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Review Article

Adenocarcinoma of Seminal Vesicle: Review and Update

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Abstract

Primary adenocarcinoma of the seminal vesicle is a rare condition with only approximately 60 cases reported in the literature. The unusual characteristics of the neoplasm makes its diagnosis difficult and treatment strategies differ as there are no specific guidelines available. Diagnosis of primary adenocarcinoma of prostate gland is confirmed microscopically. Primary adenocarcinoma neoplasms of the seminal vesicle are localized primarily within the seminal vesicle and in order to confirm a diagnosis of primary adenocarcinoma of seminal vesicle, it is important to exclude invasion of malignant neoplasm from the prostate gland (by undertaking PSA / PAP tests), the rectum or other sites of the body. Primary adenocarcinoma of seminal vesicle usually exhibits a papillary adenocarcinoma simulating the architecture of normal seminal vesicle. Primary adenocarcinoma of seminal vesicle resembles prostatic duct adenocarcinoma Gleason patterns 3 or 4 or mucinous (colloid) carcinoma. Primary adenocarcinoma of seminal vesicle, is usually unresectable and patients who are afflicted by primary adenocarcinoma of seminal vesicle die within 2 years. The ensuing article has discussed in detail various aspects of primary adenocarcinoma of seminal vesicle, including an overview of primary adenocarcinoma of seminal vesicle, as well as miscellaneous narrations and discussions from some case reports, case series, and studies related to primary adenocarcinoma of seminal vesicle.

Keywords: primary adenocarcinoma of seminal vesicle; prostate cancer; bladder cancer; adenocarcinoma of rectum; biopsy; microscopy; histopathology; immunohistochemistry; papillary architecture

Introduction

Yin et al. [1] stated the following:

- Primary seminal vesicle adenocarcinoma (PSVA) is a very rare malignant tumour with only about 60 cases reported up to 2021 as documented by Campobasso et al. [2]
- It had been pointed out thar PSVA usually does not manifest with any symptoms during the early stages of the tumour, and when the tumour is progressing, it might typically manifest as bloody urine, bloody sperm, or obstructive uropathy.
- No clear aetiological factors had yet been demonstrated for PSVA.
- In view of a lack of symptoms within the early stages of the tumour, most cases of PSVA are found at a late stage at the time of diagnosis, with direct invasion of the prostate gland or metastasis to the lung, emanating in a poor prognosis. [3]
- It has been iterated that it is obvious that primary carcinoma emanating within the prostate gland, rectum, or urinary bladder is much more common in comparison with primary carcinoma originating within the seminal vesicles, so PSVA should be carefully distinguished from malignancies that originate within nearby tissues; specifically, PSVA with prostate invasion should be definitely distinguished from primary prostate carcinoma of the prostate gland which has invaded the seminal vesicles, in view of the fact that the latter is more common in comparison with the former. [4]
- 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). [5] [6]
- At the time of publication of the article, there was 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 [7] Nevertheless, complete resection is always difficult to undertake in view of the complex anatomy around the seminal vesicles. Following en bloc surgery, it is disputed whether to follow up with

chemotherapy, radiotherapy or endocrine (anti-androgen) therapy.

- Undoubtedly, for patients who have residual tumour pursuant to undergoing surgery, it is necessary to provide chemotherapy and/or radiotherapy. For metastatic PSVA, it is effective to undertake chemotherapy, anti-androgen therapy or a combination of both therapies. [7]

Considering the rarity of PSVA, it would be envisaged that majority of clinicians all over the world would not have encountered or managed a case of PSVA before. The ensuing article on primary adenocarcinoma of the seminal vesicle is divided into two parts: (A) Overview which has discussed general overview aspects of adenocarcinoma of seminal vesicle and (B) Miscellaneous narrations and discussions from some case reports, case series and studies related to primary adenocarcinoma of the seminal vesicle.

Aim

To review and update the literature on primary adenocarcinoma of the seminal vesicle.

Methods

Internet data bases were searched including: Google; Google Scholar; Yahoo; and PUBMED. The search words that were used included: Adenocarcinoma of seminal vesicle; seminal vesicle adenocarcinoma; carcinoma of seminal vesicle; and seminal vesicle carcinoma. --- references were identified which were used to write the article which has been divided into two parts: (A) Overview which has discussed general overview aspects of adenocarcinoma of seminal vesicle and (B) Miscellaneous narrations and discussions from some case reports, case series and studies related to primary adenocarcinoma of the seminal vesicle.

Results

[A] Overview

Definition / general statements

The ensuing general statements and definition had been provided on primary adenocarcinoma of seminal vesicle: [8]

- Primary adenocarcinoma of seminal vesicle is very rare, and its diagnosis needs to be confirmed by microscopically examination of a specimen of the seminal vesicle tumour. [8]
- Primary adenocarcinoma of seminal vesicle tumours should be localized primarily to the seminal vesicle and the clinician must exclude invasion from prostate gland by undertaking serum PSA / PAP tests as well must exclude origin of the tumour from the rectum or other sites. [8]
- Usually, a papillary adenocarcinoma resembling architecture of normal seminal vesicle is found. [8]
- Primary adenocarcinoma of seminal vesicle simulates prostatic duct adenocarcinoma Gleason patterns 3 or 4 or mucinous (colloid) carcinoma. [8]
- Usually, primary adenocarcinoma of seminal vesicle is unresectable and patients die within 2 years [8]
- Primary adenocarcinoma of the seminal vesicle is very rare, and the clinician needs to rule out prostate primary carcinoma; which is often mucin producing, and ulcerates through skin of scrotum [8]

Epidemiology [9]

It has been iterated that primary adenocarcinomas of the seminal vesicles are very rare [9] [10] [11] and they could be observed at a wide age range [9] [11].

