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Primary embryonal carcinoma of the prostate

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ABSTRACT

Extragonadal germ cell tumors originating in the prostate are extremely rare. Thus far, less than 20 cases were described in the literature. To our knowledge, there are no published cases of primary embryonal carcinoma of the prostate. The present study presents a case of a 24-year-old male with primary prostate embryonal carcinoma. The patient received cisplatin-based chemotherapy. The patient refused a surgical treatment, which resulted in relapse of the disease and death in a short follow-up period. The present case shows that primary embryonal carcinoma may also be found in prostate and indicates the potential importance of timely surgical resection.

1. Introduction

Extragonadal germ cell tumors (EGGCTs) are a heterogeneous group of tumors of neoplastic germ cells arising from extragonadal anatomical locations, without evidence of gonadal primary tumors.[1] Their morphology varies widely and includes mature teratoma, immature teratoma, seminoma, yolk sac tumor, embryonal carcinoma, choriocarcinoma, and mixed GCTs.[2] Primary EGGCTs are rare, accounting for 1–3% of all GCTs, of which 60 % are seminomas.[3] Extragonadal germ cell tumors (EGGCTs) originating in the prostate are extremely rare, with <20 cases described in the literature.[4] To the best of our knowledge, there are no published cases of primary embryonal carcinoma of the prostate to this day. The present study describes the case of a 24-year-old male with primary embryonal carcinoma of the prostate who sought medical assistance due to urinary retention. Seeing that the patient passed away, his relative gave informed written consent for this study. The authors declare no conflict of interest.

2. Case report

In January 2022, a 24-year-old man first presented himself at the Urology Clinic of the University Clinical Center of Serbia due to urinary retention. A digital rectal examination following the placement of a urinary catheter showed a firm, nodular, and vaguely circumscribed prostate without a palpable sulcus. The local findings in the examination of testicles were normal. The testicles were indolent, homogeneous in structure and without palpable nodules. PSA value was 2.53 ng/ml. Computer tomography of abdomen and pelvis with contrast material was indicated and showed an inhomogeneous prostate 50 × 45mm without clearly visible tumor in the prostate. The bladder wall was diffusely thickened with signs of calcification. Abdominal and pelvic lymph nodes were not enlarged or described as suspicious. TRUS guided biopsy of prostate followed. Pathohistology showed cells with large pleoform nuclei, prominent nucleoli with high mitotic activity. Tumor cells are of solid, tubular and papillary growth. Fields of necrosis and hemorrhage were observed. The immunohistochemical findings were markedly positive for the following markers: OCT3/4, SALL4, CD30 (Fig. 1). Accordingly, a diagnosis of embryonal carcinoma was made. Tumor markers were additionally determined in serum and showed the following values: AFP 28.5 ng/ml (normal values 1.1–8 ng/ml), β-HCG 19.5 ng/ml, LDH 576 IU/L (normal values 101–233 IU/L). Ultrasonography and the bilateral biopsy of the testicles that followed showed a completely normal finding, which together with the above-mentioned pathohistological finding was the basis for establishing the diagnosis of primary extragonadal embryonal carcinoma in prostate tissue. After the case was presented to the multidisciplinary tumor council, a decision was made to start chemotherapy with a total of 4 cycles of bleomycin, etoposide and cisplatin (BEP – Protocol). The control computer tomography that was performed at the end of the chemotherapy cycles in September 2022 showed still locally limited disease without the

