Oncology

Laparoscopic port-site metastasis as the manifestation of neuroendocrine prostate cancer: Case report and literature review

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A B S T R A C T

Introduction: The neuroendocrine differentiation in prostate cancer is a rare entity that may occur as de novo, or as a result of treatment with androgen deprivation. It is characterized by its rapid progression and poor prognosis, without elevation of the prostate specific antigen (PSA), which is why it is often diagnosed by biopsy of a site of metastasis; there are no established treatment regimens. In this case, metastasis was presented as implantation to a laparoscopic port. These implantations subsequent to laparoscopic procedures in prostate cancer are very rare, with an incidence between 0.09 and 0.7%. The exact pathogenesis of the tumor implantation at the insertion site is not clear, there are several theories.

Materials and methods: We describe the case of a 53-year-old patient with a diagnosis of prostate adenocarcinoma who underwent laparoscopic radical prostatectomy plus lymphadenectomy, staged as PT3B N0 (0/6) M0 R1 Gleason 4 + 5. The patient never had negative PSA levels after the treatment, and presented elevation of the same, so radiotherapy was performed at a dose of 66 Gy plus antiandrogen deprivation therapy with leuprolide acetate for 30 months, with a decrease in PSA to 0.011 ng/ml, which remained stable. After 3 months of hormonal therapy, he presented with an umbilical mass on the scar of the laparoscopic port; ultrasound and computed tomography were performed, showing a solid mass dependent of the umbilical upper edge with a defect in the abdominal wall of 3 cm, as well as hepatic nodules suggestive of metastatic lesions and peritoneal implantations.

Results: A biopsy of the abdominal wall lesion was performed, documenting poorly differentiated carcinoma with an immune-profile consistent with neuroendocrine carcinoma; immunohistochemistry showed strong and diffuse positivity with cytokeratin cocktail and chromogranin. In conjunction with oncology, treatment with chemotherapy was decided. He received six cycles of cisplatin and etoposide, with progression of his disease and death seven months after diagnosis.

Conclusions: Prostate cancer with neuroendocrine differentiation is a rare entity, usually occurring in the castration resistance stage, with poor prognosis and survival of less than 1 year. It presents as clinical and radiological progression without elevation of the PSA. Although it is very rare, the possible causes include tumor implantation in laparoscopic ports and/or open surgery scars, so caution and certain precautions must be taken when performing radical prostatectomy. In case of suspecting a tumor with neuroendocrine differentiation, biopsy and immunohistochemistry studies should be performed in order to clarify the diagnosis and provide a multimodal treatment based on surgery, radiotherapy and chemotherapy.

Introduction

PCa with neuroendocrine differentiation is a rare entity, very aggressive, poorly diagnosed, and with a high mortality rate. It can present as a primary disease or as a late differentiation of prostate cancer in ADT, and so far there are no management schemes determined. We report the case of a patient with PCa who presented metastasis in a laparoscopic port-site scar with neuroendocrine differentiation.
Clinical case

53 years-old male, with PSA elevation (9.72 ng/ml), presents a slightly enlarged prostate at physical examination, with a fibrous and painful area in the right lobe. Transrectal prostate biopsy reported prostate adenocarcinoma Gleason 3 + 4 in the apex, middle and base of both lobes, with 10/12 fragments involved and presence of perineural invasion. Radical prostatectomy plus lymphadenectomy was performed by laparoscopy in March/2013. The result of the surgical pathology showed prostate adenocarcinoma with Gleason 4 + 5 in the 4 quadrants, with extra prostatic extension, multifocal involvement in border of section in bilateral apex and compromised seminal vesicles without ganglionic invasion. It was classified as a prostate adenocarcinoma PT3BN0(0/6)M0R1 Gleason 4 + 5. He never had negative PSA levels, and subsequently presented elevation of the same (Aug/13): 0.38 ng/ml; (Feb/14): 0.86 ng/ml; (Mar/14): 1.75 ng/ml. In April/2014, treatment with pelvic radiotherapy began with a dose of 66Gy, ending in August 2014, plus hormonal therapy with Leuprolide acetate 22.5mg quarterly until October/2016.

In January 2017, the patient reported a sensation of mass at the abdominal level; he had nodules in the laparoscopic umbilical port wound and in two more ports. Abdominal computed tomography showed a localized lesion towards the midline on the scar of the laparoscopic port, in the subcutaneous cellular tissue in front of the abdominal wall of 3cm, multiple nodular lesions in the peritoneum of 1–4cm, which could correspond to peritoneal carcinomatosis, hypodense lesion of 3cm in the liver, which could correspond to metastasis, and multiple abdominal adenopathies (Figs. 1 and 2). A biopsy of the umbilical port-site lesion was performed, and the anatomopathological study confirmed a poorly differentiated carcinoma with immune-profile consistent with neuroendocrine carcinoma; immunohistochemical studies showed strong and diffuse positivity with cytokeratin cocktail and chromogranin, weak positivity with synaptophysin and were negative to cytokeratin 7, cytokeratin 20, p63, PSA and ttf-1 (Fig. 3).

