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UROLOGY - CASE REPORT

A pure primary low-grade neuroendocrine carcinoma (carcinoid tumor) of the prostate

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Abstract The first time in Scandinavia we present a case report of a pure primary low-grade neuroendocrine carcinoma (carcinoid tumor) of the prostate. Our patient is a 34-year-old male with a long history of symptomatic chronic prostatitis/prostatodynia. After developing severe obstructive uropathy, a transurethral resection was performed. An unexpected diagnosis of a low-grade neuroendocrine carcinoma was made. Subsequently, in radical prostatovesiculectomy, we noted metastases to both seminal vesicles and two inguinal lymph nodes. Follow up is ongoing.

Keywords Prostate · Low-grade neuroendocrine carcinoma · Carcinoid tumor · Neuroendocrine differentiation

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Case report

Primary low-grade neuroendocrine carcinoma, formerly known as a carcinoid tumor, of the prostate is a very rare tumor derived from the amine precursor uptake and decarboxylation cells of the gland [6]. Neuroendocrine differentiation in prostate cancer is detected by immunohistochemistry as single cells in conventional adenocarcinoma. Pure and primary prostatic neuroendocrine tumors, such as carcinoid or small cell carcinoma, although rare, have been documented in the literature, mostly in case reports [1–4, 6, 7, 9, 10].

Here, we report the first patient in Scandinavia who was diagnosed with primary low-grade neuroendocrine carcinoma of the prostate with patient's consent.

A 34-year-old man first presented to our unit at the age of 31 years with a long history of symptomatic chronic prostatitis and approximately one-year history of dysuria. Cystometric and fiberscopic examinations were performed, and the results showed a low, non-pathologic detrusor contraction manageable with pharmacological therapy. Rectal examination revealed a large regular prostate with diffuse pain in the palpation. In prostatic ultrasound, the volume detected was 16.1 cm^3 , and the initial diagnosis was chronic prostatitis.

After 2 years, the symptoms became worse. New clinical examinations revealed obstructive uropathy and a transurethral resection of the prostate (TURP)

with about 8 g of prostate biopsy were performed. The specimen was interpreted as a low-grade neuroendocrine carcinoma of the prostate. Because of malignant appearance of the removed tissue, an octreotide mapping, 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) and abdominal computed tomography were performed and were unremarkable showing no signs of metastatic disease (Fig. 1).

A radical prostatovesiculectomy was performed and evaluated. According to the pathologist's report, the margins of resection were free and 2/5 of regional lymph nodes showed metastatic invasion on the left side. Pre-operative serum chromogranin A was 3.9 nmol/L.

The tumor was staged as pT3bN1M0. The primary histological diagnosis based on morphology in the TURP specimen was a low-grade neuroendocrine carcinoma (carcinoid tumor) that expressed common features for a malignancy: infiltrative growth pattern, desmoplastic stromal reaction, elevated rate of mitosis and perineural invasion (Fig. 2). Subsequently, the diagnosis was confirmed by immunohistochemistry. Pancytokeratin was positive in tumor cells. Prostate-specific antigen (PSA) and vimentin were negative (Fig. 3). Synaptophysin was strongly positive in all tumor cells, and chromogranin A was intermediately positive in all tumor cells (Fig. 4). Ki-67 rate was high (ad 30%) although variable depending on focus (Fig. 5). The results confirmed the primary diagnosis. In the prostatovesiculectomy preparate, predominantly periurethral growth with infiltrations to ambilateral seminal vesicles was seen. In addition, two microscopic metastases to two inguinal nodes, which were not apparent in the frozen sections, were identified. The tumor consisted of intermediate-sized cells with dark staining enlarged concentric oval nuclei with coarse chromatin. The growth pattern was trabecular with fused trabecules and pseudoacini. In the peripheral foci, there was an intensive perineural invasion. The immunohistochemical staining profile was in accordance with the original sample with some additional stainings: AMACR and CD117 were negative. The final pathological diagnosis was a low-grade prostatic neuroendocrine carcinoma.

Two weeks postoperatively, a left femoral vein thrombosis was detected by ultrasounds and treated pharmacologically. No additional therapy has been planned for the cancer.

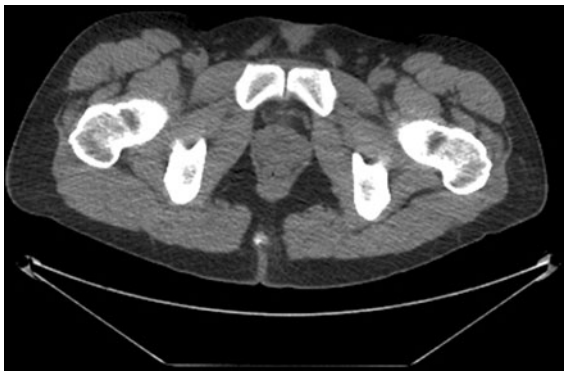

Fig. 1 Abdominal computed tomography scan of the prostate tumor before the operation

Discussion

Primary low-grade neuroendocrine carcinoma of the prostate is an exceedingly rare tumor, which may metastasize to loco-regional lymph nodes, liver, lungs and bones [3].