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presence of pathologically enlarged lymph nodes in the abdomen and pelvis. Liver and kidney function tests, electrolyte values and coagulation parameters did not show any abnormalities. The values of the corresponding tumor markers (β-HCG, AFP, LDH and PSA) were all normal. The case was again presented at multidisciplinary tumor council, where a recommendation was made for radical surgical intervention (cystoprostatectomy with urinary diversion), with the idea of definitive disease treatment in accordance with the latest recommendations for treatment of EGGCTs.[5] The patient refused the proposed surgical intervention. The patient presented himself again in February 2023 and asked for operative treatment. Obstructive lower urinary tract symptoms were still present as well as occasional diarrhea. For the purpose of preoperative preparation, in March 2023, a computer tomography of the abdomen and pelvis was again performed, which showed disseminated as well as locally infiltrative disease (with infiltration of the urinary bladder wall) with multiple pathologically enlarged and metastatic suspect lymph nodes in the abdomen (Fig. 2). Corresponding laboratory findings also spoke in favor of disease relapse (AFP 25 ng/ml, β- HCG 45.1 ng/ml, LDH 800 IU/L). The initially planned surgical intervention was abandoned in favor of starting 4 cycles of chemotherapy with Cisplatin, Etoposide and Ifosfoamide (VIP - Protocole). After the first cycle of therapy, there was a significant worsening of the patient's general condition with signs of acute kidney injury. It was indicated to pause further systemic treatment and start with supportive measures until the general condition improves. Death occurred during the follow-up period after 2 months.

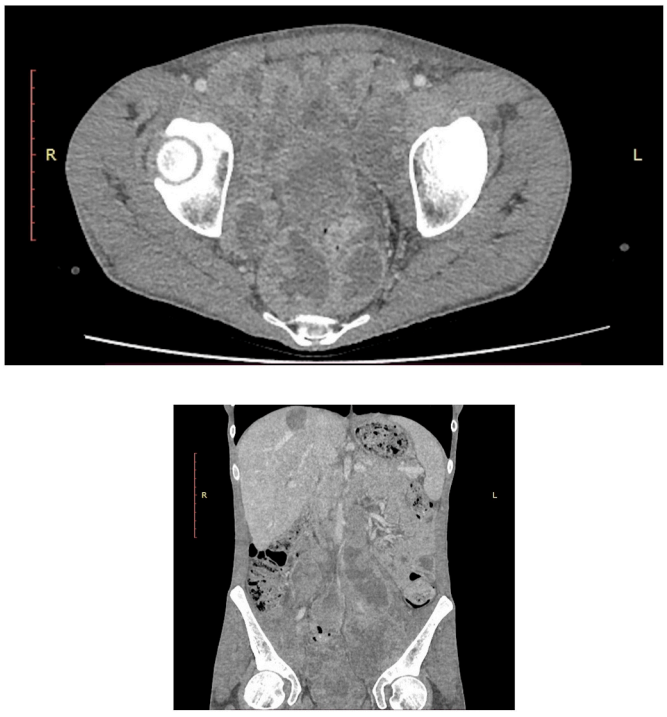

Fig. 2. Computer tomography of the abdomen and pelvis – Disease relapse with locally infiltrative disease with infiltration of the urinary bladder wall as well as multiple pathologically enlarged and metastatic suspect lymph nodes.

3. Discussion

Primary EGGCTs are uncommon, and the majority of these tumors likely originate from the midline of the body. The etiology of primary prostate EGGCTs is unclear. One hypothesis suggests that prostatic pluripotent stem cells transform neoplastic cells into gonadal cells, which results in the formation of tumors. Symptoms of primary EGGCTs in prostate are, due to low number of cases, insufficiently examined and documented. The cases published so far, as well as our report, suggest that obstructive lower urinary tract symptoms (LUTS) are the most frequent first symptom in prostate EGGCTs.[6] The elevated serum markers of β- HCG and/or AFP also point to the diagnosis of prostate EGGCTs in patients with LUTS.[7] Data on survival and long-term comorbidities of patients with EGGCTs are scarce. Published data suggest that EGGCTs present in general an inferior prognosis than their gonadal counterparts.[8] During the last three decades, the clinical outcome of non-seminomatosus EGGCTs (NSEGGCTs) has been

