

A 5-year follow-up of primary seminal vesicle adenocarcinoma

A case report

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Abstract

Rationale: Primary seminal vesicle adenocarcinoma (PSVA) is an extremely rare malignancy that should be carefully differentiated from cancer originating in the prostate, colon or bladder. Without standard guidelines, radical resection is considered a mainstay treatment, providing the best prognosis. However, as manifestations of PSVA are not detected in early stages, the majority of cases of PSVA are diagnosed at late stages, contributing to poor prognosis.

Patient concerns: We described the case of a PSVA patient confirmed by histopathology and immunohistochemistry (IHC) staining positive for carbohydrate antigen-125 (CA-125) and negative for prostate specific antigen (PSA).

Diagnosis: Primary seminal vesicle adenocarcinoma.

Interventions: Surgery was carried out at the beginning, however, residual tumor was verified; thus 3 cycles of chemotherapy with a regimen of paclitaxel and cis-platinum were performed, followed by radical pelvic radiotherapy with a dose of 60 Gray in 30 fractions; then, another 3 cycles of the same chemotherapy were carried out.

Outcomes: At the moment, the patient is still under follow-up and has been disease-free for more than 5 years.

Lessons: Our manuscript describes a patient with PSVA with long-term survival and supplies a successful management strategy for this malignancy.

Abbreviations: CA-125 = carbohydrate antigen-125, CEA = carcinoembryonic antigen, CK = cytokine, CT = computed tomography, EUS = endoscopic ultrasound, IHC = immunohistochemistry, MRI = magnetic resonance imaging, MUC6 = mucin-6, PAP = prostatic acid phosphatase, PSA = prostate specific antigen, PSVA = primary seminal vesicle adenocarcinoma.

Keywords: case report, diagnosis, long-term survival, primary seminal vesicle adenocarcinoma, treatment

1. Introduction

Primary seminal vesicle adenocarcinoma (PSVA) is an extremely rare malignancy; only approximately 60 cases have been reported to date.^[1] It usually manifests no symptoms in early stages, and when progressing, it may characteristically present as bloody urine, bloody sperm, or obstructive uropathy. No clear etiological factors have yet been demonstrated. Due to a lack of symptoms in early stages, the majority of cases are found at a

late stage at the time of diagnosis, with direct invasion of the prostate or metastasis to the lung, resulting in a poor prognosis.^[2] It is obvious that primary carcinoma originating in the prostate, rectum, or bladder is much more common than primary carcinoma originating in the seminal vesicles, so PSVA should be carefully differentiated from malignancies originating in nearby tissues; specifically, PSVA with prostate invasion should be definitely differentiated from primary prostate carcinoma that has invaded the seminal vesicles, as the latter is more common than the former.^[3] Fortunately, immunohistochemistry (IHC) staining of most PSVAs is characterized by staining that is positive for carbohydrate antigen-125 (CA-125) and negative for prostate specific antigen (PSA).^[4,5]

Currently, there is no standard guideline for the treatment of PSVA. It has been accepted that complete resection of local disease is the most reliable treatment with the best prognosis.^[6] However, complete resection is always difficult due to the complex anatomy around the seminal vesicles. After en bloc surgery, it is disputed whether to follow up with chemotherapy, radiotherapy or endocrine (anti-androgen) therapy. Undoubtedly, for patients with residual tumor after surgery, it is necessary to carry out chemotherapy and/or radiotherapy. For metastatic PSVA, it is effective to perform chemotherapy, anti-androgen therapy or a combination of both therapies.^[6]

Herein, we report on a PSVA patient whose disease was confirmed by histopathology in July 2012. After surgery, residual tumor was verified by post-surgery magnetic resonance imaging (MRI). Three cycles of chemotherapy were performed, and radical radiotherapy was then performed, followed by another 3

Editor: N/A.

The case report has been approved by the ethics committee of Tongji Hospital affiliated with Tongji Medical College of Huazhong University of Science and Technology.

