

Primary T-Cell Lymphoma of the Prostate in a Dog – Case Report

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Abstract: The prostate gland is considered an accessory sexual organ of the male reproductive system which in dogs can vary in size influenced by age, weight and breed. The most frequent anomalies found in the canine prostate are due to Benign prostatic hyperplasia, prostatitis, abscesses, prostatic and paraprostatic cysts, squamous metaplasia and prostate neoplasia in adult and geriatric dogs. Prostate lymphoma, unlike some neoplasms, is not routinely seen. An abnormal prostate is presumptively diagnosed based on the patient's history and clinical signs, blood markers and abnormal anatomical outline detected on palpation and imaging. The present report describes the case of a 13-year-old male, 26 kg, intact dog, referred to the Centro Universitário Barão de Mauá Veterinary Campus manifesting dysuria and diagnosed with primary prostatic lymphoma.

Keywords: Canine; Neoplasm; Prostate gland; Prostate neoplasm.

1. Introduction

The prostate gland is considered an accessory sexual organ of the male canine reproductive system and is located inside the pelvic cavity, caudally to the bladder. Its main purpose is to produce the seminal fluid which facilitates sperm life and transportation [1, 2]. The canine prostate can vary in size because of the natural aging process. Different sized prostate glands can be found in dogs of different sizes and breed [3]. As age advances, an increase in prostate volume and consequent benign prostatic hyperplasia (BPH) can occur [4] although many other abnormalities such as: prostatitis, abscesses, prostatic and paraprostatic cysts, squamous metaplasia and prostatic neoplasia, are also commonly found in adult to geriatric dogs [5, 6].

Prostate neoplasia occurs in castrated as well as in intact dogs, with adenocarcinoma being the most found in routine clinical care [7, 8]. Nevertheless, transitional cell carcinoma, squamous cell carcinoma, leiomyosarcoma, primary lymphoma, fibro sarcoma and metastases can also occur [9]. Studies show that a lymphoma is typically a proliferation of malignant lymphocytes, originating from lymphoid organs such as bone marrow, thymus, liver, spleen and lymph nodes. Lymphoma represents, in dogs, around 8-9% of all neoplasms, being the most common hematopoietic neoplasm in this species [10]. Although its exact origin remains unknown, causes of occurring lymphoma are mostly attributed to immunological mechanisms and gene modification, or as result of exposure to ionic and carcinogenic chemicals [11]. Lymphoma can occur in different tissue types due

to continual lymphocyte migration throughout the body. Primary lymphomas of the prostate are globally rare, representing <0.1% of all prostatic neoplasms. Their rarity and non-specific symptomatology at presentation usually instigate a clinical diagnosis of benign prostatic hyperplasia or chronic prostatitis, leading to significant retardation in diagnosis [12].

When abnormalities are detected in the canine prostate, a presumptive diagnosis is usually made based on clinical signs and the patient's history, blood profile and altered organ anatomy detected by palpation and imaging [13]. When neoplasia is suspected, a suggested diagnosis can be supported by fine needle aspiration cytology (FNAC), whereas confirmation can be provided by histopathological evaluation of the affected tissue [10, 14]. In patients with lymphoma, CD3 marking indicates the origin of this neoplasm in T cells. On the other hand, CD79a marking indicates its origin in B cells. To evaluate lymphoma, it is necessary to use both markers, so that the lymphoma immunophenotype [14]. The immunophenotype is regarded as an independent prognostic factor in high-grade lymphomas, seeing that lymphomas of T-cell origin are associated with shorter survival time [15].

The present case reports a dog presenting a hyperplastic prostate gland, detected upon abdominal palpation and confirmed by ultrasonography, diagnosed with primary T cell prostatic lymphoma.

2. Case Report

A 13-year-old sexually intact male dog of indistinct breed, weighing 23 kg, was referred to the Campus Veterinário Escola do Centro Universitário Barão de Mauá, Ribeirão Preto, São Paulo, presenting dysuria. A urine sample showed normal physical parameters and the patient's physiological parameters presented as normal on physical examination. On abdominal palpation, a firm, consistent mass in the hypogastric area was noted and then further investigated by abdominal ultrasonography. The imaging obtained showed the urinary vesicle cranially dislocated but with an apparently normal content volume. The prostate was found displaced, beyond its habitual topography. Also, the gland did not present a normal bi-lobulated outline, and showed a diffuse heterogenic parenchyma, suggestive of permeated cysts. Prostatic measurements were 9.0 X 7.8 cm. Further abdominal assessment showed no other abnormalities. Assessment of blood samples showed normal hemogram and blood chemistry values. A fine needle aspiration cytology guided by ultrasound was then performed on the prostate, with the results showing the parenchyma with moderate cellularity, anisocytosis (inequality in cell size) and anisochariosis (nuclear size variation).

