

## CASE REPORT

# Clinical evidence of neuroendocrine differentiation in a patient with prostate cancer and bone marrow micrometastases

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### Case report

A 58-year-old man had a biopsy taken in November 1998 and was diagnosed as having prostatic adenocarcinoma of Gleason score 5 (3+2); his serum PSA was 86.7 ng/mL. A DRE revealed a palpable nodule of increased consistency on the left lobe of the prostate; TRUS showed a hypoechoic area 1.5 cm in diameter in the peripheral zone of the left lobe of the prostate, with no evidence of capsular or seminal vesicle infiltration. CT of the abdomen and pelvis showed no lymphadenopathy, and the bone scan and chest X-rays were normal.

Laboratory tests showed a significant reduction in haemoglobin (94 g/L, normal 132–170), platelet count (89 000; normal 150 000–450 000) and neutrophils (33.8%, normal 55–70). In November 1998 the patient underwent an iliac bone marrow biopsy and the histology showed tumour cell clusters; immunohistochemical staining for PSA was positive at the tumour cell sites. Histological sections from the prostate biopsy were assessed for chromogranin A expression by immunohistochemistry [1], and more than one focus with extensive staining for chromogranin A was detectable in the tumour cells (Fig. 1). Moreover, high

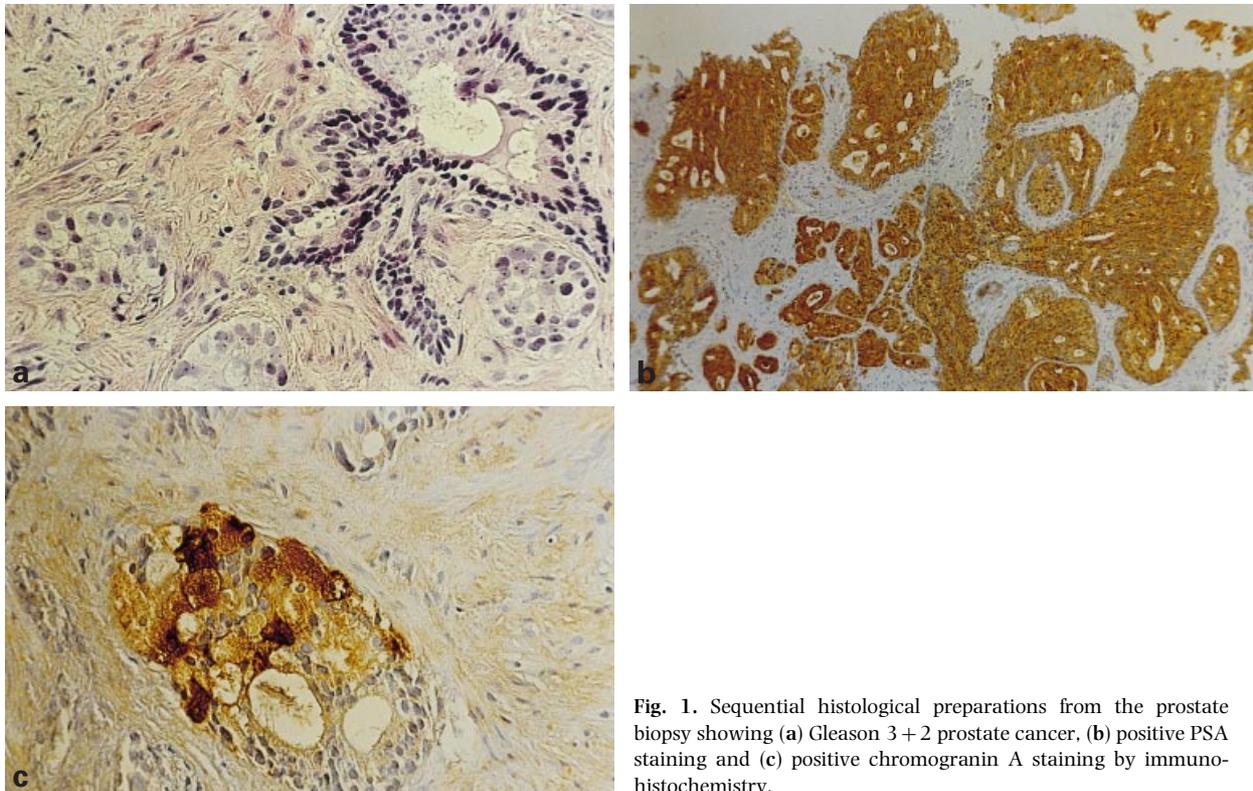
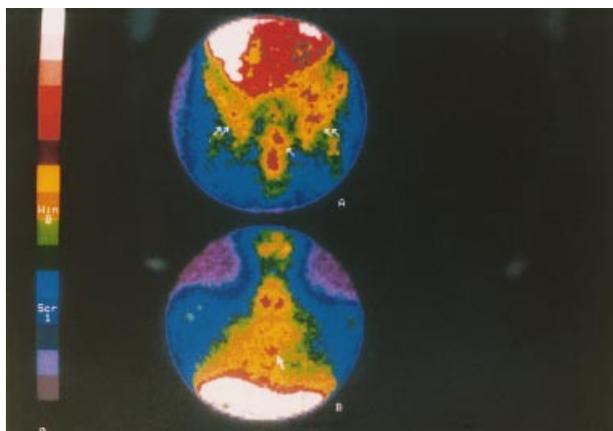
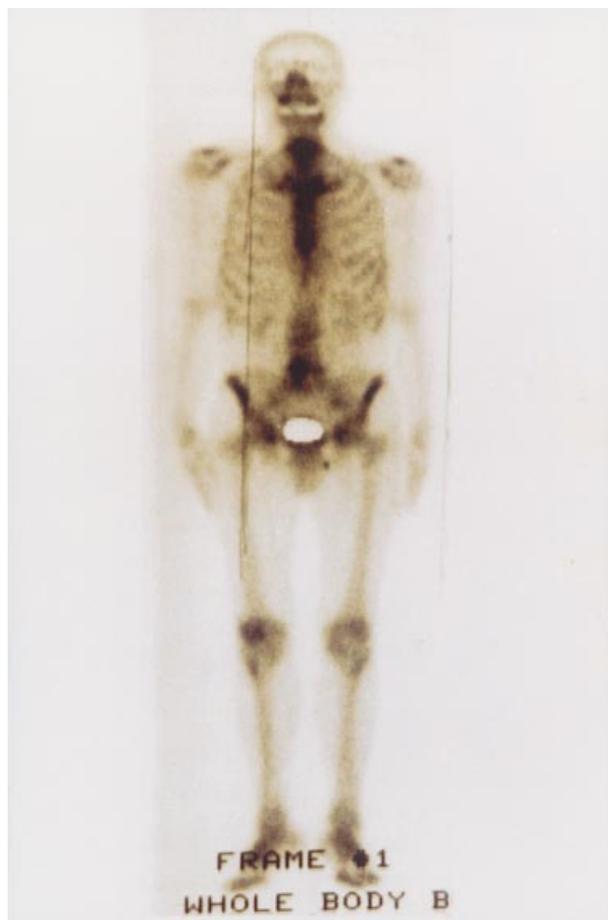