The patient has given his consent for this case report to be published.

The authors declare no conflicts of interest.

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Medicine (2018) 97:41(e12600)

Received: 8 May 2018 / Accepted: 3 September 2018

<http://dx.doi.org/10.1097/MD.0000000000012600>

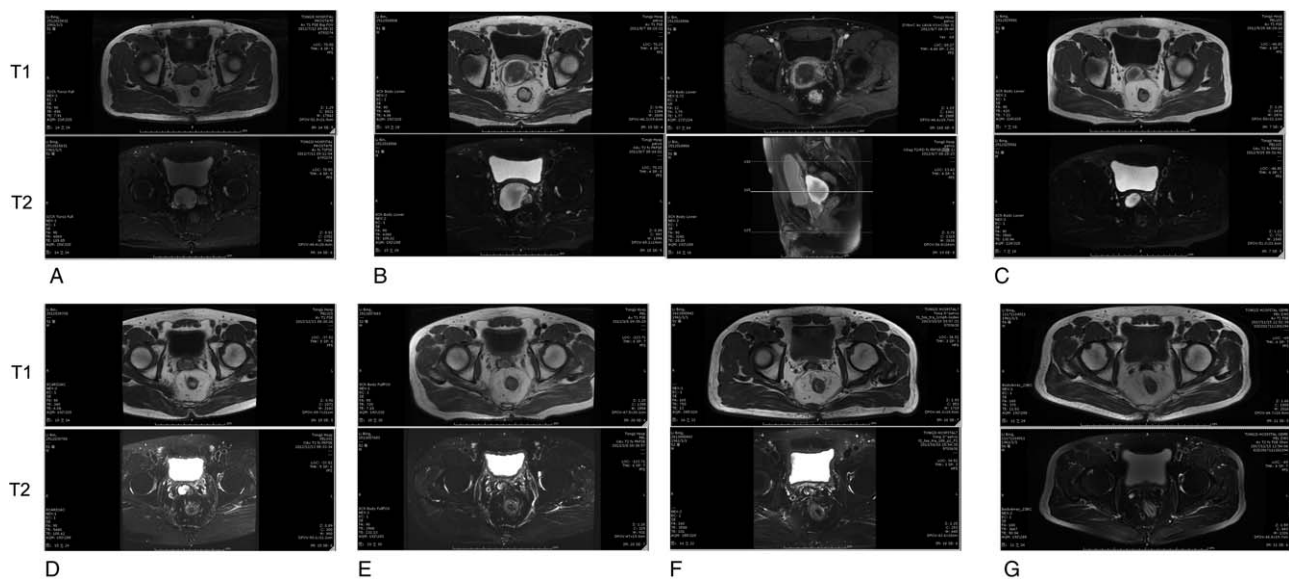


Figure 1. Representative MRI for the patient. A, pre-surgery; (B) post-surgery; (C) after 2 cycles of chemotherapy; (D) after 3 cycles of chemotherapy plus radiotherapy; (E) 6 months after surgery; (F) 1 year after surgery; (G) 5 years after surgery. T1, MRI T1 weight; T2, MRI T2 weight.

cycles of chemotherapy. To date, the patient has been monitored for more than 5 years and still remains disease-free.