A predominance of round cells was noted in the samples. These presented as medium to large lymphocytes with moderate to ample basophilic cytoplasm, some vacuolated, round to pleomorphic nuclei with uncondensed chromatin and evident nucleoli, and high mitotic activity, suggestive of lymphoid neoplasia. With this diagnostic possibility in mind, the patient was then submitted to an exploratory midline celiotomy and prostate incisional biopsy. During the procedure, a thick prostatic neoformation adhered to the bladder (Figure 1) was noted and assessed by palpation. The bladder was then submitted to retrograde hydropropulsion using a 0.9% sterile saline solution and the procedure showed points of bleeding and rupture in the organ's wall. As the bladder was deemed functionally non-viable, the patient was euthanized per the owner's consent and tissue samples from the prostate were taken for histopathological evaluation. No other macroscopic abnormalities were found in other organs or lymph nodes in the abdominal cavity.

Histopathological examination of the prostate tissue samples showed malignant round cell neoplasia, diffusely invading the sampled tissue with neoplastic cells surrounding prostate glands (Figure 2). It is possible to observe hyperplastic prostate glands, with the presence of prostatic secretion inside them. Hematoxylin and eosin

(H&E) staining indicated a round cell neoplasm, and immunohistochemistry was required for definitive diagnosis.

Figure 1. Photograph of an excised surgical piece from a dog. A: enlarged prostate with neoplastic infiltrate; B: non-viable, hyperemic urinary bladder, thickened and adhered to the prostate.

