Annals of Clinical Case Reports

Case Report
Published: 21 Mar, 2022

Primary Signet Cell Adenocarcinoma of the Prostate pT2aN0 in Radical Prostatectomy Specimen of a Young Male: Case Report and Literature Review

Ana Marinho[1,2], Rui Almeida[2,3], Vitor Sousa[2,3], Edgar Tavares-da-Silva[1,2], Pedro Simões[1] and Arnaldo Figueiredo[1,2]*

[1]Department of Urology and Renal Transplantation, Hospital and University Center of Coimbra, Portugal

[2]Department of Medicine of Coimbra, University of Coimbra, Portugal

[3]Department of Pathological Anatomy, Hospital and University Center of Coimbra, Portugal

Abstract

Primary signet cell adenocarcinoma of the prostate occurs in 2.5% of cases of prostate adenocarcinomas. Signet ring is a term used to describe the histologic appearance of a tumor cell characterized by compression of the nucleus into the form of a crescent by a large cytoplasmatic vacuole. Generally, it is diagnosed at a later stage and has a worse prognosis when compared to classic prostatic adenocarcinoma. We report a case of a 54-year-old asymptomatic man referred to Urology in June 2021. He had a total PSA of 4.23 ng/ml with a 12% Free/Total PSA ratio. A multiparametric magnetic resonance image, performed in August 2021, revealed a suspected area in the right side, poorly defined, located in the middle third and apical region at anterior and posterolateral location, measuring 28 mm × 9 mm, PI-RADS 5. A prostate biopsy identified acinar adenocarcinoma in 15% of the fragments of the right lobe, Gleason 8 (4+4). Staging PET-PSMA described a right lobe focus with high intensity of uptake. The patient underwent radical prostatectomy and extended pelvic lymph node dissection in November 2021. The histology revealed a poorly differentiated acinar adenocarcinoma of the prostate, variant signet cells (30%), Gleason grade 9 (4+5), involving 10% of the right lobe tissue (peripheral zone of apex, lower and middle floor), pT2aN0, negative margins. After surgery the PSA was <0.06 ng/ml.

OPEN ACCESS

Correspondence:
Ana Catarina de Oliveira Marinho, Department of Urology and Renal Transplantation, Hospital and University Center of Coimbra; Praceta Mota Pinto, 3000-075 Coimbra, Portugal, Tel: 351 239400400; Fax: 239 822291; E-mail: anacatarina.marinho.fmuc@gmail.com

Received Date: *05 Jan 2022*
Accepted Date: *09 Mar 2022*
Published Date: *21 Mar 2022*

Citation:
Marinho A, Almeida R, Sousa V, Tavares-da-Silva E, Simões P, Figueiredo A. Primary Signet Cell Adenocarcinoma of the Prostate pT2aN0 in Radical Prostatectomy Specimen of a Young Male: Case Report and Literature Review. Ann Clin Case Rep. 2022; 7: 2141.

ISSN: 2474-1655

Introduction

Primary Signet Cell Adenocarcinoma of the Prostate (PSCADCP) was first described in 1979 and occurs in 2.5% of cases of prostate adenocarcinoma. Signet ring is a term used to describe the histologic appearance of a tumor cell with a crescent-shaped nucleus made by cytoplasmic vacuole compression. It is more common in the stomach, followed by colon, pancreas and less commonly in the bladder. Generally, PSCADCP is diagnosed at a later stage and, consequently, has a worse prognosis when compared to conventional prostatic adenocarcinoma [1]. The grim prognosis and rarity of PSCADCP warrant closer investigation, and much of the literature on this neoplasm is based on case reports. We report a very rare case of early diagnosis in a young man. The treatment and follow-up protocol of these cases has not been established due to the rarity of the disease. However, the literature describes the need for aggressive treatment and very close surveillance.

Case Presentation

A 54-year-old man was referred for evaluation by urology in June 2021. He had lower urinary tract symptoms, but he was asymptomatic on observation by the urologist. The calculated IPSS was 9. Symptoms improved with an alpha-adrenergic blocker. The rectal examination revealed a prostate with about 40cc, unsuspected. He performed an uroflowmetry which was inconclusive because urine volume was <150 ml. The total PSA was 4.23 ng/ml with a 12% free/total PSA ratio. A multiparametric Magnetic Resonance Imaging (MRI) was performed in August 2021 and revealed a suspicious area in the right lobe, poorly defined, involving the anterior and posterolateral zones of the middle third and apical region, measuring 28 mm × 9 mm. There was capsular irregularity, which increases the suspicion of extracapsular extension. The findings classified the lesion as PI-RADS v2.1-5. A prostate biopsy identified acinar adenocarcinoma in 15% of the fragments of the right lobe, Gleason 8 (4+4). Staging was performed with PET-PSMA, which described a high