2. Case report

A 51-year-old man without a history of past illness whose main complaints were repeated hemospermia for 2 years and hematuria for 2 weeks came to Tongji Hospital in July 2012. Physical examination, including digital rectal examination (DRE), did not reveal any indications. Pelvic MRI showed a mass with mixed cystic and solid signals in the district of the right seminal vesicle (Fig. 1A). No distant metastases were found in this patient. Serum tumor markers indicated that carcinoembryonic antigen (CEA) and PSA levels were both normal, while CA-125 levels were above normal at 137 U/mL. Surgery was carried out, and a tumor with a diameter of approximately 4 centimeters with an unclear border was detected adhering to peripheral tissue and was carefully removed. Local lymphadenectomy was not performed. Post-operative histopathology confirmed the diagnosis of PSVA with IHC staining of that was negative for CEA, negative for PSA, and positive for CA-125 (Fig. 2A–E). Unfortunately, the tumor was not resected en bloc according to the surgeon and was confirmed by a post-surgery MRI (Fig. 1B) that showed a ring-like cystic cavity with marginal enhancement above the prostate, behind the bladder, and in front of the rectum. After a multidisciplinary discussion, 3 cycles of chemotherapy using a regimen of 150 mg/m² paclitaxel plus 60 mg/m² cis-platinum were performed; then, radical pelvic radiotherapy with a dose of 60 Gray in 30 fractions was carried out followed by 3 cycles of the same chemotherapy. The draining lymph node was not prophylactically irradiated since pre-surgery MRI imaging showed no metastasis to the lymph node. Concurrent chemoradiotherapy was not considered since there was no evidence to support its use at that point. The side effects of sequential chemotherapy and radiotherapy were acceptable, and no severe adverse effects were observed in this patient. Endocrine therapy was not performed on this patient. After finishing treatment, the patient was assessed every 3 months in the first

year and every 6 months in the following 2 years (Fig. 1C,D). The last follow-up was November 2017 (Fig. 1E). We know this patient is still disease-free, and he has been followed for longer than any other PSVA patient in a published report.

3. Discussion

The first case of PSVA was reported in 1925 by Lyons.^[7] However, less than 60 cases have been reported to date, showing the exceedingly rare incidence of this malignancy.^[1] The age of onset is quite varied, ranging from 19 to 90 years old.^[6] Interestingly, there are also cases of bilateral PSVA and primary seminal vesicle squamous cell carcinomas and sarcomas.^[1,8–12]

Diagnosis of PSVA is very difficult at an early stage due to a lack of specific symptoms. At an advanced stage, hemospermia, hematuria, or obstructive uropathy may occur; however, it is difficult to diagnose a definite location and cause, such as inflammation or tumors. Even if a mass is found in the seminal vesicles or nearby, tumors originating in surrounding organs with seminal vesicle invasion are more common.^[6] Therefore, when a diagnosis of PSVA is made, it should be carefully differentiated from potential surrounding malignancies such as tumors in the rectum, bladder or prostate, especially prostate carcinoma, that often exhibit invasion of the seminal vesicle in the clinic.

Local imaging is useful and necessary for the diagnosis of PSVA. Endoscopic ultrasound (EUS) through the rectum, pelvic computed tomography (CT) or MRI could provide a considerable amount of helpful information about a seminal vesicle tumor, which is very valuable for differentiating between types of tumors, designing operations, and predicting possible complications. Interestingly, there was one PSVA case that was diagnosed by a biopsy with no abnormal findings by EUS through the rectum, so it is possibly more reliable to use high resolution CT or MRI to detect the disease.^[12] However, EUS through the rectum should not be abandoned. In our case, MRI was always performed to detect the disease through the entire treatment and follow-up.