Diagnosis

Diagnostic criteria [9]

The following modified diagnostic criteria have been described for diagnosis [1] [11]:

- The main primary adenocarcinoma of seminal vesicle has its localization within the seminal vesicle
- Seminal vesicle invasion by other cancers needs to be ruled out (for example: PSA, PAP and CEA negative)
- Preferable papillary growth pattern resembling the seminal vesicle architecture is identified upon microscopy examination of the seminal vesicle tumour

Clinical Manifestation [9]

- Primary adenocarcinoma of seminal vesicle generally tends to be associated with a lack of specific symptoms and hence patients usually manifest with advanced stages of the tumour. [9]
- Haematospaermia, haematuria, dysuria, other obstructive symptoms, or pelvic pain are possible forms of manifestation with digital rectal examination the only clinical examination which could indicate the presence of a tumour within the seminal vesicles in up to 30% of patients. [1] [10] [11] [12] [13].

Complications [9]

- With regard to complications, it has been iterated that primary adenocarcinoma of the seminal vesicles tends to metastasize to pelvic, paraaortic and other lymph nodes as well as to the lungs and liver. Other sites of metastases including bone had been reported [9] [10]

Macroscopy pathology examination appearance [9]

- It has been iterated that primary adenocarcinoma of seminal vesicle tumours are required to be mainly or exclusively localized in the seminal vesicle [9] [10] [13]

Microscopy pathology examination appearance

It has been iterated that for a diagnosis of primary adenocarcinoma of the seminal vesicle to be made, microscopically, the tumours need to be consistent with adenocarcinomas [9] [13]. The histological examination features had been summated to include the following: [9] [11]:

- Hobnail appearance of tumour cells
- Transparent cytoplasm
- Papillary glandular architecture

Immunophenotype [9]

- It has been iterated that immunohistochemistry stains are usually positive for CA-125 and CK7 and negative for CK20 and prostatic markers such as PSA and PAP [10]

Markers [9]

- It has been stated that Ca-125, is usually elevated in primary adenocarcinoma of the seminal vesicles and is rarely normal, whereas **prostate-specific antigen (PSA)**, **prostate specific acid phosphatase (PSAP)** and **CEA** are usually, tend to be normal [9] [10] [11] [12]

Immunohistochemistry studies summations related to primary adenocarcinoma of seminal vesicles: [8]

Positive stains

It has been iterated that primary adenocarcinoma tumour cells exhibit positive staining for: [8]

- CK7, CA125, [6]

Negative stains

It has been iterated that primary adenocarcinoma tumour cells exhibit negative staining for: [8]

- **PSA, PAP, CK20**

Radiographic features [9]

- It had been iterated that magnetic resonance imaging scan and computed tomography scan had been mainly utilised for the visualization of the seminal vesicles [10] [11]
- It had also been iterated that seminal vesicle adenocarcinomas are usually circumscribed and confined or mainly located within the seminal vesicles and might appear solid or cystic [12] [13].

Computed Tomography (CT) scan [9]

- It had been iterated that the CT scan findings in primary adenocarcinoma of the seminal vesicle include various descriptions of solid heterogeneously enhancing masses that are centred around the seminal vesicles [10] [12].

Magnetic Resonance Imaging (MRI) scan [9]

- It had been stated that with regard to primary adenocarcinoma of seminal vesicle, the findings on MRI had been reported with heterogeneous and lobulated features as papillary or cystic necrotic with solid components and often high signal in T1 weighted images [10] [11] [12] [13]

Nuclear Medicine [9]

- It has been iterated that positron emission tomography – computed tomography (PET-CT) scan demonstrates FDG-uptake within the primary tumour and had been used for the diagnosis, staging and evaluation of treatment of primary adenocarcinoma of seminal vesicle [10] [11] [12]

Radiology Report [9]

It has been advised that the radiological report of primary adenocarcinoma of seminal vesicle should include a description of the following: [9]

- The form, the location and the size of the tumour
- The tumour margins
- Prostatic invasion
- Urinary bladder invasion
- Suspicious or enlarged lymph nodes

Treatment and prognosis [9]

- It has been iterated that the management of primary adenocarcinoma of seminal vesicle is usually multimodal including radical surgery in combination with radiation therapy hormone and chemotherapy [10].
- Prognosis of primary adenocarcinoma of seminal vesicle is considered poor with the vast majority of patients dying within less than 3 years probably party due to the advanced stage at the time of diagnosis in most cases [10] [11] [12] [13]

History and etymology [9]

- It has been iterated that primary adenocarcinoma of the seminal vesicles was first reported by O. Lyons in 1925 [10] [11]
- It has also been iterated that Dalgaard and Giertson had initially described the criteria for the diagnosis in 1956 [10] [1] which were subsequently modified [11]

Differential diagnoses [9]

Some of the conditions simulating the clinical manifestation or radiology imaging appearance of primary adenocarcinoma of the seminal vesicles had been summated to include [10]