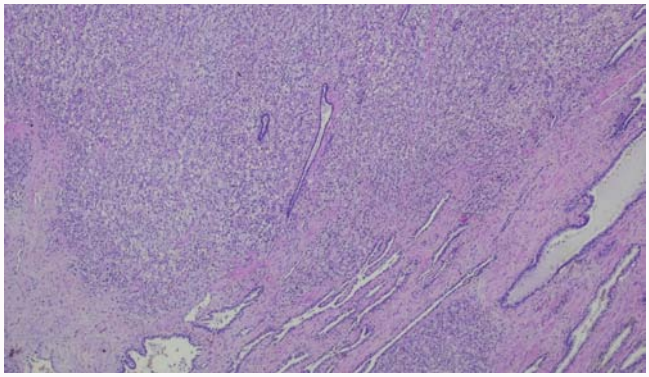

Figure 1: HE 20x, prostate acinar adenocarcinoma.

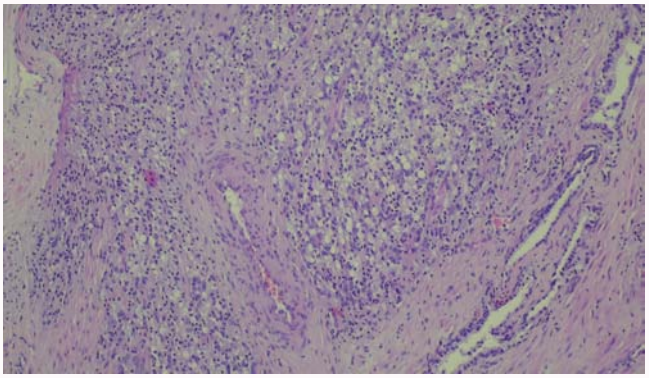

Figure 2: HE 100x, prostate acinar adenocarcinoma Gleason 4 pattern and signet ring cells.

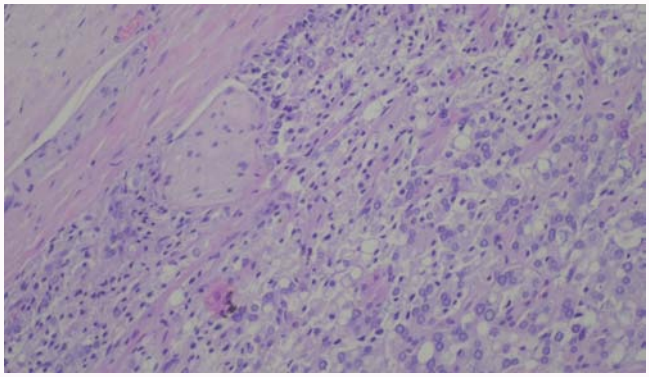

Figure 3: HE 200x, prostate acinar adenocarcinoma with signet ring cells and perineural invasion.

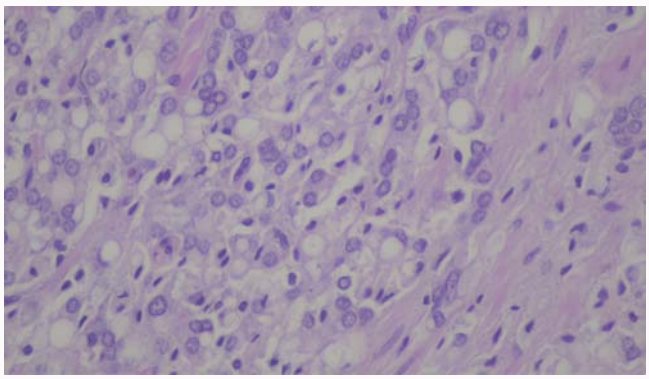

Figure 4: HE 400x, prostate acinar adenocarcinoma with signet ring cells.

intensity focus on the right lobe, centered on the middle floor, lateral and posteriorly and nonspecific bilateral pulmonary nodules. Chest computed tomography detected uncharacteristic micronodules. Thus, the patient underwent retropubic radical prostatectomy and extended pelvic lymph node dissection in November 2021. There were no complications, and the patient was discharged on the third postoperative day. The histology revealed a poorly differentiated acinar adenocarcinoma of the prostate, histological variant signet-like cells (30%). About 60% of neoplasia was classified as Gleason pattern 4 (cribriform pattern) and 10% as pattern 3 (Figures 1-4). The neoplasia was graded Gleason 9 (4+5), pT2aN0, negative margins, International Society of Urological Pathology (ISUP) Grade 5. The neoplasia involved 10% of the right lobe tissue (peripheral zone of apex, lower and middle floor). After surgery, he had PSA<0.06 ng/ml.

