Sclerosing Adenosis of the Prostate—A Benign Lesion Similar to Prostate Cancer: A Case Report and Literature Review

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Abstract
Sclerosing adenosis of the prostate (SAP) is a rare benign non-neoplastic small acinar hyperplasia. Like sclerosing adenosis of the breast, which is confused with breast cancer, SAP is a trap in the pathological differential diagnosis of benign and malignant lesions of the prostate. We report such a case to help colleagues better distinguish and diagnose such diseases. A 75-year-old patient with SAP had a prostate specific antigen (PSA) level of 11.0 ng/mL, and he had been suffering from progressive dysuria for 3 years. The central glandular area and the right periphery of the prostate were found to have nodular low signals on magnetic resonance imaging (MRI). Prostate biopsy showed that basal cells were positive for P63 and P504s, few basal cells were positive for S-100, and the positive rate of Ki-67 was approximately 2%. We consider that the possibility of SAP is high. The patient was treated conservatively and was discharged in good health, free of dysuria and other problems. SAP is a rare benign lesion that is easily misdiagnosed as prostate cancer. The prostatic gland tube has a complete basal cell layer surrounding it, as well as myoepithelial cell metaplasia of basal cells, which is a key trait in distinguishing it from prostate cancer. Although the latest research indicates that SAP does not require treatment, the question of whether it is a risk factor for prostate cancer remains unanswered.

Keywords
prostate, sclerosing adenosis, prostate cancer, pathology, case report

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Introduction
Prostate biopsy is the gold standard for the diagnosis and evaluation of prostate cancer. However, a growing number of benign prostate lesions that could be mistaken for prostate cancer have been discovered in prostate biopsy, drawing the attention of physicians and pathologists (Luque et al., 2003). Sclerosing adenosis of the prostate (SAP) is one of the rare benign prostate lesions; according to statistics, 2% of patients diagnosed with T1a of prostate cancer in the past actually have sclerosing adenosis (Bostwick & Chang, 1999). In the late 1980s, Young and Clement characterized the histological and immunohistochemical features of SAP, noting that it was similar to homonymous breast lesions (Young & Clement, 1987). This disease most commonly affects the transitional area of the prostate and is typically discovered by chance in the pathology report following a transurethral resection of the prostate (TURP) or prostate biopsy. SAP has a distinct microscopic structure and immunophenotype. There is a complete and continuous basal cell layer around the gland tube, and some of the basal cells are prone to myoepithelial metaplasia (Grignon et al., 1992). We must be aware of the histological features of SAP to avoid misdiagnosis.

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This paper describes the characteristics of SAP and discusses its differential diagnosis with prostate cancer by reviewing related literature and analyzing the pathology report and immunohistochemistry results.

**Case Presentation**

A 75-year-old man with a 3-year history of progressive dysuria and a 10-day catheterization visited our hospital. For 3 years, the patient had dysuria, prolonged micturition time, reduced urinary flow, short distance, endless dripping urine, and other symptoms without evident reason but had not received therapy. In addition, there was no urgent urination, no painful urination or gross hematuria. He smoked for 30 years with an average of 30 cigarettes per day and has given up smoking for 15 years. He has a 15-year history of hypertension and takes valsartan orally every day for treatment, and the impact of blood pressure management was ideal. He had no previous history of diabetes, tuberculosis, or surgical, trauma, or transfusion procedures. In addition, there were no other patients in the family who had similar symptoms.

Digital rectal examination showed that the prostate was enlarged and tough. Its surface was smooth without nodules, and the central sulcus disappeared. In addition, there was no tenderness in the prostate and no blood stain on the finger-cot. The routine blood test showed that there were no abnormalities, and routine urine tests showed that the number of white blood cells, red blood cells, and epithelial cells increased and the urine protein was positive. PSA and carcinoembryonic antigen (CEA) concentrations were 11.0 and 5.85 ng/mL, respectively, which exceeded the normal range and other tumor indicators were normal.

Ultrasound of the urinary system showed that the prostate volume increased significantly (5.4 * 4.8 * 4.6 cm), the shape was full, and the boundary was clear and regular. The echo of the parenchyma was uneven, and patchy hyperechoic areas could be seen. Magnetic resonance imaging (MRI) confirmed the enlarged prostate (5.8 * 4.7 * 5.5 cm), and irregular nodular abnormal signals were found in the central gland area and the right peripheral zone (Figure 1). T2W and T2W SPAIR images showed slightly low signals and high signals, respectively, and the prostate imaging reporting and data system (PI-RADS) score was 5 points.

Subsequently, the patient underwent ultrasound guided transperineal prostate biopsy, with a total of 16 cores, including 12 systematic core biopsies and four targeted core biopsies. Pathological results demonstrated that six of 16 prostate biopsy tissues showed hyperplasia disorder of some glandular epithelium and nuclear enlargement and heterogeneity. Immunohistochemistry showed that P63 was positive, suggesting that most of the hyperplasia basal cells still exist, but the characteristics are not easy to identify. In addition, epithelial cells were positive for P504S, and few basal cells were positive for S-100. The positive rate of Ki67 was approximately 2%. Combined with the above results, it is concluded that the possibility of SAP is high (Figure 2).