- **Seminal vesicle invasion by tumour from elsewhere**
    - Adenocarcinoma of prostate gland.
    - Carcinoma of the urinary bladder.
    - **Adenocarcinoma of rectum.**
- **Cystadenoma**

Differential diagnoses extra information

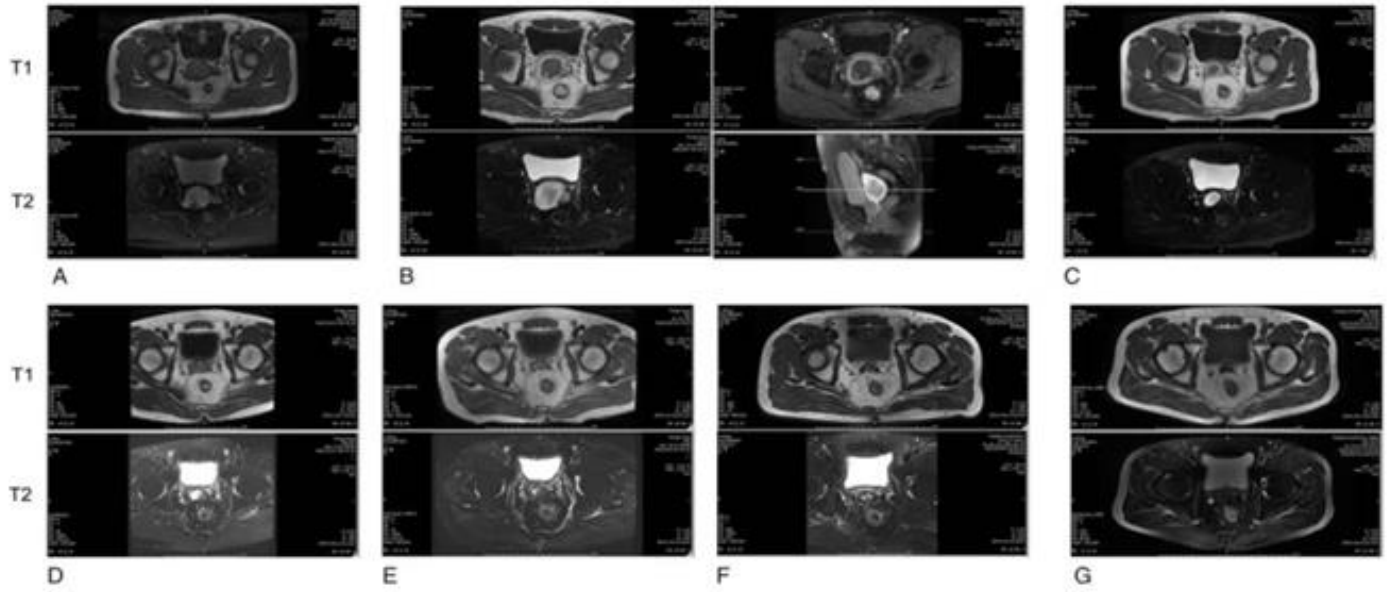
The ensuing summating documentations had been made about the differential diagnoses of primary adenocarcinoma of seminal vesicles: [8]

- **Adenocarcinoma of urinary bladder:** CA125-
- **Urothelial carcinoma of urinary bladder:** CK20+, CA125-
- **Adenocarcinoma of prostate gland:** PSA+, PAP+, CA125-
- **Adenocarcinoma of rectum**: CA125-, CK7 neg, CK20+

[B] Miscellaneous narrations and discussions from some case reports, case series, and studies related to primary adenocarcinoma of seminal vesicles.

Yin and Jiang [1] reported a 51-year-old man who did not have any history of past illness whose main manifestations were repeated hemospermia over the preceding 2 years and haematuria over the preceding 2 weeks and who came to Tongji Hospital in July 2012. His clinical examination, including digital rectal examination (DRE), did not demonstrate any abnormal findings. He had pelvic MRI scan which demonstrated a mass with mixed cystic and solid signals in the district of the right seminal vesicle (see figure 1A). No distant metastases were found in this patient. The results of his serum tumour markers had indicated that his carcinoembryonic antigen (CEA) and serum PSA levels were both normal, while CA-125 levels were above normal at 137U/mL. Surgery was undertaken, and a tumour with a diameter of about 4 centimetres with an unclear border was identified adherent to the peripheral tissue and was carefully removed. Local lymphadenectomy was not undertaken. Post-operative histopathology examination of the

excised specimen confirmed the diagnosis of primary seminal vesicle adenocarcinoma (PSVA) with immunohistochemistry (IHC) staining of that was negative for CEA, negative for PSA, and positive for CA-125 (see figures 2A to 2E). Unfortunately, the tumour was not resected en bloc according to the surgeon and was confirmed by a post-surgery MRI scan (see figure 1B) that demonstrated a ring-like cystic cavity with marginal enhancement above the prostate, behind the bladder, and in front of the rectum. After a multidisciplinary team discussion, 3 cycles of chemotherapy utilising a regimen of 150 mg/m^2 paclitaxel plus 60 mg/m^2 cis-platinum were undertaken; 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 eradiated since pre-surgery MRI imaging had shown no metastasis to the lymph node. Concurrent chemoradiotherapy was not considered in view of the fact that 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 the patient. Endocrine treatment was not provided to the patient. After completion of his treatment, the patient was assessed every 3 months in the first year and every 6 months in the following 2 years (see figures 1C and 1D. His last follow-up was November 2017 (see figure 1E). The authors reported that the patient was still disease-free, and he had been followed for longer than any other PSVA patient in a published report.