Discussion

PSCADCP can present with voiding problems, but it can present with symptoms related to metastasis since the diagnosis is usually made at an advanced stage of the disease. In our case the patient reported lower urinary tract symptoms that resolve with an alfa-adrenergic blocker. The diagnosis of PSCADCP requires histopathologic examination of the tissue, and it is necessary to prove the prostatic origin of the primary tumor, classically it was necessary to exclude metastases of other organs to the prostate, namely gastrointestinal tract. Currently, available imaging tests allow targeting the origin of the tumor in the prostate. Due to a slightly elevated PSA with a free/total PSA ratio <15%, the patient underwent a multiparametric MRI that was compatible with right lobe prostate carcinoma (PI-RADS v2.1-5) which was confirmed by biopsy. Staging PET-PSMA also revealed intense marking of the right lobe of the prostate, which indicates a neoplasm of prostatic origin. Adjacent foci of more typical prostatic adenocarcinoma strongly favor a prostatic origin, as described in the literature [2]. There are reviews that admit that the minority of patients (31%) had a documented gastrointestinal work-up to determine the primary signet cancer cells source [3].

The name signet cell was given because of the appearance of the cell, since large vacuoles push the cell nucleus to the periphery. The 4th edition of the Classification of Tumors of the Urinary System and Male Genital Organs, from World Health Organization, in agreement with other authors, considers that to diagnose PSCADCP, signet cells should comprise more than 25% of the tumor [2,4]. Immunohistochemical techniques can be performed when there are doubts. In fact, certain histologic appearance can be like the signet ring cell, such as vacuolated lymphocytes and altered smooth muscle cells after radiotherapy or hormone therapy. Guerin et al. [5] suggested that signet ring carcinoma cells should be classified as a variant of high-grade adenocarcinoma rather than a separate histologic classification. In support of this proposition, a signet ring carcinoma cell is often found in the presence of other high-grade prostatic adenocarcinoma patterns. The diagnosis of PSCADCP is certainly a histologic diagnosis that can be done using needle biopsy, endoscopic resection specimens, or prostatectomy specimens. Gleason score sum of 9 or 10 is typical and is usually associated with a high stage, early spread to bones and viscera, and poor outcomes. In our patient, the radical prostatectomy specimen revealed 30% of the tumor formed by signet ring cells. About 60% of the neoplasia is classified as Gleason pattern 4 (cribriform pattern) and 10% as pattern 3. Thus, the prostate

cancer was classified as Gleason 9 (4+5), ISUP grade group 5.

Warner et al. [3] in their review of 9 cases of PSCADCP calculated that mean age was 68.2 years. Blas et al. [6], in 2019, reviewed 5 cases of PSCADCP and found a mean age of 77.8 years and mean PSA level of 18 ng/ml (10.6 ng/ml to 331 ng/ml). The patient described in this article is young when compared to the mean ages described in the literature. In addition, it had a slightly increased PSA level, little suspicious of neoplasia, different from the values described in some reviews. Wang et al. [7] identified that younger age (40 to 50 *vs.* >70) was a predictor of worse cancer specific survival, despite more aggressive therapy. This information could be useful when counseling these patients and emphasizes the need for new strategies and molecular-based therapeutic approaches for these cases.

Fujita et al. [2] presented a case series of 42 patients with PSCADCP and found that up to 75% of cases present with locally advanced or metastatic disease at the time of diagnosis. Stage IV disease was a predictor of poor survival. Furthermore, they showed that the survival rates after the initial diagnosis was 82.3% in the first year, 54.7% in the third year and 11.7% in the fifth year. Warner et al. [3] showed an average survival time of 29 months and 33% of patients presented at diagnosis with stage IV cancer. Bronkema et al. [8] also concluded that metastatic disease was most common with PSCADCP (10.3%) compared to non-variant cases (4.2%); PSCADCP presents with higher local stage than non-variant tumors. Warner et al. [3] reviewed 9 cases and all were diagnosed at an advanced stage and, despite multidisciplinary treatments, the mortality rate was very high, around 66%. Recent case reports continue to alert for diagnosis at a very advanced stage of the disease, which implies a poor prognosis [1,9]. Kim et al. [9] reported a 56-year-old man with hematuria which exams identified a bladder mass. Consequently, transurethral resection was performed, and histological evaluation revealed a signet ring cancer invading muscularis propria. He was submitted to radical cystoprostatectomy. The histology revealed that tumor involved both prostate and bladder, but its center was in the prostate and definitive diagnosis was PSCADCP. Chemoradiotherapy was initiated two months later, but patient developed bone and liver metastases and died. Despite the poor prognosis and description of mortality in practically all cases, there are more recent case reports of therapeutic success. Gök et al. [10] presented a case without any evidence of disease 16 months after combination of hormone therapy and radiotherapy. Fortunately, the case described in this case report was diagnosed at a very early stage, which is very rare and may imply a better prognosis for the patient.