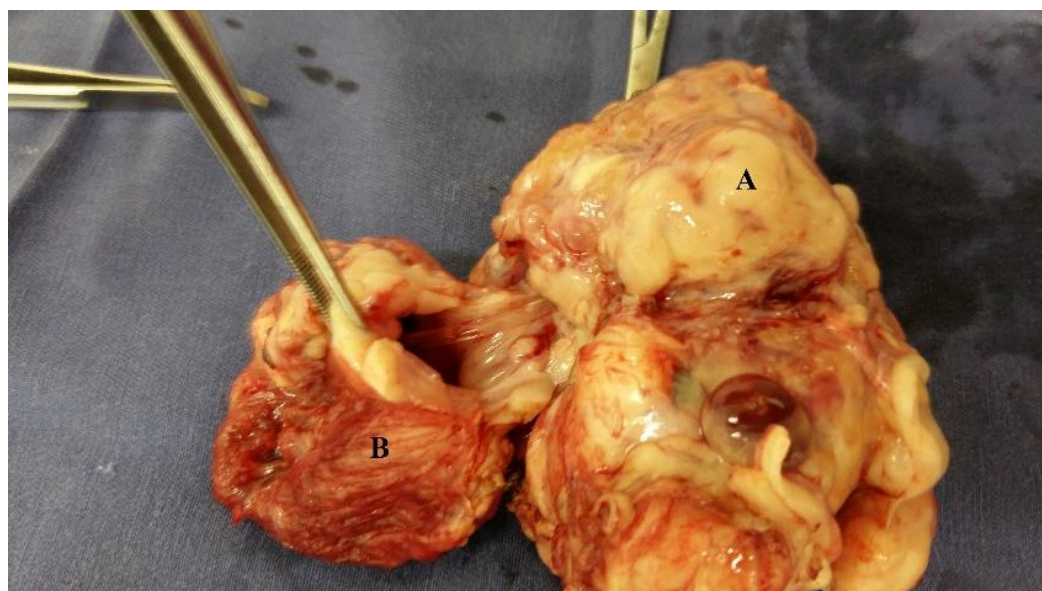
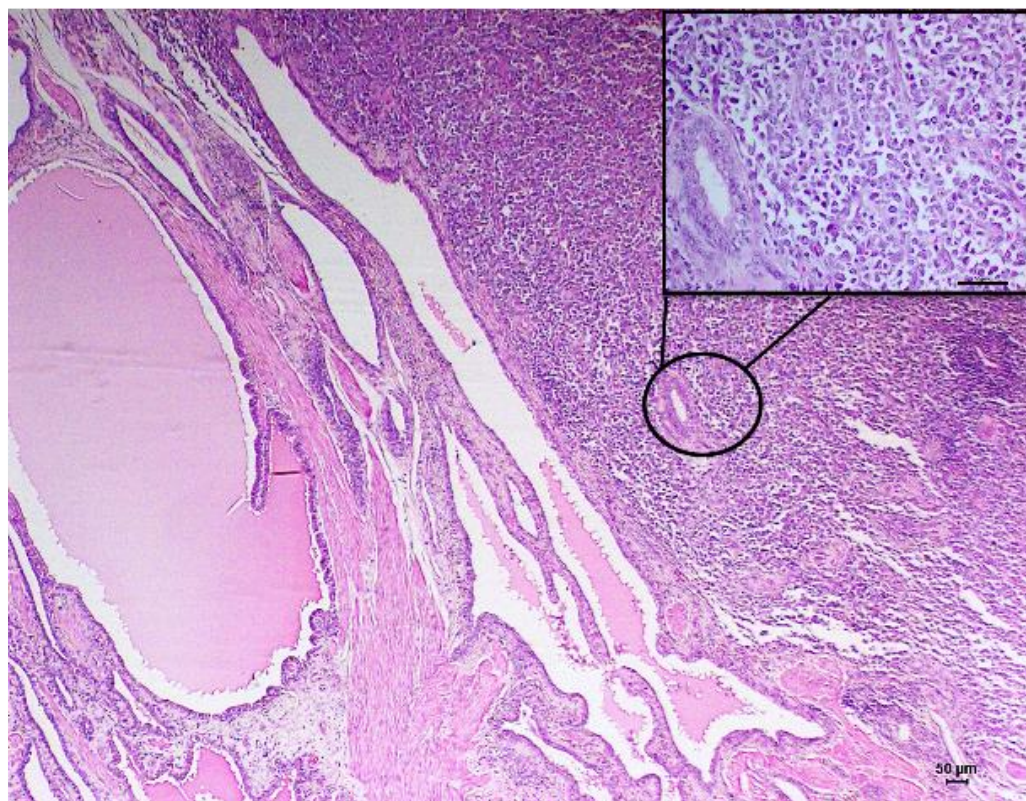


Figure 2. Hematoxylin and eosin stained (H&E) canine prostate, magnification 50x. Note proliferation of round cells around hyperplastic prostatic glands. Note the proliferation of neoplastic lymphocytes surrounding a prostate gland (circled, 440x).