The patient received conservative treatment after discharge and took tamsulosin and finasteride orally once a day and one tablet at a time. Three months later, we followed up the patient and found that the patient was in good condition without dysuria or other complications. Prostate specific antigen, urinary system ultrasound and computed tomography (CT) were not reexamined because the patient did not return to the hospital after discharge.

**Figure 1. Ultrasound and MRI Images**

*Note.* A. Ultrasound showed that the prostate volume increased, and patchy hyperechoic areas could be seen in the parenchyma. B and C. MRI revealed abnormal signals in the central gland area and the right peripheral zone (B. T2W-TSE; C. T2W-TSE SPAIR). MRI = Magnetic Resonance Imaging.
Discussion

SAP is considered to be a rare type of adenosis and was first reported by Young et al. in the 1980s (Young & Clement, 1987). In addition, Young also identified that the lesion is a rare benign prostatic hyperplasia that is similar to sclerosing adenosis of the breast in terms of histology and immunophenotype. As this disease in the breast is easily confused with breast cancer, SAP is a difficulty in the pathological differential diagnosis of benign and malignant prostate lesions.

The differential diagnosis between SAP and prostate carcinoma is mainly manifested in the following aspects (Sakamoto et al., 1991): (a) SAP is mainly located in the transitional zone, and the lesion boundary is clear although there is no capsule. In contrast, prostate cancer exhibits diffuse invasive growth and is more likely to occur in the peripheral zone. (b) The mesenchyme of SAP is mainly composed of fibroblasts and a small number of smooth muscle cells. The glandular ducts are often squeezed into cords as a result of interstitial edema and hyperplasia, and the glandular cavity narrows or vanishes. (c) Around the gland, complete basement membrane thickening can be detected in SAP, but the prostate carcinoma gland lacks complete basement cells. (d) Despite the disappearance of amyloid bodies in the glandular cavity, there is a lack of eosinophilic crystals common in well-differentiated adenocarcinoma. (e) The atypia of SAP is not obvious and the matrix has acidic mucin and collagen deposition.

Although there are the above differences between SAP and small acinar carcinoma in hematoxylin-eosin (HE)-stained sections, the final diagnosis of the disease depends on immunohistochemistry (Collina et al., 1992; Jones et al., 1991). There were intact basal cells with 34βE12, CK5/6, and P63 positivity around the glandular duct in SAP. At the same time, basal cells exhibit a proclivity for myoepithelial metaplasia, as evidenced by the presence of S-100 protein, smooth muscle actin (SMA), and other myoepithelial markers. The features mentioned above are the diagnostic basis of SAP.
P504S, which is also known as alpha-methylacyl-CoA racemase or AMACR, is a cancer stem cell marker. In 2001, Jiang et al. first identified that P504S was a highly sensitive and specific positive marker for prostate cancer, while Hameed subsequently thought that P504S expression could be found in high-grade prostatic intraepithelial neoplasia (PIN), atypical adenomatous hyperplasia (AAH) and benign prostate (Hameed & Humphrey, 2005; Jiang et al., 2001). In our case, we found that some epithelial cells in SAP were positive for P504S and that the expression of S-100 protein was weak. As the number of cases was small, we still do not know whether this is a new trap in the immunohistochemical expression of sclerosing adenopathy or a precancerous lesion such as high-grade PIN.

PI-RADS, jointly proposed by the European Society of Urogenital Radiology and the American College of Radiology, is applicable to prostate MRI evaluation. PI-RADS makes prostate imaging reports standardized and reduces fuzzy image descriptions and diagnosis results through scoring (Turkbey et al., 2019). The patient in this case had a PI-RADS score of 5, indicating that there is a great possibility of cancer, which is also a reason why SAP is easily misdiagnosed as prostate cancer.

To date, no relationship between SAP and prostate cancer has been found. Some studies have identified that SAP does not require special treatment, and its prognosis is good. After an average follow-up of 33 months in five SAP patients, it was reported that none of the patients progressed to prostate cancer (Cheng & Bostwick, 2010; Jones et al., 1991). However, this pathological phenomenon should still attract our attention.

This article also has some limitations. For example, the patient was in a state of catheterization due to difficulty in urination. Indwelling catheter may also be a reason for the increase in PSA, which makes diagnosis difficult. Second, the patient did not return to the hospital for a reexamination of PSA and related imaging examinations so that we could not evaluate the prognosis of patients in detail. Third, the case amount of SAP is too small to be convincing. We will continue to pay attention to this disease in the future and expand our sample size.

Conclusion
In summary, SAP is an uncommon benign hyperplasia with distinct histological, immunophenotypic, and histochemical characteristics. Some markers in basal cells around prostate glands, such as 34βE12, P63, S-100, and SMA, can be utilized to distinguish SAP from adenocarcinoma. The latest studies have reported that SAP does not require treatment, but whether it is a risk factor for prostate cancer remains controversial. Therefore, we should pay attention to the differential diagnosis and avoid confusion with prostate cancer.
Data availability statement
All data in this paper can be obtained by contacting the correspondence author.

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