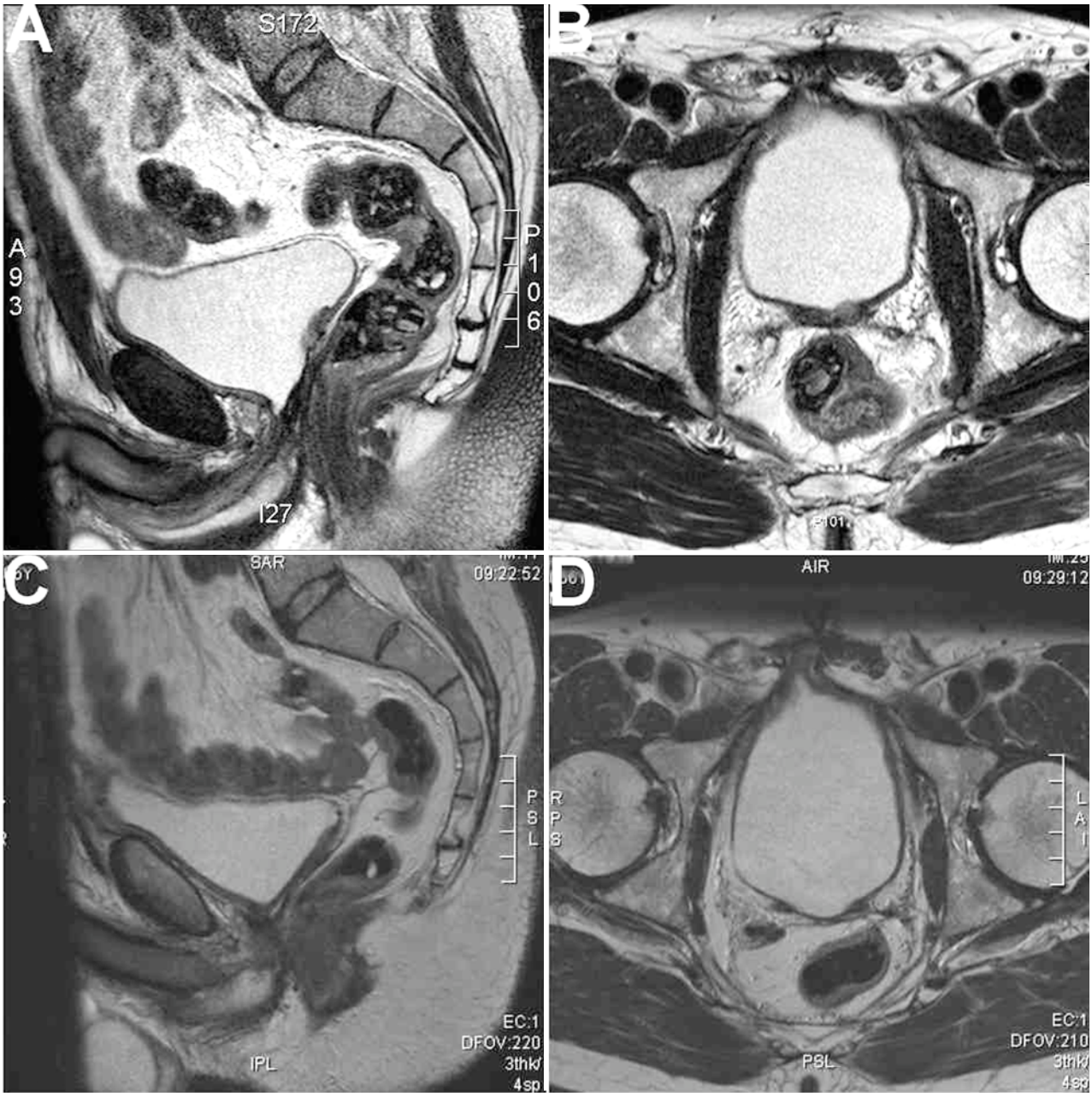

Fig. 2. A and B, Magnetic resonance imaging (MRI) five years following radical prostatectomy shows a 14 mm x 10 mm x 10 mm suspicious mass at the posterior wall of the urinary bladder 3 cm cranial the bladder neck. There are no additional suspicious lesions in the pelvis. C and D, MRI six months following the resection of the tumor. There are no signs of residual tumor.

efit for the patients' outcome would be unlikely, as studies concerning cyproterone acetate demonstrate.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. Cancer statistics, 2006. CA Cancer J Clin. 2006 56(2):106-130.
2. Aus G, Abbou CC, Bolla M, Heidenreich A, Schmid HP, van Poppel H, Wolff J, Zattoni F. EAU guidelines on prostate cancer. Eur Urol. 2005 48(4):546-551.
3. Eri LM, Svindland A, Tveter KJ. The effect of bicalutamide on prostate histology. Prostate. 2001 46(4):275-280.
4. Scattoni V, Montironi R, Mazzucchelli R, Freschi M, Nava L, Losa A, Terrone C, Scarpa RM, Montorsi F, Pappagallo G, Rigatti P. Pathological changes of high-grade prostatic intraepithelial neoplasia and prostate cancer after monotherapy with bicalutamide 150 mg. BJU Int. 2006 98(1):54-58.
6. Bullock MJ, Srigley JR, Klotz LH, Goldenberg SL. Pathologic effects of neoadjuvant cyproterone acetate on non-neoplastic prostate, prostatic intraepithelial neoplasia, and adenocarcinoma: a detailed analysis of radical prostatectomy specimens from a randomized trial. Am J Surg Pathol. 2002 26(11):1400-1413.
7. Armas OA, Aprikian AG, Melamed J, Cordon-Cardo C, Cohen DW, Erlandson R, Fair WR, Reuter VE. Clinical and pathobiological effects of neoadjuvant total androgen ablation therapy on clinically localized prostatic adenocarcinoma. Am J Surg Pathol. 1994 18(10):979-991.

8. Kollermann J, Feek U, Muller H, Kaulfuss U, Oehler U, Helpap B, Kollermann MW. Nondetected tumor (pT0) after prolonged, neoadjuvant treatment of localized prostatic carcinoma. Eur Urol. 2000 38(6):714-720.
9. Kollermann J, Hopfenmuller W, Caprano J, Budde A, Weidenfeld H, Weidenfeld M, Helpap B. Prognosis of stage pT0 after prolonged neoadjuvant endocrine therapy of prostate cancer: a matched-pair analysis. Eur Urol. 2004 45(1):42-45.
10. Scolieri MJ, Altman A, Resnick MI. Neoadjuvant hormonal ablative therapy before radical prostatectomy: a review. Is it indicated? J Urol. 2000 164(5):1465-1472.

Received: December 20, 2006 / Accepted: March 7, 2007

Address for correspondence
Dr. med. Jörg Ellinger
Klinik und Poliklinik für Urologie
Universitätsklinikum Bonn
Sigmund-Freud-Strasse 25
53105 Bonn, Germany
Phone: ++49-228-28716236
Fax: ++49-228-28719484
email: joerg.ellinger@ukb.uni-bonn.de