Several cases have been reported in the literature [2–4, 6, 9, 10], mostly in men aged over 60 years. A single case of primary prostatic carcinoid in conjunction with multiple endocrine neoplasia (MEN) 2B in a child has also been reported [9]. Our patient was a 34-year-old otherwise healthy man with negative family history for malignancies or inflammatory bowel disease (IBD) but with a long-standing chronic prostatitis.

Chronic inflammation has been shown to contribute to carcinogenesis in various organs. The incidence of carcinoid tumors seems also to be elevated in patients with Crohn′s disease [8]. The role of chronic inflammation, infectious agents, apoptosis and proliferation has been intensively studied in prostate carcinogenesis [5]. A primary low-grade neuroendocrine carcinoma of prostate is so rare that we may never be able to have a reasonable judgement to its relation to inflammation, let alone to any other etiological factor.

A proper identification and classification of prostate neuroendocrine carcinoma is very important because it is possible that a conventional adenocarcinoma includes neuroendocrine features, the so-called carcinoid-like growth pattern [4]. As some authors have speculated that tumors with neuroendocrine

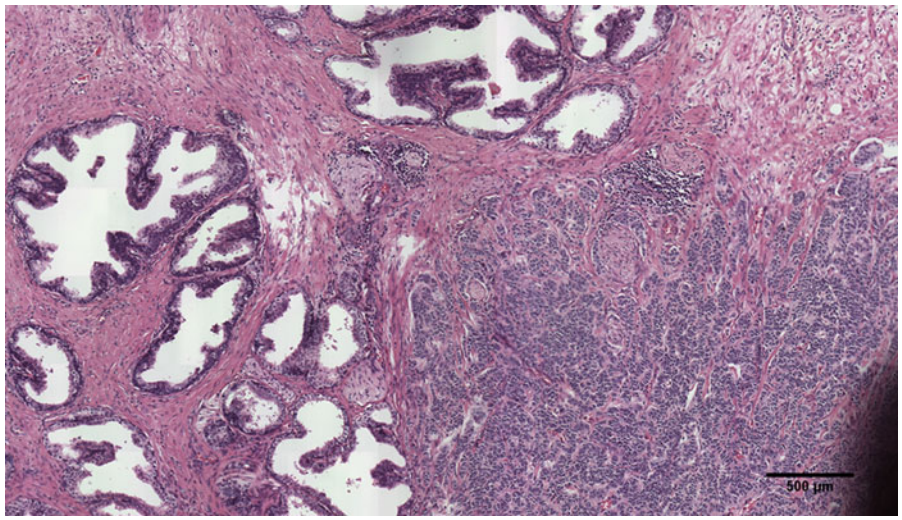

Fig. 2 A characteristic focus with trabecular growth pattern and intervening normal prostatic glands. Note also intensive perineural growth. HE staining. A *scale bar* present on *lower right*

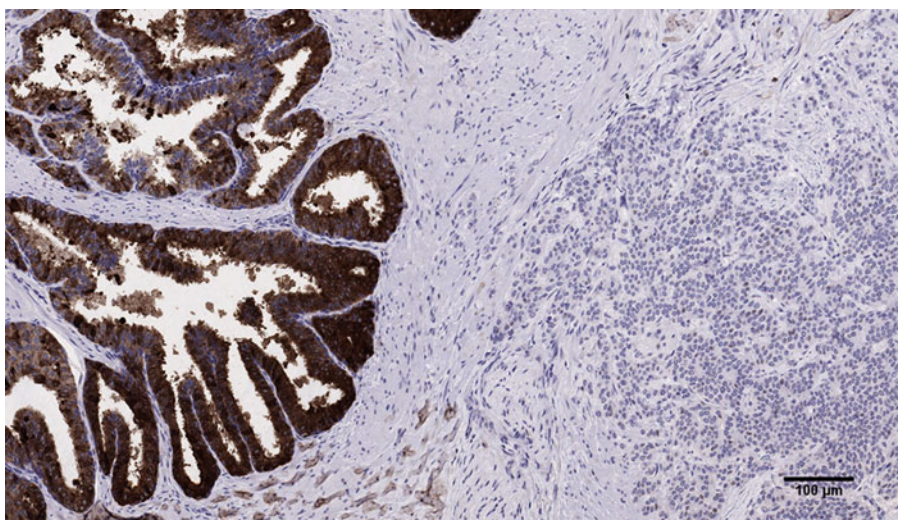

Fig. 3 Carcinoma completely negative for PSA on the *right*. Prostatic glandular epithelium strongly positive on the *left*. A *scale bar* present on *lower right*

differentiation behave more aggressively, it is also necessary to determine whether the tumor is a conventional adenocarcinoma with neuroendocrine differentiation or a pure neuroendocrine carcinoma.