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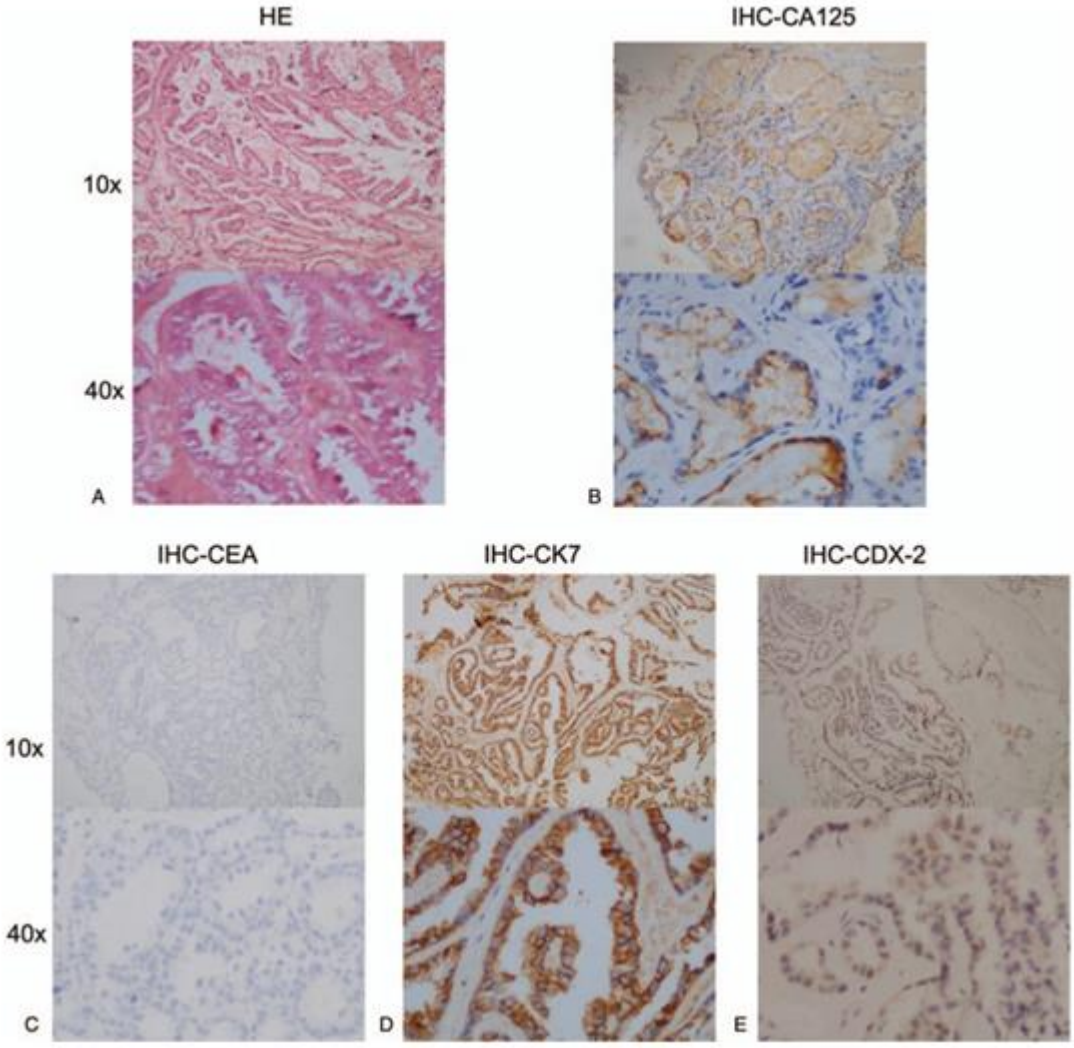

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Representative pathology images of the patient's tumour by haematoxylin and eosin (HE) staining and IHC.A, HE staining; (B-E) IHC of CA-125, CEA, CK7, and CDX-2 respectively. 10 x amplified; 40 x, 40 times amplified. Reproduced from:

Yin and Jiang [1] made the ensuing educative discussions:

- The first case of PSVA was reported in 1925 by Lyons. [14]
- Nevertheless, less than 60 cases had been reported up to the time of publication of their article, demonstrating the exceedingly rare incidence of this malignancy. [2]
- The age of onset has been quite varied, ranging from 19 years to 90 years of age [7].
- Interestingly, there had also been reported cases of bilateral PSVA and primary seminal vesicle squamous cell carcinomas and sarcomas. [1] [2] [15] [16] [17] [18] [19]
- Diagnosis of PSVA is very difficult at an early stage of the tumour in view of a lack of specific symptoms.
- During an advanced stage of the tumour, hemospermia, haematuria, or obstructive uropathy might occur; nevertheless, it is difficult to diagnose a definite location and cause, such as inflammation or tumours.
- Even if a mass is found within the seminal vesicles or nearby, tumours originating within encompassing organs with seminal vesicle invasion are stated to be more common. [7]
- In view of this, when a diagnosis of PSVA is made, it should be carefully differentiated from potential encompassing

malignancies such as tumours within the rectum, urinary bladder or prostate gland, especially carcinoma of prostate gland, which often exhibit invasion of the seminal vesicle in the clinic.