There was no evidence that the tumor had another origin. The lesion was in the right point of laparoscopy port site. The transformation to neuroendocrine differentiation can occur and has been reported after androgenic deprivation treatment.

Six cycles of chemotherapy with cisplatin and etoposide were indicated. The patient presented progression of his disease and died in September 2017.

Discussion

PCa with neuroendocrine differentiation may present itself as a primary entity, and more commonly, during the castration resistance stage. As a result of their secretory products, these cells stimulate the proliferation of tumor cells and increase their aggressiveness by inhibiting apoptosis and stimulating angiogenesis. The over-expression of the proto-oncogene Bcl-2 (an inhibitor of apoptosis), is highly correlated with cancer progression and androgen resistance.1 Its diagnosis is based on the histopathological study of prostate biopsy, or biopsy of metastatic lesions, characterized by the presence of neuroendocrine changes, and the absence of adenocarcinoma cells. The most frequent findings in immunohistochemistry are the presence of chromogranin A, GRP bombesin, enolase and synaptophysin, and low or absent levels of PSA, PSAP, PSMA, when compared with adenocarcinoma.1

This type of PCa has high rates of short-term mortality; systemic treatment with radiotherapy plus chemotherapy tends to improve survival when compared to palliative management.

In our patient, the appearance of tumor seeds in the scars of laparoscopic ports was unexpected, a finding never before seen in our institution; the reported incidence is low, between 0.09 and 0.73%.2 Castillo and collaborators reported that in 1280 laparoscopic procedures were performed for malignant urological tumors for 10 years, and only two patients presented tumor seeding, with an incidence of 0.1%; in addition, they conducted a review of the literature in 2008, finding only 31 reported cases.3 Rassweiler and colleagues found in a study of 450 patients who underwent laparoscopic radical prostatectomy, and 60 who underwent pelvic lymphadenectomy after radiotherapy for laparoscopic, that none of the cases presented metastasis to the port of laparoscopy.3 We did not find any case of tumor in the port of laparoscopy of prostate cancer with neuroendocrine differentiation reported in the literature.

These cases present mainly as a palpable mass at the abdominal level, specifically in the scars corresponding to the ports of laparoscopy.

The exact pathogenesis of the tumor implantation at the insertion site is not completely known; there are several factors that can favor this event, among which are the spread of tumor cells by inadvertent tumor cuts, direct implantation of tumor cells in the surgical wound, and tumor trauma by laparoscopic instruments.4 Other risk factors are the patient's immune status, advanced tumor stages and aerosolization of tumor cells.5

Regarding the treatment of PCa with neuroendocrine differentiation, the available literature is scarce, and there is no established regimen. Usually, treatments based on chemotherapy with platinum are offered. Other authors add androgen blockade since there is a high rate of mixed tumors (neuroendocrine and adenocarcinoma).1 However, relapse is common in this type of tumors, and survival is less than one year. If presented as a localized primary entity, the most appropriate treatment is radical surgery.

Other possible treatment modalities have been found, and are under study, among which are: somatostatin analogues, bombesin antagonists, serotonin antagonists and mTOR blockers, but none of them with

Fig. 1. Abdominal CT, axial (A) and coronal (B). A nodule (arrow) is seen in the subcutaneous fat tissue in the supraumbilical region, over the port-site scar. This lesion slightly enhances with contrast, and does not present a cleavage plane with the abdominal wall muscles.
enough weight to make clinical decisions and define management.1

Conclusions

PCa with neuroendocrine differentiation is a rare entity, usually occurring in the castration resistance stage, with poor prognosis and survival of less than 1 year. It presents itself as clinical and radiological progression without elevation of the PSA. Although it is very rare, the possible causes include tumor implantation in laparoscopic ports and/or open surgery scars, so caution and certain precautions must be taken when performing radical prostatectomy. When suspecting a tumor with neuroendocrine differentiation, biopsy and immunohistochemistry studies should be performed in order to provide a multimodal treatment based on surgery, radiotherapy and chemotherapy.

Informed consent

Informed consent was signed by the patient.

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Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2019.100845.

References

1. Parimi V, Goyal R, Poropatich K, et al. Neuroendocrine differentiation of prostate cancer: a review. Am J Clin Exp Urol. 2014;2(1):273–285. https://doi.org/10.1200/JCO.2011.36.0487.
2. Bruyne P De, Schatteman P, Naeyer G De, Carpentier P. Port site metastasis in prostate cancer. Can Urol Assoc J. 2015;9(June):387–389.
3. Castillo OA, Vitagliano G. Port site metastasis and tumor seeding in oncologic laparoscopic urology. Urolgy. 2008;71(3):372–378. https://doi.org/10.1016/j.urology.2007.10.064.
4. Savage SJ, Wingo MS, Hooper HB, Smith MT, Keane TE. Pathologically confirmed port site metastasis after laparoscopic radical prostatectomy: case report and literature review. Urolgy. 2007;70(4) https://doi.org/10.1016/j.urology.2007.09.004, 1222.e9-11.
5. Lee BH, Tan BJ, Smith AD. Laparoscopic port site metastasis: incidence, risk factors, and potential preventive measures. Urolgy. 2005;65(4):639–644. https://doi.org/10.1016/j.urology.2004.09.067.