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SMALL CELL PROSTATE CANCER WITH BONE MARROW INVASION—A CASE REPORT

Small cell carcinoma (SCC) of the prostate is an uncommon disease. About 40 cases have been reported since 1977 with one series of 20 patients (1). The histogenesis of the disease remains unclear. There is a great variety in its clinical presentation and evolution. SCC of the prostate is in about half of the cases accompanied with a prostate adenocarcinoma of ordinary type. All patients with SCC of the prostate have one feature in common: a rapid and fatal progression due to metastatic spread to liver, lungs and bone. In the literature no cases are described with metastases to the brain or the bone marrow. No information exists on optimal therapy for primarily localized disease.

Case report. A 63-year-old man was referred to our hospital with a history of two months' perineal and pelvic pain. For the last two years he had also had progressive symptoms of prostatism. On physical examination a tumor of the prostate T3NxMx (UICC 1986) was detected without other clinical abnormalities. Biopsy showed tumor tissue, composed of small round cells with large nuclei and inconspicuous cytoplasm. Foci of tumor cells with fusiform morfology were noted. The chromatin was distributed in a granular fashion; there were no nucleoli. The number of mitoses was high. Foci of necrosis were noted. Immunohistochemical staining for neuron specific enolase (NSE) was positive in the cytoplasm of the tumor cells. A poorly differentiated small cell neuro-endocrine tumor was diagnosed

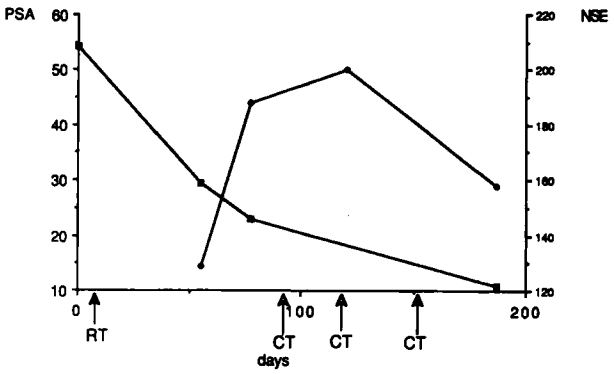

Figure. Serum level of prostate specific antigen (—□—) and neuron specific enolase (—◆—). RT = radiotherapy; CT = chemotherapy.

In the following three weeks the tumor progressed rapidly into a mass that infiltrated the bladder, rectal wall, seminal vesicles and with pathological lymph nodes along the obturator muscle. The patient developed urine retention due to tumor encompassing both ureters. At that time no distant metastases were detected. After nephrostomy, irradiation was started against the pelvis, given up to a total dose of 50 Gy with daily fractions of 1.8 Gy. Already after 20 Gy the pain and the urinary obstruction resolved and miction became normal. At the end of radiotherapy, echography showed a rather enlarged prostate without clear evidence of tumor. Two months after irradiation the patient was again hospitalized in a poor general condition and extremely exhausted. His blood count showed marked anemia, leukopenia and thrombopenia. The serum level of prostate specific antigen (PSA) had dropped from initially 54.2 ng/ml (normally below 2.7 ng/ml) to 10.8 ng/ml, whereas the neuron specific enolase (NSE) increased from 130 μg/ml to 200 μg/ml (normal range: 3–12.5 μg/ml). Bone marrow biopsy showed bone marrow invasion by SCC of neuro-endocrine origin. Monthly courses of cis-platinum and etoposide were started. After the first course the peripheral blood count normalized. The patient was feeling well but the NSE level in the blood remained at a level of around 200 μg/ml. He subsequently died from pneumonia after the third course of chemotherapy. On autopsy several metastases in lungs, liver, right kidney and lymph nodes in the retroperitoneum and mediastinum were found. Histologic examination revealed tumor tissue with the same cytologic features as described above. In the prostate no residual tumor was found. Microscopic examination showed scar tissue only.

Discussion. SCC of the prostate is a very aggressive disease with a median survival of about 5 months due to distant metastases. Most reported cases have distant metastases at presentation and no clear information exists about the optimal therapy for patients with limited disease at the time of diagnosis. Our patient, presenting with clinically localized disease, was initially treated by pelvic radiotherapy to avoid chemotherapy-related problems caused by the patient's renal malfunction and to obtain pain release and renal recovery in the shortest possible time. This was indeed achieved and the patient had at autopsy complete remission within the irradiated volume. The further evolution was, however, similar to SCC of the lung with rapid development of distant metastases. The best treatment for SCC of the prostate remains to be determined due to insufficient data. Loco-regional treatment (by irradiation) is recommended for patients with disease confined to the prostate. Adjuvant systemic treatment seems logical because of the usually rapid dissemination of the disease. Hindson et al. (2) reported one patient with a transient complete response to

chemotherapy. In the series of Têtu et al. (1) 4 out of 13 patients responded temporary to chemotherapy and none out of 12 to hormonal treatment. Actually a combined approach employing loco-regional irradiation and combination chemotherapy seems warranted for patients with limited, as well as for those with disseminated, SCC of the prostate.

Little is known about the different tumor markers during the course of prostatic SCC. Increased serum levels of prostate specific antigen (PSA) and of prostate acid phosphatase (PAP) are probably expression of an adenocarcinoma component in the prostate although not always observable in biopsy specimens. According to Têtu et al. (1) virtually all cases of prostatic SCC might be associated with an ordinary adenocarcinoma. In two cases where loco-regional treatment was given to the prostate (ref. (4) and our patient) the PSA levels decreased in spite of further dissemination. The neuron specific enolase (NSE) level in our patient remained high, even during chemotherapy (Figure). Moreover, in the report by Freeman & Doolittle (3) of an SCC of unknown primary the PAP level remained unchanged up to the moment where a bilateral orchiectomy was performed. Freeman & Doolittle (3) and Hagood et al. (4) considered a decrease in PSA or PAP levels towards the terminal phase of the disease to be an expression of dedifferentiation of the tumor. We merely think this to be therapy-induced, suggesting two concomitant tumor strains: the differentiated adenocarcinoma and the undifferentiated SCC.

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