Fig. 1. Sequential histological preparations from the prostate biopsy showing (a) Gleason 3 + 2 prostate cancer, (b) positive PSA staining and (c) positive chromogranin A staining by immunohistochemistry.



**Fig. 2.** Total-body somatostatin receptor scintigraphy (at 4 h after injection). The arrows show an intense focus of abnormal  $^{111}\text{In}$ -pentatetreotide uptake (red areas) in the left part of the prostate (the central arrow in A) and other multiple foci of abnormal  $^{111}\text{In}$ -pentatetreotide uptake (red areas) of low intensity in the iliac crest bilaterally (A) and in the sternum (B).

chromogranin A plasma levels (126 ng/mL, normal <90) were shown by RIA and the patient underwent total-body somatostatin-receptor scintigraphy (SRS). This method takes advantage of the overexpression of type II somatostatin receptors on the cell surface of most neuroendocrine tumours. Previously, some authors showed that positive SRS strongly predicts the presence of tumour with neuroendocrine differentiation [2]. SRS was undertaken after an intravenous injection with  $^{111}\text{In}$ -pentatetreotide, a radioactive somatostatin analogue. Radiolabelling of pentatetreotide (Mallinckrodt Medical, Petten, The Netherlands) with  $^{111}\text{In}\text{-Cl}_3$  and imaging were carried out as described previously [2]. In particular, planar images of the body from the head to the leg ( $128 \times 128$  word matrix, 1 million counts or 10–15 min acquisition time) were taken in anterior and posterior projections at 4 and 24 h after the injection of  $^{111}\text{In}$ -pentatetreotide. The planar images were analysed qualitatively and semi-quantitatively. With this technique, the presence of neuroendocrine differentiation both at the primary and metastatic sites of tumour can be detected [2]. An intense focus of abnormal  $^{111}\text{In}$ -pentatetreotide uptake in the left part of the prostate (Fig. 2) and other multiple foci of lower intensity in the iliac crest bilaterally and in the sternum (Fig. 2) were detected at 4 h after injection; there were no further changes after 24 h. In December 1998, the patient underwent hormone therapy (LHRH analogue and bicalutamide, 5 mg/daily). At 6 months of follow-up a new bone scan was positive and areas of abnormal uptake were detected in the sternum, iliac crest bilaterally, and in the cervical and lumbosacral segment of the spinal cord (Fig. 3). The patient's serum PSA level was then 60 ng/mL.



**Fig. 3.** A radionuclide bone scan with  $^{99\text{m}}\text{Tc}$  at the 6-month follow-up (May 1999). Areas of abnormal uptake of the radioactive marker were detected in the sternum, iliac crest bilaterally and in the cervical and lumbosacral segment of the spinal cord.

### Comment

The detection of micrometastases in bone marrow may identify individuals destined to develop clinically detectable systemic metastases [3]. Neuroendocrine differentiation of the prostate is a recently appreciated phenomenon that has important diagnostic and prognostic implications [4–6]. Neuroendocrine-like cells appear to be involved in the emergence of androgen-independent tumours [4]. In the present case, the presence of neuroendocrine cells in the primary prostate cancer was confirmed by immunohistochemistry. This is the first report describing the use of SRS to locate the presence of neuroendocrine differentiation at the primary and metastatic sites of prostate cancer. The immunohistochemical results and SRS imaging seemed to agree. Moreover, after only 6 months after the SRS-positive results, conventional bone scintigraphy showed the presence of skeletal metastases.

## References

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