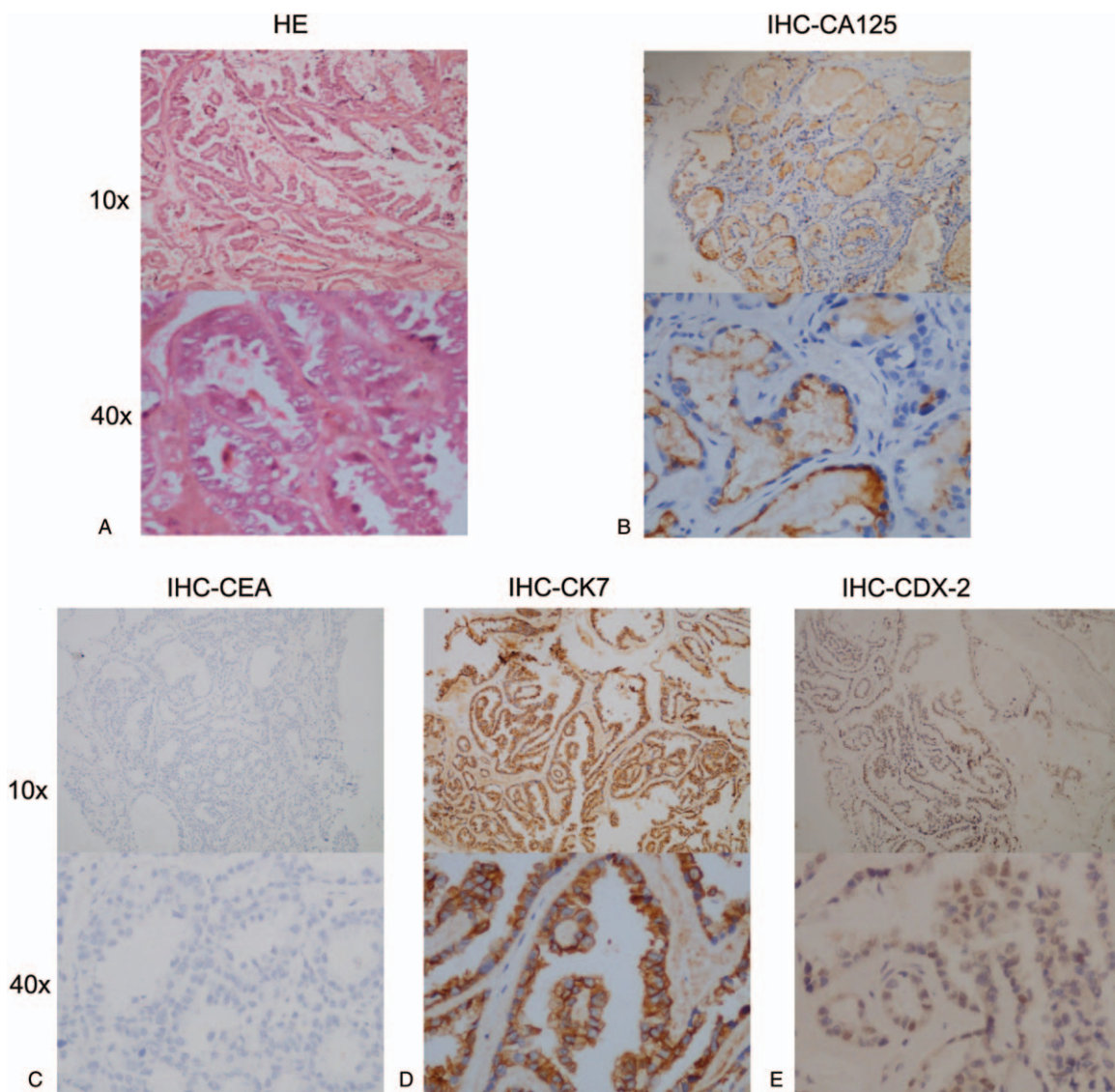


Figure 2. Representative pathologic images of the patient's tumor by hematoxylin and eosin (HE) staining and IHC. A, HE staining; (B–E) IHC of CA-125, CEA, CK7, and CDX-2, respectively. 10 ×, 10 times amplified; 40 ×, 40 times amplified.

The definite diagnosis of PSVA depends on histopathology. It should always exclude the possibility that a surrounding tumor invaded the seminal vesicle because that disease state is more common than PSVA. In 1956, the diagnostic criteria for histopathology were proposed by Dalgaard and mentioned that: the tumor should be inside or mainly located in the seminal vesicle, with basic characteristics of carcinoma under macroscopy and microscopy; there should be no signs of other primary malignant tumors; and it was best for tumors to be papillary with normal seminal vesicle structure. These are the earliest pathologic criteria that depended on cell and tissue morphology without molecular markers, which are difficult to diagnose in poorly differentiated tumors.^[9] In 1984, Benson improved the former criteria by adding IHC markers of a negative PSA stain and a positive CEA stain.^[13] However, later on, it was noted that a negative CEA stain was much more common than a positive stain.^[14,15] Moreover, a positive signal for CA-125 in pathology or serum strongly supports the diagnosis of PSVA.^[4,5] However, for poorly differentiated tumors, CA-125 measurements could also be negative in serum or IHC, so negative staining of CA-125