- Local radiology imaging is useful and necessary for the diagnosis of PSVA.
- Endoscopic ultrasound (EUS) scan assessment through the rectum, pelvic computed tomography (CT) or MRI could provide a considerable amount of helpful information about a seminal vesicle tumour, which is very valuable for distinguishing between types of tumours, designing operations, and predicting possible complications.
- Interestingly, there was one PSVA case which was diagnosed based upon the undertaking of a biopsy with no abnormal findings by EUS through the rectum, so it is possibly more reliable to utilise high resolution CT scan or MRI scan to identify the disease. [19]
- Nevertheless, EUS through the rectum should not be abandoned.
- In their case, MRI was always performed to identify the disease throughout the entire treatment and follow-up.
- The definite diagnosis of PSVA depends upon histopathology examination of the tumour specimen. It should always exclude the possibility that a surrounding tumour invaded the seminal vesicle because that disease state is more common than PSVA.
- In 1956, the diagnostic criteria for histopathology of primary adenocarcinoma of seminal vesicle were proposed by Dalgaard and this mentioned that: the tumour should be inside or mainly located within the seminal vesicle, with basic characteristics of carcinoma under macroscopy and microscopy; there should be no signs of other primary malignant tumours; and it was best for tumours to be papillary with normal seminal vesicle structure.
- These were the earliest pathological criteria which depended on cell and tissue morphology without molecular markers, which are difficult to diagnose in poorly differentiated tumours. [16]
- In 1984, Benson improved the former criteria by adding immunohistochemistry (IHC) markers of a negative PSA stain and a positive CEA stain. [20]
- Nevertheless, later on, it was noted that a negative CEA stain was much more common than a positive stain. [21] [22]
- Moreover, a positive signal for CA-125 in pathology or serum strongly supported the diagnosis of PSVA. [5] [6]
- Nevertheless, for poorly differentiated tumours, 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 tumour marker which is 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 pathology examination diagnosis of PSVA.
- It is understood 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.[6] [21] [23]
- In addition, mucin-6 (MUC6) is believed to commonly stain positive in PSVA [24] (see table 1).
- In their patient, CA-125 expression was positive by both serum and IHC pathology, CK7 expression is positive by IHC, and CEA and PSA expression levels were both negative by IHC (see figure 2).

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

Table 1. Reproduced from: [1] Medicine (Baltimore). And Wolters Kluwer Health, Inc. for granting permission for reproduction of contents of their journal article under copyright: Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non-Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal. http://creativecommons.org/licenses/by-nc/4.0 Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6203478/

Common IHC marker for cancer.

- Until 2018, there had been no standard treatment for PSVA.
- Complete excision the seminal vesicle tumour is the mainstay for primary treatment, providing the best prognosis. [3] [7] [25]
- Nevertheless, operating on PSVA is difficult in view of its cystic structure and complicated anatomical relationships with the surrounding tissue.
- In addition, it was still debated whether to prophylactically resect draining lymph nodes.
- There is no evidence on repeating the operations after a first excision with residual tumour or positive-tumour surgical resection margins.
- It had also been disputed whether to follow adjuvant chemotherapy or radiotherapy after complete resection of PSVA. Nevertheless, it was certain that radiotherapy is necessary for residual tumours or tumours with positive margins after surgery.
- It had been iterated that radiotherapy is a useful compensatory method for partial excision or residual tumour. [26]
- In view of a few reports about chemotherapy in PSVA, the effect of adjuvant chemotherapy after surgery had remained not clear.
- The chemotherapy regimen is diverse, from a single drug to combined drugs, varying the prognosis. [3] [5] [23]
- It had been reported by Campobasso et al [2] that a patient with residual tumour after surgery was treated with 4 cycles of chemotherapy using a regimen of gemcitabine plus cis-platinum and then radical radiotherapy.
- Their patient with residual tumour 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 treatment could be effective as an adjuvant or palliative treatment for androgen-dependent PSVA. [27]
- Nevertheless, it was not clear whether long-term anti-androgen therapy is necessary for patients with complete excision, even if their tumours are androgen-dependent.

Yin and Jiang [1] made the ensuing conclusions:

- PSVA is an extremely rare malignant tumour which originates from the Wolffian duct of the male reproductive system.
- Until 2018, there had been no aggregated standard for its diagnosis and treatment.
- In the clinic, it should be carefully differentiated from tumours that originate in surrounding tissues with the help of some useful markers, such as CA-125, PSA, PAP, CK7, and CK20.
- Even though en bloc dissection could afford the best prognosis, it is always difficult to undertake.
- For patients who have residual tumours or positive margins after surgery, chemotherapy and radiotherapy could be an effective approach with tolerable side effects.
- Their patient who, as far as they knew, had the longest disease-free survival time that had been reported, provided a useful example of the diagnosis and treatment of PSVA.

