v. 5, n. 28, 2025

International Journal of Health Science

Acceptance date: 15/08/2025

METASTATIC NEUROENDOCRINE TUMOR OF THE PROSTATE IN A YOUNG PATIENT ASSOCIATED WITH HOSTILE TUMOR BEHAVIOR: A CASE REPORT

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Keywords: Prostate tumor. Neuroendocrine. Young patient.

INTRO

Prostate cancer is the neoplasm with the highest incidence and mortality in Latin America (GCO, 2024). The increase in incidence is related to age, with 3.9 cases per 100,000 in the 30-49 age group recorded in Latin America in 2022. In men over 70 years of age, there were 619.3 cases per 100,000 (GCO, 2024).

Adenocarcinomas account for more than 95% of prostate cancer cases. Approximately 5% of men diagnosed develop distant metastases, in which the overall survival rate is 30% in five years (Wasim, 2022).

Prostate neoplasia is pathophysiologically dependent on androgens, and testosterone deprivation therapy is a fundamental step in treatment. However, there may be a phase of the disease in which there is a castration-resistant variant after treatment with hormonal agents (Spetsieris, 2020).

Among the castration-resistant variants, there is a rare and aggressive subtype called neuroendocrine, which affects approximately 2% of patients with prostate cancer (Wasim, 2022). Based on these data, there is interest in clinical studies on neuroendocrine prostate neoplasia, aiming to describe the clinical case of a young patient with this disease and the particularities of its behavior at an early age, in addition to contemplating the third goal, Health and Well-being, of the Sustainable Development Goals (SDGs) established by the UN.

METHOD

This paper discusses a case report experienced by members of the Academic Oncology League (LIONCO) of the Regional University of the Northwest of the State of Rio Grande do Sul (UNIJUÍ). This study was based on a clinical case report, consented to by the patient through a Free and Informed Consent Form and supplemented by a literature review. The objective was to analyze the association between prostate neuroendocrine tumors and young age and aggressive tumor behavior, incorporating a literature review obtained from a search using the keywords "prostate tumor," "neuroendocrine," and "young patient," which are related to the topic. The database used was the National Library of Medicine (PUBMED).

CLINICAL CASE REPORT AND DISCUSSION

A 35-year-old patient, previously healthy and without risk factors, began experiencing urinary hesitancy and bone pain in 2019, without associated weight loss. He has a family history of bladder cancer in his brother and skin cancer in his maternal uncle. He underwent

Laboratory tests showed PSA (Prostate-Specific Antigens) results of 55.83 ng/ml. Investigation continues with a transrectal prostate biopsy, with anatomopathological results of Malignant Epithelioid Cell Neoplasm suggestive of Gleason 8 (4+4) Adenocarcinoma.

Investigation continues with staging bone scintigraphy showing multiple

secondary implants to the underlying neoplasm in the axial and appendicular skeleton (more than 7 scattered foci of lesions).

Referred to the Oncology Service, staged as TxNxM1, stage IV. Somatic genetic mutation testing was performed on a tumor sample, which showed no clinically relevant mutations, and treatment was initiated with chemotherapy and hormone blockade, with 8 cycles of docetaxel and quarterly gosserelin. He progressed with a good clinical and biochemical response. However, three months after starting treatment, there was a worsening of pain symptoms in the dorsal spine, with increased osteoblastic activity in other pre-existing lesions on the new bone scan, and he underwent antalgic radiotherapy due to disease progression.

In addition, there was an increase in PSA, classifying him as castration resistant from that moment on.

The patient continued to have genitourinary symptoms of increased frequency, lower abdominal pain, and persistent gross hematuria in 2023, with cystoscopy showing a large irregular mass in the bladder neck. A new tumor sample was collected with immunohistochemical analysis to better clarify the new expansive mass in the prostate, with a diagnosis of Prostatic Acinar Adenocarcinoma with Neuroendocrine differentiation.

The collection of a new tumor sample with immunohistochemistry with neuroendocrine differentiation was crucial for a better understanding of the disease. Thus, it was possible to elucidate some relevant aspects of the behavior of this tumor, starting with the association of the neuroendocrine subtype with early age. Although rare, this differentiation has a significant incidence in young patients, with family history being the most significant risk factor. This is because it involves hereditary genetic alterations, which, in turn, participate in the carcinogenesis of neuroendocrine tumors in young patients, who have approximately twice the incidence of known hereditary syndromes than those diagnosed at an older age (Fogassa, 2023). In the present case, the patient also has a positive family history of neoplasia; however, his somatic test for genetic mutation was negative. It should be noted, however, that the patient did not have access to germline testing, which could still reveal some clinically significant alteration.

Furthermore, there is also an association between neuroendocrine tumors and aggressive tumor behavior. This phenomenon can be attributed to the ability of neuroendocrine cells to promote greater growth of prostate adenocarcinoma cells, inhibiting apoptosis and promoting tumor angiogenesis (Wang, 2019). Furthermore, micromolecular characteristics capable of determining the hostile tumor behavior of neuroendocrine tumors are explained by the expression of cell proliferation markers, such as Ki-67, which is elevated in neuroendocrine tumors (Araújo, 2012), as well as the condition found in the reported patient, in whom Ki-67 expression is 80%. Furthermore, the hostility of neuroendocrine tumor differentiation can also be explained by the transformation into a hormone-resistant phenotype, that is, resistant to androgenic castration (Freschi, 2003), a situation described in our case. In addition, there is a greater predisposition to metastasis, especially in young patients, as published by Maqdasy (2017), who associates early diagnosis with a greater propensity to develop metastases.

With regard to metastasis, Wang (2019) demonstrates higher rates of bone metastasis in neuroendocrine prostate tumors (81.08%) than in other histological types (65.65%). Furthermore, he correlates reduced PSA levels with neuroendocrine content, a situation in which even with low PSA levels, there may be a higher proportion of neuroendocrine tumor cells and, thus, more aggressive tumor behavior.

In short, considering that neuroendocrine tumors have more aggressive tumor behavior, it can be inferred that there will be impacts on survival in this population. In this sense, the study by Wang (2019) presents a median survival of 19 months for patients with prostate neuroendocrine tumors, regardless of age. Although the evidence for survival is unfavorable, the age of the patient studied should be considered a strong predictor of survival, given better health conditions to tolerate treatment. In this sense, Fogassa (2023) points out that young patients have better survival regardless of clinical stage, with the patient reported exceeding the average survival of 19 months, since the neuroendocrine diagnosis was established in 2019 and, therefore, he has a higher survival rate (49 months) than the sample from Wang (2019).

FINAL CONSIDERATIONS

Prostate cancer is an uncommon finding in the young population, especially the neuroendocrine subtype. Furthermore, the hostile behavior of neuroendocrine tumors is related to the mechanism of neuroendocrine cells to promote exponential growth of adenocarcinoma cells and increase the possibility of metastasis. In addition, it presents a hormone--resistant phenotype, a greater propensity for bone metastasis, and reduced PSA biomarker levels, reinforcing its hostile behavior. For this reason, the approach to prostate neoplasia in young patients should pay special attention to immunohistochemical diagnosis in order to enable more appropriate treatment for the histological subtype and, consequently, offer better survival and quality of life to the patient. Thus, whenever possible, somatic and germline genetic testing should be offered for a deeper understanding of the course of the disease and hereditary risk.

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