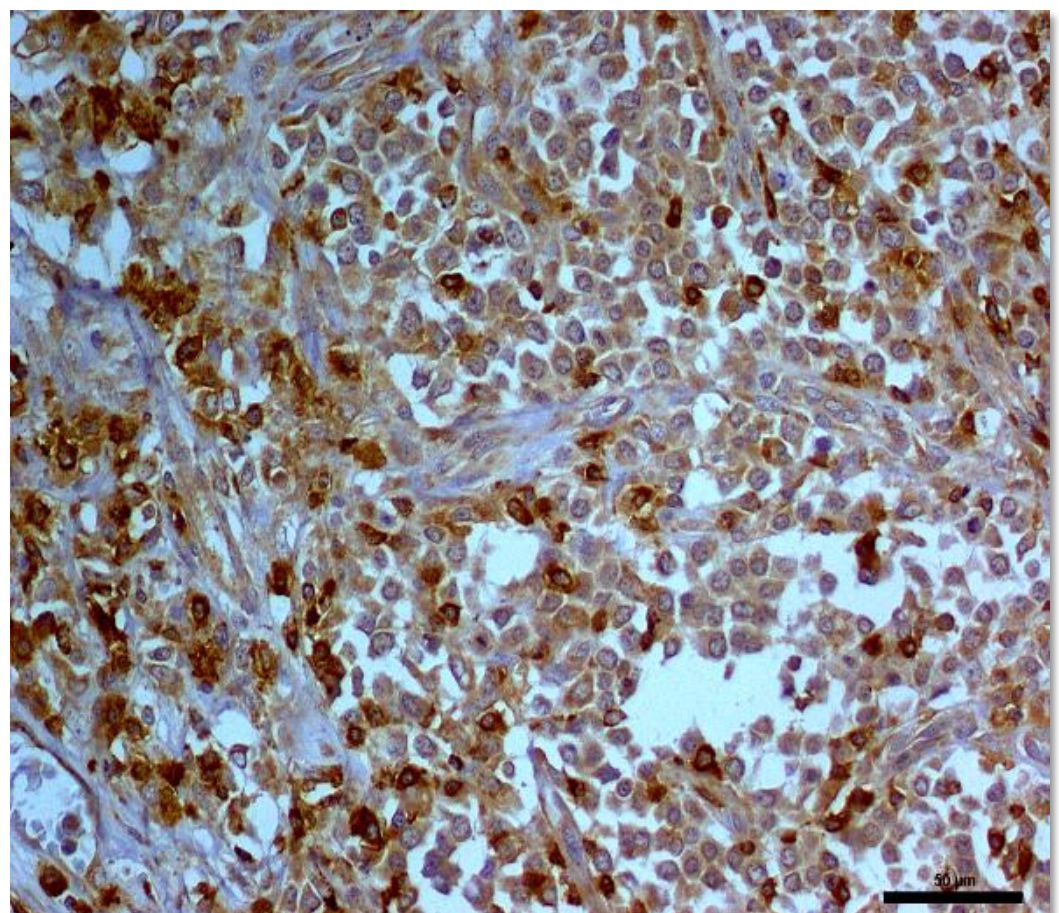


To complement the diagnosis, the immunohistochemistry technique was performed for pan-cytokeratin antibodies (Monoclonal - Invitrogen) and prostate-specific antigen (PSA) (Polyclonal - Dako Cytomation) to confirm the prostate origin of the epithelial glands surrounding neoplastic cells. With this marking, it was possible to exclude the prostatic epithelial origin of the cells found, as well as identifying the remaining prostate glands. In addition, immunostaining for CD3 (Polyclonal - Dako Cytomation) and CD79a (Monoclonal, Dako Cytomation) was performed. This staining was performed to evaluate the lymphocytic origin of the tumor, as well as to determine whether they were of T or B origin. Immunohistochemical staining was performed using the peroxidase method and 3,3' diaminobenzidine tetrachloride (DAB). Slides were dewaxed in xylene and rehydrated in graded ethanol. For antigen retrieval, slides were incubated in citrate buffer (pH 6.0) in a pressure cooker (Pascal®; Dako, Carpinteria, CA, USA).

Pan-cytokeratin detection was done at a dilution of 1/200 for 45 minutes. Samples were exposed to anti PSA antibodies at a dilution of 1/300 for 45 minutes. Exposure to CD3 and CD79a antibodies was done at a dilution of 1/100 and 1/50 respectively for 45 minutes. The Histofine (414154F, Nichirei Biosciences, Tokyo, JP) method was used for immunolabeling. Slides were counterstained with hematoxylin, dehydrated and then mounted under a cover slip in Etellan and examined by light microscopy at 400x. Negative control was buffered Tris saline solution in substitution of primary antibody. Normal canine prostate values for cytokeratin and PSA were considered as reference and a normal canine lymph node was used as a positive control for CD3 and CD79a.

