Primary adenocarcinoma of the seminal vesicles: a phantom tumor
Seminal vezikülün primer adenokarsinomu: bir fantom tümör

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ABSTRACT
Primary adenocarcinoma of the seminal vesicles (ASV) is a very rare neoplasm with less than 50 histologically confirmed cases reported in the literature. The diagnosis is complex and is based on a combination of immunohistochemical, clinical and radiological findings. Biopsy is not always conclusive, and surgical resection is usually required to determine whether the tumor originated from the seminal vesicles. We present a case of primary ASV that was discovered upon investigation of inguinal lymphadenopathy. A history of recent hormonal manipulation for the treatment of infertility may be associated with the development or the progression of this rare tumor.

Key words: Adenocarcinoma; seminal vesicle.

ÖZET
Seminal vezikülün primer adenokarsinomu (SVA), histolojik olarak doğrulanmış ve literatürde rapor edilmiş 50'den az vakaya çok nadir görülen bir neoplazmadır. Teşhisi karmaşık ve immünohistokimyasal, klinik ve radyolojik bulguların bir kombinasyonuna dayanıyor. Biyopsi her zaman ediciliği de olsa ve tümörün seminal veziküllerden orijin alıp almadığına karar vermek için genellikle cerrahi reseksiyon gereklidir. Inguinal lenfadenopati incelemesine dayanarak bulunan primer SVA'lı bir olgu sunmaktadır. İnfertilite tedavisi için yakın zamanlı hormonal manipülasyon öyküsü, bu nadir tümörün gelişmesi veya ilerlemesiyle ilişkili olabilir.

Anahtar sözcükler: Adenokarsinoma, seminal vezikül.

Introduction
The seminal vesicle is often invaded by locally advanced prostate cancer but is rarely the site of primary tumors. In fact, carcinomas arising from the seminal vesicles are very rare neoplasms and most of them are adenocarcinomas. Less than 50 histologically confirmed cases have been reported in the literature.[1]

The presenting symptoms are not cancer specific and clinical examination is of limited value in the initial stages of the disease. For these reasons, the diagnosis is extremely difficult and in most cases, the diagnosis is established at a disease stage when a cure is not possible.[2] We present a case, conduct a literature review and discuss the diagnostic and treatment-related issues.

Case report
A 46-year-old Caucasian man was admitted with bilateral inguinal lymphadenopathy and lymphedema. He reported a medical history of a left inguinal hernia repair (3 months prior to presentation), a history of chronic prostatitis that was partially treated with oral quinolones (5 years prior to presentation) and a history of a gastric ulcer (3 years prior to presentation). Cigarette smoking and alcohol abuse were also reported. There was no history of sexual transmitted diseases (STD). The patient underwent a work-up for infertility six months prior to his admission and was found to have oligospermia despite his normal testosterone levels; he had then undergone hormonal therapy for six months prior to his presentation. No history of cryptorchidism was reported.
On physical examination, the patient presented with extended edema involving the groin, suprapubic area, scrotum, body of the penis and the lower limbs. The left superficial inguinal lymph nodes were moderately enlarged, palpable and painful. A pair of palpable, painless left subclavian lymph nodes was also noted. The patient had a normal, painless digital rectal examination. On admission, his blood count and blood chemistry profile were normal. The tumor marker values, including prostate specific antigen (PSA), were within normal limits.

Plain radiography of the chest and computed tomography (CT) of the chest and brain were negative for primary and metastatic disease. Because the chest CT confirmed the presence of left subclavian lymph nodes, the patient underwent gastroscopy. A biopsy of an ulcerous duodenal lesion showed edema, congested blood vessels and scarce inflammatory infiltrations. Both CT and magnetic resonance imaging (MRI) of the abdomen failed to identify the primary tumor.

A biopsy of the left superficial inguinal lymph nodes revealed inflammatory infiltrations in the entire specimen. One node was focally infiltrated by a malignant neoplasm showing histologic and immunohistochemical characteristics of a non-mucin producing, poorly differentiated carcinoma (Figure 1). Staining was positive for cytokeratins and negative for alpha1-fetoprotein (A1FP), CD117 and human chorionic gonadotropin (HCG).

Due to the non-specific radiology, laboratory and pathology findings, the patient underwent a positron emission tomography (PET) scan. Abnormal PET findings appeared to be limited to the right lung and the lower abdomen (Figure 2).

