Case Study of the Month

Complete Response to the Combination Therapy with Androgen Blockade and Somatostatin Analogue in a Patient with Advanced Prostate Cancer: Magnetic Resonance Imaging with 1H-Spectroscopy

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1. Case history

In October 2005, a 74-yr-old man was diagnosed at prostate biopsy as having prostatic adenocarcinoma with a Gleason score 7 (4 + 3); his serum prostate-specific antigen (PSA) level was 680 ng/ml and the determination of serum chromogranin A (CgA, 121 ng/ml; normal, <90 ng/ml) suggested neuroendocrine (NE) activity. Performance status (Eastern Cooperative Oncology Group) score was 3 and the bone pain and analgesic requirement score was 3. A bone scan showed several areas of diffuse skeletal metastases (Fig. 1A). In October 2005, the patient had a magnetic resonance
1H-spectroscopic imaging (1H-MRSI) of the prostate (Fig. 2A). The 1H-MRSI showed an area of low signal intensity (1.8 cm) involving the left lobe of the prostate and infiltrating the left seminal vesicle (Fig. 2A). At spectroscopy, in this area the metabolic ratio modification was highly suggestive for neoplastic tissue (choline + creatine/citrate > 1; Fig. 2A). Considering that the patient was at first treatment and on the basis of a possible NE activation at the prostate adenocarcinoma level, he underwent (November 2005) combination therapy using complete androgen blockade (CAB; leuprorelin acetate 3.75 mg every 4 wk plus bicalutamide 50 mg daily) and a somatostatin analogue (lanreotide acetate 60 mg every 4 wk). After 2 mo of combination therapy (January 2006), PSA and CgA levels were 0.09 ng/ml and 82 ng/ml, respectively. At follow-up, the reduction of serum PSA and CgA levels progressively continued (PSA nadir = 0.05 ng/ml at 6 mo; CgA nadir = 9 ng/ml at 12 mo; Table 1). After 6 mo of therapy (May 2006), an objective complete response to therapy was demonstrated by a normal PSA level (PSA = 0.05 ng/ml) and bone scan imaging (Fig. 1B) response. At the 12-mo follow-up (November 2006) the normal serum markers (PSA = 0.05 ng/ml, CgA = 9 ng/ml) were accompanied by a 1H-MRSI response (Fig. 2B). In particular, the normal choline + creatine/citrate analogue.

1H-spectroscopic imaging (1H-MRSI) of the prostate (Fig. 2A). The 1H-MRSI showed an area of low signal intensity (1.8 cm) involving the left lobe of the prostate and infiltrating the left seminal vesicle (Fig. 2A). At spectroscopy, in this area the metabolic ratio modification was highly suggestive for neoplastic tissue (choline + creatine/citrate > 1; Fig. 2A). Considering that the patient was at first treatment and on the basis of a possible NE activation at the prostate adenocarcinoma level, he underwent (November 2005) combination therapy using complete androgen blockade (CAB; leuprorelin acetate 3.75 mg every 4 wk plus bicalutamide 50 mg daily) and a somatostatin analogue (lanreotide acetate 60 mg every 4 wk). After 2 mo of combination therapy (January 2006), PSA and CgA levels were 0.09 ng/ml and 82 ng/ml, respectively. At follow-up, the reduction of serum PSA and CgA levels progressively continued (PSA nadir = 0.05 ng/ml at 6 mo; CgA nadir = 9 ng/ml at 12 mo; Table 1). After 6 mo of therapy (May 2006), an objective complete response to therapy was demonstrated by a normal PSA level (PSA = 0.05 ng/ml) and bone scan imaging (Fig. 1B) response. At the 12-mo follow-up (November 2006) the normal serum markers (PSA = 0.05 ng/ml, CgA = 9 ng/ml) were accompanied by a 1H-MRSI response (Fig. 2B). In particular, the normal choline + creatine/citrate analogue.

Fig. 1 – Radionucleotide bone scan with $^{99m}$Tc. (A) At diagnosis, areas of abnormal uptake of the radioactive marker were detected in the sacral, dorsal, and cervical segments of the spinal cord, right iliac crest, and chest bilaterally. (B) At response to combination therapy, normal or significant reduction of the radionuclide uptake was found in all the areas described at diagnosis, in particular, in the right iliac crest, sacral and dorsal segments of the spinal cord, and chest bilaterally.

| Table 1 – Serum PSA and CgA variations at different intervals of follow-up during therapy |
|---------------------------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Baseline | 1-mo FU | 2-mo FU | 3-mo FU | 6-mo FU | 12-mo FU |
| PSA, ng/ml                     | 680      | 102     | 0.09    | 0.07    | 0.05    | 0.05    |
| CgA, ng/ml                     | 121      | 106     | 82      | 70      | 48      | 9       |

FU = follow-up; PSA = prostate specific antigen; CgA = chromogranin A.
ratio (<0.2) at 1H-MRSI confirmed a complete response to the combination therapy at the prostate level. The clinical response was associated with concomitant normal ECOG (1 score) and bone pain scores (0 score), beginning at 2 mo of follow-up. Therefore, after 12 mo of follow-up the patient is alive without disease progression and with a complete objective and symptomatic response.

Fig. 2 – Magnetic resonance 1H-spectroscopic imaging (1H-MRSI; Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) of the prostate, equipped with surface phased-array and endorectal coil. Imaging protocol: transverse spin-echo T2-weighted sequences on the axial, sagittal, and coronal planes for the morphologic imaging and three-dimensional chemical shift imaging (CSI) sequence with spectral/spatial pulses optimised for quantitative detection of choline and citrate (spectral resolution of 0.28 cm⁻³). (A) At diagnosis: transverse fast spin-echo T2-weighted MRI (5000/99 [effective]) showed an area of low signal intensity of 18 mm in the left middle region of the prostate involving the left seminal vesicle (arrows). Selected MR spectra obtained in this area showed a the metabolic ratio modification (choline + creatine/citrate > 1); these findings were suggestive of neoplastic tissue. (B) At response to therapy: transverse fast spin-echo T2-weighted MRI (5000/99 [effective]) showed a reduction (50%) of the low signal intensity area in the left middle region of the prostate and no seminal vesicle involvement (arrows). MR spectra obtained in this area demonstrated normalisation of the metabolic ratio (choline + creatine/citrate < 0.5).

EU-ACME question

Please visit www.eu-acme.org/europeanurology to answer the below EU-ACME question on-line (the EU-ACME credits will then be attributed automatically). The answer will be given in Case Study of the Month: Part 2, which will be published in next month’s issue of European Urology.
Question:

Neuroendocrine differentiation could be considered one of the factors related to the progression of prostate adenocarcinoma in hormone-refractory disease. How has it been proposed to manage this neuroendocrine hyperactivation in prostate cancer?

A. To continue complete androgen blockade (CAB).
B. To discontinue androgen-deprivation therapy and start chemotherapy.
C. To discontinue androgen-deprivation therapy and start somatostatin analogues.
D. To add a somatostatin analogue to androgen-deprivation therapies.