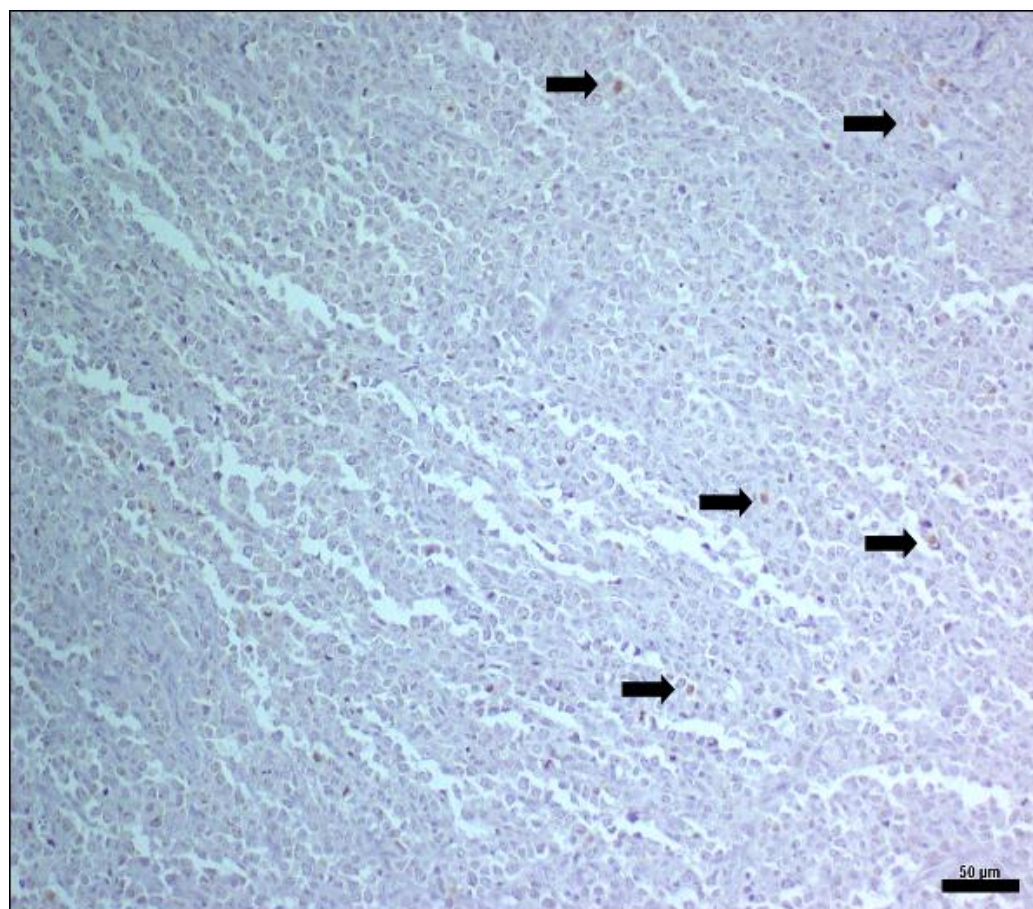
All analyzed samples showed strongly positive for anti-CD3 antibodies (Figure 3) and were negative for anti-CD79a antibodies (Figure 4), considered typical of a T cell source.

Figure 3. CD3 staining in the prostate of the described patient. Note the intense positive staining of neoplastic lymphocytes (brown staining), indicating a T immunophenotype. Immunohistochemistry, dog prostate, 400x magnification.



When submitted to immunolabeling, both epithelial cells and prostatic secretion were labeled with PSA antibodies (prostatic specific antigen) (Figure 5). The immunohistochemical profile performed allowed the identification of the definitive diagnosis (lymphoma), as well as providing the immunophenotype of the tumor (cellular origin - T cells).

Figure 4. Note proliferation of round cells negative for CD79a (B cell marker). However, there is the presence of tumor-infiltrating lymphocytes (arrows) positive for the CD79a protein (positive internal control). Immunohistochemistry, dog prostate, 200x magnification.