does not exclude the diagnosis of PSVA. CA-125, a tumor marker expressed in the Mullerian duct that is also elevated in PSVA, indicates some intrinsic homology between the female and male reproductive systems. Cytokines (CK) also play an essential role in the pathologic diagnosis of PSVA. It is believed that CK7 should stain strongly positive by IHC, while CK20 staining should be negative in PSVA; in contrast, in colorectal cancer, CK7 staining should be negative, while CK20 staining should be strongly positive.^[5,14,16] Furthermore, mucin-6 (MUC6) is thought to commonly stain positive in PSVA^[17] (Table 1). In

Table 1

Common IHC marker for cancer.

Marker	CEA	CA-125	PSA/PAP	CK7	CK20	MUC6
PSVC	–	+	–	+	–	+
Prostate cancer	–	–	+	–	–	–
Colorectun cancer	+	–	–	–	+	–
Bladder cancer	+	–	–	+	+	–

our patients, CA-125 expression is positive by both serum and IHC pathology, CK7 expression is positive by IHC, and CEA and PSA expression levels are both negative by IHC (Fig. 2).

Until now, there has been no standard treatment for PSVA. Complete excision is the mainstay for primary treatment, providing the best prognosis.^[2,6,18] However, operating on PSVA is difficult due to its cystic structure and complicated anatomical relationships with the surrounding tissue. Moreover, it is still debated whether to prophylactically resect draining lymph nodes. There is no evidence on repeating operations after a first excision with residual tumor or positive margins. It is also disputed whether to follow adjuvant chemotherapy or radiotherapy after complete resection of PSVA. However, it is certain that radiotherapy is necessary for residual tumors or tumors with positive margins after surgery. It has been reported that radiotherapy is a useful compensatory method for partial excision or residual tumor.^[19] Due to a few reports about chemotherapy in PSVA, the effect of adjuvant chemotherapy after surgery remains unclear. The chemotherapy regimen is diverse, from a single drug to combined drugs, varying the prognosis.^[2,4,16] It is reported by Campobasso et al^[1] that a patient with residual tumor after surgery was treated with 4 cycles of chemotherapy using a regimen of gemcitabine plus cisplatin and then radical radiotherapy. Our patient with residual tumor after surgery underwent 6 cycles of chemotherapy with a regimen of paclitaxel plus cis-platinum and radical radiotherapy with a dose of 60 Gy in 30 fractions between the third and fourth chemotherapy cycles. There are a few reports on endocrine therapy for PSVA. Anti-androgen therapy could be effective as an adjuvant or palliative treatment for androgen-dependent PSVA.^[20] However, it is unclear whether long-term anti-androgen therapy is necessary for patients with complete excision, even if their tumors are androgen-dependent.

In conclusion, PSVA is an extremely rare malignant tumor originating from the Wolffian duct of the male reproductive system. Until now, there has been no aggregated standard for its diagnosis and treatment. In the clinic, it should be carefully differentiated from tumors originating in surrounding tissues with the help of some useful markers, such as CA-125, PSA, PAP, CK7, and CK20. Although en bloc dissection could afford the best prognosis, it is always difficult to perform. For patients with residual tumors or positive margins after surgery, chemotherapy and radiotherapy could be an effective approach with tolerable side effects. Our patient who, as far as we know, has the longest disease-free survival time that has been reported, provides a useful example of the diagnosis and treatment of PSVA.

Author contributions

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Investigation: Yueqiang Jiang.

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