The patient then underwent a colonoscopy and a transrectal ultrasound of the prostate (TRUS). While colonoscopy revealed no pathology, the TRUS showed a non-specific inhomogeneous left transitional zone of the prostate but failed to identify a focal lesion. The seminal vesicles appeared normal although the left one was slightly larger. A filing defect in the bladder neck was suspicious for a bladder tumor (Figure 3). Urine cytology revealed few urothelial and squamous cells and non-specific high-grade malignant cells arranged in groups. On cystoscopy, the bladder neck was congested and edematous, while the remaining bladder mucosa was normal. The biopsy specimens from the bladder neck, prostate and seminal vesicles were obtained during the transurethral resection and TRUS. According to the pathology report, the specimens consisted of fibromuscular tissue containing hyperplastic prostate acini and solid accumulations of malignant cells of various sizes. Immunohistochemically, these malignant cells were found to react with polyclonal cytokeratin; however, they exhibited negative PSA, prostatic acid phosphatase (PAP) and R63 staining. Normal seminal vesicles epithelia were not observed. Malignant cells from the prostate and seminal vesicle biopsies were found to have morphological and immunological characteristics that were similar to those of the malignant cells of the lymph node block specimen. Malignant cells from the bladder neck specimens also exhibited a similar immunophenotype.

Patient medical records were reviewed and a missed lesion that was located in the left seminal vesicle on the CT scan was identified (Figure 4). A diagnosis of primary adenocarcinoma of the seminal vesicle (ASV) was eventually made and the patient...
underwent further evaluation. Because the patient was found to have metastases based on the bone scan, the poor prognosis was explained and he was started on chemotherapy (docetaxel). Unfortunately, he died two months later due to complications.

**Discussion**

ASV typically presents with advanced, symptomatic disease. Among the most common presenting symptoms are hematuria and hematospermia, but urinary infection, dysuria, painful defecation and pelvic pain have also been reported.[3] These symptoms are not cancer-specific and when they occur as the presenting symptoms of cancer, other malignancies are far more common than SVC. Actually, our patient had no similar symptoms and thus the diagnosis was further delayed.

The diagnosis of ASV is generally based on a combination of morphological, immunohistochemical and clinical findings, including radiologic examination. CT and ultrasonography may be helpful in localizing the tumor. The radiological findings are usually consistent with a solid or cystic mass between the rectum and the bladder or prostate.[4] Rarely, an expansion of the seminal vesicle is evident, which may be misinterpreted, as occurred in the present case.[4]

The macroscopic features of ASV have not been extensively studied. It seems that ASV is associated with two main gross anatomical patterns. Some tumors have firm cut surfaces with irregular margins,[5,6] whereas others are predominantly cystic and are often filled with brownish fluid, pus or necrotic material.[7,8] In cases with cystic appearance, the cystic appearance of ASV can be suggestive of an old hemorrhage or abscess rather than cancer.

The histological diagnosis of primary ASV has been debatable over the past 30 years. The accepted criteria include no other demonstrable tumor and either an anaplastic or papillary histological appearance.[3] In several cases however, some mucinous differentiation is present.[9] Desmoplasia may also be observed around infiltrating glands.[10] The most recent World Health Organization (WHO) classification criteria also include the lack of PSA and PAP immunostaining.[8]

All published reports on the immunohistochemistry of ASV have shown that these tumors are always negative for PSA and PAP stains; however, CA125 and CGA staining is positive in most cases.[11] CK7 staining may be strongly positive, whereas CK20 staining is usually negative.[3] This keratin profile might be helpful in the differential diagnosis of adenocarcinomas whose primary site is the prostate gland (these are usually CK7 negative and CK 20 positive). Similar to ASV, urinary bladder adenocarcinomas are usually CK7 positive and CK 20 negative and thus must be distinguished from SVC based on the topography, morphology and lack of CA125 expression. Extensive immunohistochemistry performed on all the specimens from our patient confirmed the above observations.

The pathogenesis of ASV is unknown. However, the involvement of hormonal factors, as occurred in our case, should not be excluded. Although the chemopreventive activity of estrogen inhibitors (tamoxifen) has been proposed for androgen-promoted carcinomas of the rat seminal vesicle and prostate,[12] simultaneous administration of testosterone and estrogen inhibitors may result in a large amount of circulating testosterone[13] which can trigger the development of ASV.[14]

The prognosis of these tumors is extremely poor because they are often in the advanced stages of the disease when they are discovered and therefore, the majority of patients die within 3
years of diagnosis. Surgery, radiotherapy, chemotherapy and hormonal therapy have been attempted with dismal results. Recently, Thyavihally et al investigated the efficacy of chemotherapy with 5-fluorouracil plus leucovorin plus oxaliplatin along with bilateral orchiectomy.

In conclusion, primary ASV is an extremely rare and poorly understood neoplasm. Certain difficulties, such as the absence of symptoms at an early stage, the lack of well-defined diagnostic criteria and limited experience, result in delayed diagnosis. Because prompt diagnosis and treatment may improve long-term survival, the accurate recognition of this neoplasm is important.

Conflict of interest
No conflict of interest was declared by the authors.

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