Bhat et al. [28] stated the following:

- The rarity of primary seminal vesical adenocarcinoma (PSVA) coupled with mostly late and advanced presentation with high mortality makes it an unanticipated malignancy with poor prognosis.
- Even though there had been sporadic reporting of cases, the dearth of literature makes standardised care a challenge.
- The identification had incorporated immunohistochemistry for establishing the site of origin as well as the differentiation of primary from metastatic cancer.
- Surgical management with seminal vesiculectomy has continued to be the mainstay of treatment, but difficult anatomy and delayed intervention do lead to an increased chance of residual disease that may warrant further adjuvant chemoradiation.
- They had reported a case where PSVA developed in a patient with Zinner syndrome—an observation that is extremely rare.

Terrisse et al. [29] reported a 43-year-old man, who had manifested with azoospermia, perineal insensitivity, lumbar pain and rectal pus, which he had been suffering over the preceding 6 months. His clinical examination demonstrated small testicles and his digital rectal examination revealed an enlarged prostate gland with no fixed adenoma. His Prostate specific antigen (PSA) level was 1.52 ng/mL He had MRI scan of his prostate gland, which demonstrated non-specific abnormalities with: an enlarged prostatic gland, heterogeneous signal in left central and transitional parts of the prostate and loss of seminal-prostatic and deferent differentiation. He had trans-rectal biopsies of the prostate gland and pathology examination of the biopsy specimens revealed a poorly differentiated carcinoma, probably of glandular origin. The immunohistochemistry staining study results are illustrated in Table 2. Based upon these data, the diagnosis of a poorly differentiated carcinoma of probably urothelial origin with massive prostate extension was confirmed.

Table 2. Reproduced from: [29] Terrisse S, Camblor ME, Vérine J, Gauthier H, Mongiat-Artus P, Culine S. Primary adenocarcinoma of the seminal vesicle. Rare Tumors. 2017 Oct 3;9(3):7074. doi: 10.4081/rt.2017.7074. Erratum in: Rare Tumors. 2019 May 03;11:2036361319848842. Comblor, Maria Eugenia [corrected to Camblor, Maria Eugenia]. PMID: 29081928; PMCID: PMC5643883. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5643883/

Immunohistochemical analysis of prostate biopsies in patient.

Laboratory parameter	Result	Conclusion
KL1, CK 903, P504S, CD99	Positive	
Cytokeratin subsets 7 (CK7)	Negative	
Epithelial membrane antigen (EMA)	Negative	
PSA, PSAm, P501S	Negative	Reject prostatic origin
CD30, OCT3/4	Negative	Reject germinal tumor
Desmin	Negative	Reject rhabdomyosarcoma
CD57, synaptophysin, chromogranin	Negative	Reject neuroendocrine carcinoma

He had complementary assessment with computed tomography (CT) scan of thorax, which demonstrated a nodule in the left superior lobe of the lung. He had PET scanning which did not demonstrate any other metastasis. At that point, the patient had experienced an exacerbation of the symptoms with visible haematuria and perineal pain. Due to fast clinical evolution and risk of incomplete resection of the lung nodule, the patient underwent primary chemotherapy. He received six cycles of MVAC dose dense regimen (Methotrexate 30 mg/m^2 D1, Cisplatin 80 mg/m^2 D2; Vinblastine 3 mg/m^2 D2, Doxorubicin 30 mg/m^2 D2) once every 15 days. He had an excellent clinical response following his first chemotherapy cycle. A radiology imaging response was obtained following his fourth cycle with partial response at the pelvis and complete pulmonary response. Dose reductions of Cisplatin at 50 mg/m^2 were made during the fifth and sixth cycles in view of his moderate renal insufficiency (creatinin: 166 umol/L *vs* 85 umol/L at Cycle 1). One month following the end of his chemotherapy sessions, the patient underwent surgical resection, by means of a cystoprostatectomy with an extended pelvic lymphadenectomy and an enterocystoplasty. The fiinal histopathology examination of the excised surgical specimen demonstrated a carcinoma proliferation which was centred upon the seminal vesicles, negative for CK7, CK20, PSA, P63 and P504S. The lesion was diagnosed and classified as an adenocarcinoma of the seminal vesicles with invasion of the prostate gland and the lower part of the urinary bladder. The margins of the resected specimen were described as negative, without lymph nodes metastases. Two months pursuant to his surgery, the patient was still under observation when a new, 10-mm lung nodule was found, which grew to 21 mm within two months subsequently. He underwent atypical complete resection of the nodule in the left superior lobe and the immunohistochemistry confirmed a metastasis of an adenocarcinoma of the seminal vesicle. He subsequently regained control over the disease and during his last follow up visit, he was in persistent complete remission 4 years pursuant to his pulmonary metastasectomy.

Terrisse et al. [29] made the ensuing educative discussing summations:

- It has been stated that primary tumours of the seminal vesicles are a rare and poorly understood malignancy. [20]
- The symptoms are non-specific and difficult to distinguish from other retro-vesical space tumours.
- The first histologically confirmed case of carcinoma of the seminal vesicle dates back to 1925 in Lyon, France and was reported by Lazarus in 1946. [15]
- The incidence could not be known in view of the small number of cases that had been reported.
- Only about 60 cases had been reported in the literature up to the time of publication of their article. [7]
- Their review of the literature published since 2000 had described 12 cases, of which only 3 were metastatic.
- At the time of the diagnosis of the tumour, the age range goes from 19 years to 90 years but they could not find an accurate age average in the literature. In majority of reported cases, the disease had frequently appeared after 50 years of age. [7] [29]
- On the contrary, risk factors had not been formally described.
- In some cases, renal agenesis had been concomitant, although the reason of this association had remained undetermined.
- Diagnostic difficulties include the absence of symptoms at an early stage and the lack of well-defined diagnostic criteria. [3] [31]
- The manifestations in majority of cases are not specific, and commonly the manifestations had included: haematuria, hematospermia, pelvic/perineal pain and dysuria.
- Digital rectal examination is an important part of the clinical assessment, especially to exclude tumours which may be located within the prostate gland.
- Computed Tomography (CT) scan, Magnetic Resonance Imaging (MRI) scan and trans-rectal ultrasound scan are useful but there is no standard protocol.
- In their reported case, the diagnosis was not obvious from the images (prostatic MRI and transrectal image for guided biopsy).
- Immunohistochemistry stains and histomorphology are helpful for the confirmation of the diagnosis.
- Immunohistochemistry staining study is the key and demonstrates that these tumours are PSA and PSAP negatives.
- Cytokeratin profile is usually CK7 positive and CK20 negative.
- In most of the cases, CA125 is positive but was not undertaken in their case.
- CA125 could differentiate seminal vesicle adenocarcinoma from other tumours such as prostatic gland, urinary bladder and rectal adenocarcinomas, in view of its negativity.[6]
- In view of the rarity of this disease, multi-disciplinarity team management is recommended, while treatment guidelines are not available for the same reason.
- Surgical excision is the mainstay treatment. The surgical excision approach ranges from local excision to radical excision

depending upon the extent of the disease. Pelvic lymphadenectomy is also recommended. [20]

- Various adjuvant strategies had been described.
- Furthermore, radiotherapy could be used in case of positive margins or incomplete resection.[3] [32]
- Hormonal treatment had been used either in adjuvant or palliative treatment but this indication must be assessed.[2]
- Also, chemotherapy treatment had been used with only 6 cases reported. [2] [3] [5] [20] [29] [33]
- In two cases, patients had received adjuvant chemotherapy and in 4 cases, patients had received palliative chemotherapy in metastatic indication. Various treatment regimens were utilised with one drug or multiagent regimens: Folfox (Folinic acid-Fluorouraciloxaliplatin), Docetaxel, Cisplatin-gemcitabine.
- Their presented case was the only one in which the patient had received MVAC dose dense regimen and underwent surgery after the chemotherapy treatment.
- Their patient had demonstrated a noticeable response to the 6 cycles of MVAC dose dense regimen, with a complete pulmonary response and partial pelvic response. Progression had appeared in the second month after the local surgical treatment and it was the first lung metastasectomy ever described.
- Time of progression had been variable in the literature, with ranges from 2 months to 21 months.
- Their patient had exceeded all expectations with a disease-free survival of 48 months.
- Long term prognosis for this disease had been reported as extremely poor. Nevertheless, in many cases, survival rates had not been released or patients had died before progression. [7]
- In their case, the patient had a much better prognosis than had been reported in the literature, probably due to a slow growing tumour.

Terrisse et al. [29] made the ensuing conclusions:

- Their report had shown the complexity of the diagnosis, due to the lack of specific signs and symptoms.
- The final diagnosis was established retrospectively with the histopathological assessment of the resected piece.
- Efforts to establish biomolecular patterns had yet to be undertaken, in order to clarify diagnosis and therefore adapted treatment.
- In addition, their reported case was the first case of metastatic adenocarcinoma of the seminal vesicle in which chemotherapy had been used before the surgical treatment. In this way, MVAC dose dense regimen appeared to be an interesting option in the treatment of this disease.
- Yasunaga et al. [34] described an extremely rare case of poorly differentiated neuroendocrine carcinoma arising from the seminal vesicle. Yasunaga et al. [34] reported a 67-year-old man who had presented with a left humeral bone tumour which had resulted in his development of a pathological fracture. He had positron emission tomography scan, which disclosed a large pelvic tumour simulating prostate cancer invading into the seminal vesicle. His laboratory data showed an elevation of neuron-specific enolase, despite the normal prostate-specific antigen. He had trans-rectal needle biopsy that showed a poorly differentiated carcinoma of the right seminal vesicle and the metastasis of the pelvic lymph node. His immunohistochemistry results were compatible with the features of neuroendocrine carcinoma; synaptophysin, chromogranin A and CD 56 were positive. The previously biopsied bone tumour was finally diagnosed as a metastasis. A systemic chemotherapy utilising etoposide and cisplatin failed. The patient died of cancer one-and-a-half years later.

Tanaka et al. [35] reported a rare case of primary adenocarcinoma of the seminal vesicle in an 87-year-old Japanese man. The neoplastic cells, especially poorly differentiated cells, exhibited a positive reaction with periodic acid-Schiff reagent and anti-carcinoembryonic antigen. The tumour cells had invaded the urinary bladder wall but not the prostate gland. No other primary tumour was identified.