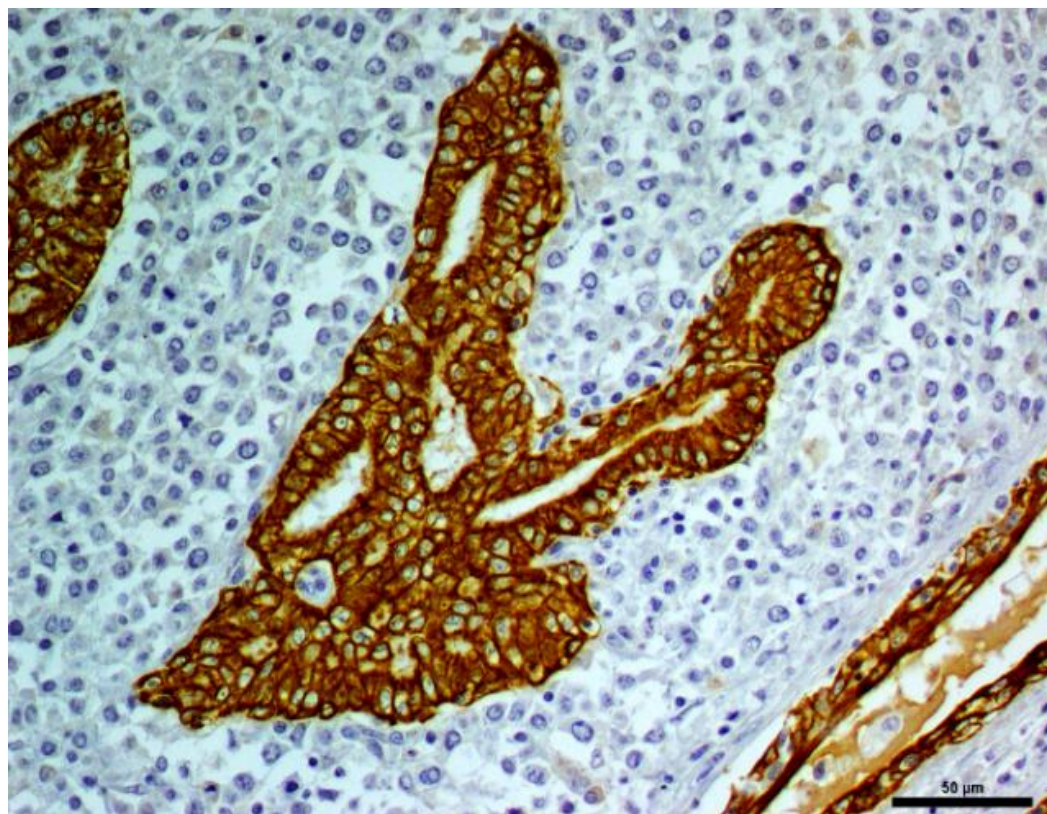
As the identified lymphoma was external to tissue source and considering the patient's clinical history, the presented clinical signs and tumor position, the lymphoma was then classified as extranodal, rarely diagnosed in dogs.

3. Discussion

Abnormalities found in the urine tract were linked to the increase in prostate volume causing compression of the urethra, similar to that reported by Watanabe [16] and Di Donato [17]. The fact that breed and age can influence prostatic size should be noted, especially in dogs of advanced age, which already tend to present prostatic hyperplasia.

Structural analysis can indicate prostatic disease, and of the many diagnostic tools available, ultrasonography is optimal in this assessment [18]. Besides position in the abdominal cavity, ultrasonography imaging can be used for assessing symmetry and echotexture. The prostate assessed in the reported case did no longer present a normal bi-lobulated outline due to the presence of neoplasia, a commonly found occurrence as corroborated by Di Donato et al. [17], who found similar structural changes in seven of five studied dogs.

Figure 5. Note intense positive staining of prostate epithelial cells and prostate secretion for prostate-specific antigen (PSA) protein. Positive expression indicates prostatic origin of the remaining epithelial tissue. Neoplastic cells are negative for PSA. Immunohistochemistry, dog prostate, 400x magnification.



A suggestive diagnosis was obtained based on FNAC results. The presence of lymphoid cells was identified by cell morphology and complement component analysis [19, 20]. A definitive diagnosis for neoplasia was established by histopathological analysis [21], concluded after evaluation of prostate parenchyma and cell structure, and identification of malignant cellular proliferation [22]. As a rule, cytology provides the presumptive result, while histopathology reveals the definitive diagnosis. The choice of cytology as the first diagnostic method was due to the fact that it is a cheap test, easy to perform and provides quick results. The labeling of specific molecules such as CD79a (in B cell lymphoma) and CD3 (in T cell lymphoma) by immunohistochemical procedure can be used to differentiate T cell and B cell lymphoma. This can provide a more precise diagnosis of tumors [10], as in the present report.

The extranodal lymphoma is classified as stage V and compared to another lymphoma, usually presents the worst prognosis. Nevertheless, when found as a solitary mass, surgical resection can mitigate aggressiveness of growth [23]. Unsuccessful treatment was due to the possible presence of dissemination in the urinary vesicle and the abnormalities of the prostate found in the reported case. If the urinary bladder was viable, treatments such as surgery, chemotherapy, radiotherapy, targeted therapy or immunotherapy could be suggested and contribute to greater patient survival [24].

4. Conclusion

The proliferation of lymphocytes externally to lymphoid tissue is considered rare and can lead to a great diversity of clinical signs according to cell source. Treatment outcome can vary, depending on biological behavior, cell differentiation, tumor progression,

occurrence of metastasis and time of diagnosis. Therefore, early investigation of prostate changes and new reports are necessary to establish appropriate therapies.

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