A large number of previously reported cases presented also areas of adenocarcinoma and, where immunoperoxidase stains were performed, these tumors often stained positive for PSA. This increases the possibility that these cases may represent adenocarcinomas with neuroendocrine differentiation rather than neuroendocrine carcinomas [1, 4, 6, 7].

In our case, there was adenocarcinoma present neither in the first TURP nor in the radical prostatectomy specimen.

The exact behavior of pure primary prostatic carcinoids is difficult to predict as only few cases have been reported in the literature and no consensus with respect to treatment is possible. Many of the previously reported cases may represent adenocarcinomas with carcinoid features, thus leading to a potentially different prognosis than with pure neuroendocrine carcinomas. Due to these speculations, no

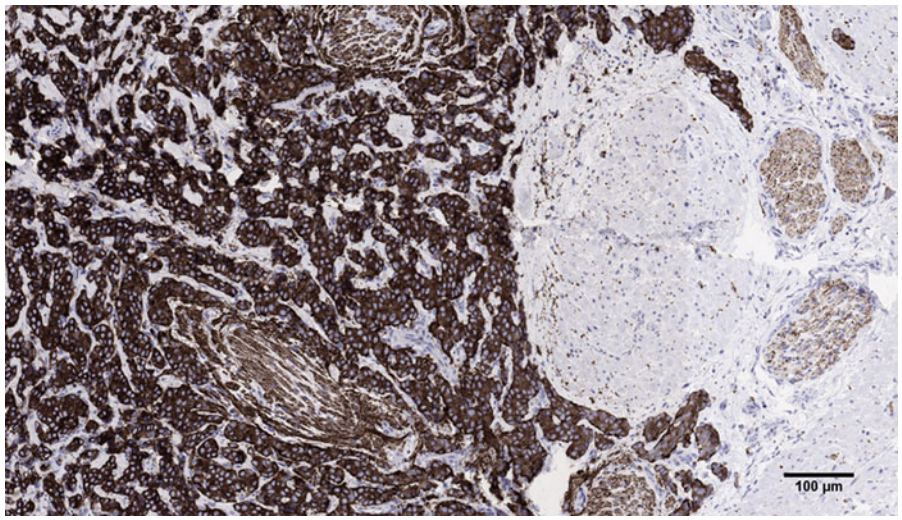

Fig. 4 Carcinoma strongly positive for synaptophysin. Some positivity also noted in perineurally invaded nerves. A *scale bar* present on *lower right*

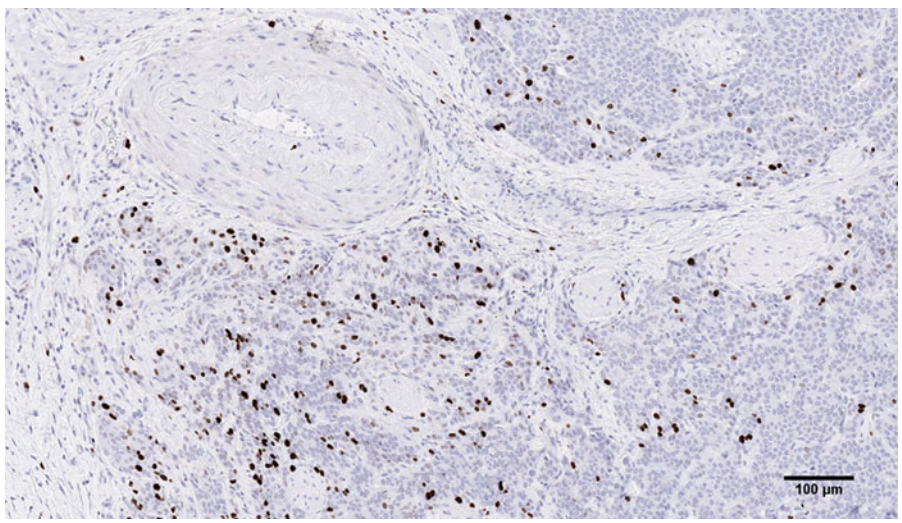

Fig. 5 High proliferation rate seen in Ki-67 staining (*black* nuclei) indicative for a malignancy. A *scale bar* present on *lower right*

further therapy (chemotherapy or radiotherapy) was planned for the patient and he remains in a follow-up program.

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