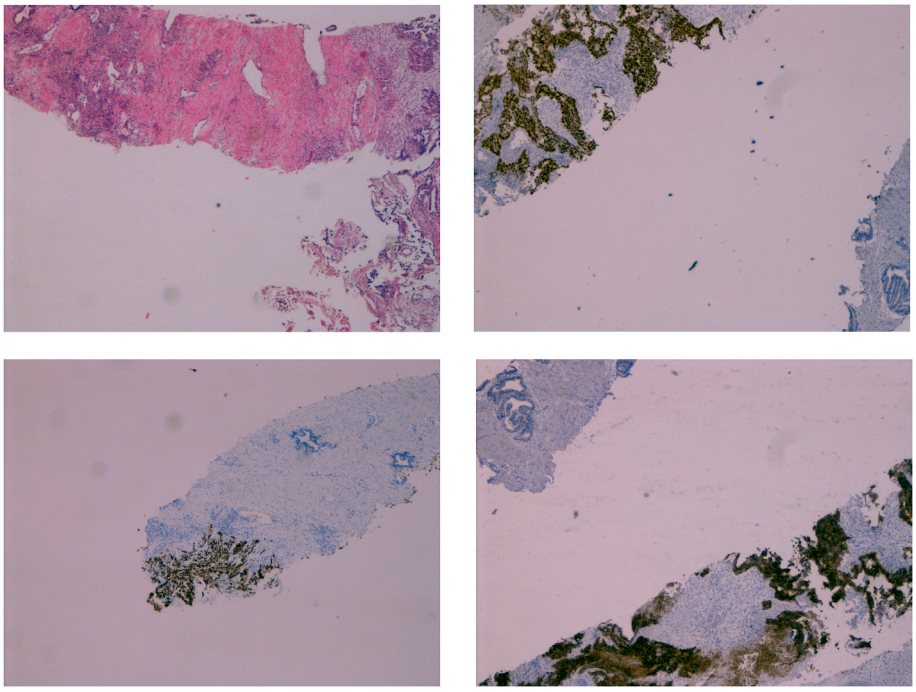

Fig. 1. Pathohistology of Tumor. H&E staining presenting the details of a tumor, and the immunohistochemical findings that were markedly positive for the following markers: OCT3/4, SALL4, CD30.

dramatically improved since the introduction of cisplatin-based chemotherapy. The standard chemotherapy regimen for patients with an (NSEGGCTs) consists of 3–4 cycles of bleomycin, etoposide, cisplatin (BEP).[9] Latest data suggest that treatment of EGGCTs with cisplatin-based chemotherapy followed by surgical resection of residual disease is currently one of the most successful approaches of multidimensional therapy.[10] In our case, the patient refused the proposed surgical treatment. In short follow-up period a relapse of the disease was established. Patients who relapse have a dismal outcome with only 10 % long-term survival. Many authors suggest that NSEGCCTs disease relapse should be further treated in a similar fashion to non-seminous GCCTs. The choice of first salvage treatment/second-line therapy here is still a matter of debate. Non-seminomas are difficult to cure with only salvage chemotherapy because of higher rates of teratoma existing in relapsed masses, sometimes with somatic malignant differentiation. This fact makes a combination of chemotherapy and surgical resection the preferred option of treatment, if it is technically feasible, which was not possible in our case. There are two chemotherapy salvage approaches, conventional-dose chemotherapy (CDCT) and HDCT followed by ASCT. Three chemotherapy options in CDCT include the TIP protocol, the combination of cisplatin, ifosfamide and vinblastine (VeIP protocol) and PEI protocol.[11] It is also worth mentioning that immuntherapies with antibodies against immunomodulators CTLA4 and PD-L1/PD-1 have shown some success in clinical application at times, but their effects on tumor treatment are not sufficiently stable, with the target effect often not achieved.[12] In our case the development of complications during the VeIP protocol caused the discontinuation of further treatment and death in a short period of follow-up.

In conclusion, the present case shows that primary embryional carcinoma, which normally affects the testicles, may also be found in prostate. Consequently, a reasonable and feasible therapy should begin with the BEP protocol. Our case also indicates the potential importance of timely surgical resection in preventing relapse and further disease progression. Further development of new treatment options for relapsed disease remains an important goal.

CRediT authorship contribution statement

Milan Radovanović: Writing – review & editing, Writing – original draft, Project administration, Data curation, Conceptualization. **Aleksa Zubelić:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Veljko Šantrić:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Uroš Babić:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Nebojša Prijović:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Predrag Nikić:** Writing – review & editing, Writing – original draft, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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