The optimal treatment strategy for this subtype of prostate cancer is unknown because few cases were reported. Historically, the treatment approach for PSCADCP has been like that for traditional prostate adenocarcinoma, involving combinations of hormonal therapy, radiation, and surgery. However, the response to hormonal therapy is unpredictable [3]. Kim et al. [9] concluded that instead of conventional hormonal therapy, aggressive treatment and close follow-up are necessary. Kwon et al. [11] reported a patient that started traditional androgen blockade and, nine months later, he was diagnosed with hormone refractory prostate cancer. The patient died after 2 cycles of chemotherapy. Wang et al. [7], in their review of 93 patients with PSCADCP, concluded that local disease, younger age and being married were predictors of radical prostatectomy. Younger age was a predictor of aggressive local therapy and was the strongest predictor for radical prostatectomy rather than external beam radiotherapy. Our patient was young and refused blood transfusions, so radiotherapy was a poor option due to its long-term sequela, for example, radiation induced cystitis.

Conclusion

PSCADCP occurs in 2.5% of cases of prostate carcinoma and requires careful histological diagnosis. It has a poor prognosis that is correlated with the diagnosis at a very advanced stage. The diagnosis in an early phase, as in our case, is very rare. Although it is difficult to define an optimum treatment strategy, early diagnosis, aggressive treatment, and close follow-up might improve prognosis.

References

1. Celik O, Budak S, Ekin G, Akarken I, Ilbey YO. A case with primary signet ring cell adenocarcinoma of the prostate and review of the literature. Arch Itali di Urologia e Andrologia. 2014;86(2):148-9.
2. Fujita K, Sugao H, Gotoh T, Yokomizo S, Itoh Y. Primary signet ring cell carcinoma of the prostate: Report and review of 42 cases. Int J Urol. 2004;11:178-81.
3. Warner JN, Nakamura LY, Pacelli A, Humphreys MR, Castle EP. Primary signet ring cell carcinoma of the prostate. Mayo Clin Proc. 2010;85(12):1130-6.
4. Moch H, Humphrey PA, Ulbright TM, Reuter VE, editors. World Health Organization Classification of tumours of the urinary system and male genital organs 4th Ed. Lyon, France: International Agency for Research on Cancer; 2016.
5. Guerin D, Hasan N, Keen CE. Signet ring cell differentiation in adenocarcinoma of the prostate: A study of five cases. Histopathol. 1993;22:367-71.
6. Blas L, Vitagliano G, Rios-Pita H, Roberti J, Guglielmi JM, Ameri C. Signet ring cell carcinoma of the prostate. Report of 5 cases and literature review. Arch Esp Urol. 2019;72(10):1051-5.
7. Wang J, Wang FW, Hemstreet III GP. Younger age is an independent predictor for poor survival in patients with signet ring prostate carcinoma. Prostate Cancer. 2010.
8. Bronkema C, Arora S, Sood A, Dalela D, Keeley J, Borchert A et al. Rare histological variants of prostate adenocarcinoma: A national cancer database analysis. J Urol. 2020;204(2):260-6.
9. Kim SW, Kim W, Cho Y-H, Kim T-J, Woo I, Sohn DW. Primary signet ring cell carcinoma of the prostate treated by radical cystoprostatectomy and chemoradiotherapy. Can Urol Assoc J. 2016;10(5-6):204-6.
10. Gök A, Tuygun C, Akmansu M, Uslu AA, Kartal IG, Sandikçi F, et al. Primary signet ring cell carcinoma of the prostate: A rare case report. J. Clin. Med. 2018;7(218).
11. Kwon W-A, Oh TH, Ahn SH, Lee JW, Park SC. Primary signet ring cell carcinoma of the prostate. Can Urol Assoc J. 2013:7(11-12):768-71.