Itami et al. [36] reported a 70-year-old man who manifested with visible haematuria and hematospermia, who was admitted for further assessment of a cystic formation of his right seminal vesicle, that measured 3.6 cm in diameter, which was detected by magnetic resonance imaging (MRI). He underwent cystoscopy which demonstrated no remarkable change, but his urine cytology was class III. His serum concentration of prostate specific antigen (PSA) was within the normal range of 1.83 ng/ml. He had trans-perineal needle biopsy of the prostate and cystic tumour of the seminal vesicle and pathology examination of the biopsy specimens revealed adenocarcinoma of the prostate gland and seminal vesicle, but immunostaining for PSA was negative, so a diagnosis of primary adenocarcinoma of the seminal vesicle was made. Bloody fluid of the cyst was obtained by trans-perineal aspiration, but no cancer cells were identified by cytological examination. Total prostatectomy was undertaken, and the pathological finding was infiltration of prostate cancer into the seminal vesicle (pT3b) because immunostaining of the PSA was positive.

Stenzel et al. [37] stated that criteria for the very rare diagnosis of primary seminal vesicle carcinoma had traditionally been highly stringent but may be relaxed with the application of immunohistochemistry to the diagnosis of mass lesions which occur within the male pelvis. Stenzel et al. [37] reported a case of disseminated carcinoma with a clinically occult primary site which apparently had its origin within the seminal vesicle. He had autopsy which demonstrated a 10-cm tumour enveloping the prostate and seminal vesicles without involvement of colonic or urothelial mucosa. Much smaller tumours were found present within other sites outside the pelvis. The tumour was noted to be composed of poorly formed glands and sheets of malignant-appearing cells, involved the seminal vesicle, and had the immunohistochemical profile of seminal vesicle carcinoma, notably strong immunoreactivity for CA-125 and no immunoreactivity for cytokeratin-20 or prostate-specific markers.

Ormsby et al. [6] stated the ensuing:

- Primary adenocarcinoma of the seminal vesicles is an extremely rare tumour.
- In view of the fact that prompt diagnosis and treatment are associated with improved long-term survival, accurate recognition of this neoplasm is important, especially when evaluating limited biopsy material.

- Immunohistochemistry staining can be used to exclude tumours that commonly invade the seminal vesicles, such as prostatic adenocarcinoma.
- Prior reports had shown that seminal vesicle adenocarcinoma (SVCA) is negative for prostate-specific antigen (PSA) and prostate-specific acid phosphatase (PAP); however, little else is known of its immunophenotype.
- Consequently, they evaluated the utility of cancer antigen 125 (CA-125) and cytokeratin (CK) subsets 7 and 20 for distinguishing SVCA from other neoplasms that enter the differential diagnosis.

Ormsby et al. [6] immunostained four cases of SVCA-three cases of bladder adenocarcinoma and a rare case of adenocarcinoma arising in a mullerian duct cyst for CA-125, CK7, and CK20. Ormsby et al. [6] reported the results as follows:

- Three of four cases of SVCA were CA-125 positive and CK7 positive.
- All four cases were CK20 negative.
- All urinary bladder adenocarcinomas and the mullerian duct cyst adenocarcinoma were CK7 positive and negative for CA-125 and CK20.
- Furthermore, CA-125 immunostaining was performed in neoplasms that commonly invade the seminal vesicles, including prostatic adenocarcinoma (n = 40), bladder transitional cell carcinoma (n = 32), and rectal adenocarcinoma (n = 10), and all were negative for this antigen.

Ormsby et al. [6] concluded that:

- Their study had shown that the CK7-positive, CK20-negative, CA-125-positive, PSA/PAP-negative immunophenotype of papillary SVCA is unique and can be used in conjunction with histomorphology to differentiate it from other tumours which enter the differential diagnosis, including prostatic adenocarcinoma (CA-125 negative, PSA/PAP positive), bladder transitional cell carcinoma (CK20 positive, CA-125 negative), rectal adenocarcinoma (CA-125 negative, CK7 negative, CK20 positive), bladder adenocarcinoma (CA-125 negative), and adenocarcinoma arising in a mullerian duct cyst (CA-125 negative).

Conclusions

Primary adenocarcinomas of the seminal vesicle is an extremely rare malignant neoplasm which afflicts the seminal vesicle in that so far it does appear form the literature that only about 60 cases of the tumour had been reported.

- In the initial stage of the tumour, primary adenocarcinoma of the seminal vesicle has tended to be asymptomatic and diagnosis of the tumour may be incidental based upon digital rectal examination palpation of the enlarged seminal vesicle as well as based upon radiology image findings following imaging for a different scenario.
- In advanced stages of the tumour, the manifestations do include: lower urinary tract symptoms, haematuria, haematospermia, urinary retention, infertility, and other non-specific symptoms.
- The ages of patients that had been diagnosed as being afflicted by primary adenocarcinoma of prostate gland has ranged between 19 years and 90 years.
- Diagnosis of primary adenocarcinoma of seminal vesicles can be established based upon microscopy and immunohistochemistry pathology examination findings of specimens of the tumour that had been identified.
- Some of the differential diagnosis of primary adenocarcinoma of seminal vesicle include: primary adenocarcinoma of prostate invading the seminal vesicle, adenocarcinoma of rectum invading the seminal vesicle, urothelial carcinoma of urinary bladder invading the seminal vesicle, adenocarcinoma of urinary bladder invading the seminal vesicle as well as other primary adenocarcinoma from sites of the body including the bowel.
- Primary adenocarcinoma of the seminal vesicle is a tumour has generally been associated with poor prognosis despite the undertaking of surgical excision and various forms of adjuvant therapy including: radiotherapy, chemotherapy and immunotherapy.

Conflict of Interest – Nil

Acknowledgements

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