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Case Report

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Metastatic prostate carcinoma: A case report on a Brca2 mutated young patient

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Abstract

Prostatic adenocarcinoma is one of the most frequent malignancy amongst men, majority patients with advanced disease end up developing bone metastases. One of the factors linked to such condition is the genectic variability of cancer types, the most aggressive of them are derived from a series of mutations in tumor suppressor genes. BRCA2 is a tumor suppressor gene and the presence of a mutation within this gene increases the chance of developing prostate cancer by more than 8 times, being present in approximately 5% of patients with advanced stages. Other than that, the diagnosis of a BRCA2 mutation may be helpful in terms of genetic counseling, risk assessement and early screening. Currently, many treatment strategies are effective for patients with prostate cancer who have germline/somatic modifications in the DNA restoration pathway mechanism for BRCA1 and BRCA2.

keywords: *prostate cancer; bone metastases; Brca2*

Introduction

Prostate cancer is the second most frequent cancer and the fifth leading cause of cancer death among men in 2020, with an estimated almost 1.4 million new cases and 375,000 deaths worldwide [1]. The risk increases significantly after the age of 50 [2] and approximately 50% of patients undergoing local radiotherapy or prostatectomy may have recurrence [1]. Current treatments have extended the overall survival by more than 10 years with a high cure rate [3], still, in most patients with advanced disease (65-75%) end up developing bone metastases, mainly in the spine, pelvis, ribs and long bones [4].

The reason for metastasis development and non-survival in some individuals is related to treatment resistance [3]. One of the factors linked to such condition is the genectic variability of cancer types, the most aggressive of them are derived from a series of mutations in tumor suppressor genes. Furthermore, the bone microenvironment and its interactions may be responsible for numerous disseminations, hindering the treatment [3]. Therefore, genomic analysis have been utilized not only for diagnostic purposes, but also used as a therapeutic optimization resource [5].

Less than 1% of the cases of prostate cancer are detected in patients under the age of 50 years [6]. BRCA2 is a tumor suppressor gene and the presence of a mutation within this gene increases the chance of developing prostate cancer by more than 8 times, being present in approximately 5% of patients with advanced stages. Furthermore, mutations in BRCA2 have been reported to result in an aggressive pattern of disease, usually associated with Gleason greater than or equal to [8], as well as the development of distant metastases, with a reduced survival rate, especially in metastatic cases resistant to castration [7]. Thus, genetic tests are essential for the assessment and screening of cancer risk, especially in younger patients, in addition to allowing genetic counseling for men in families with a hereditary condition of BRCA28.

Case presentation

A previously healthy 37-years-old man, reported to the Emergency Department with a chief complaint of weakness, hyporexia, a 32 kilos weight loss, associated with episodes of epistaxis, bruises and multifocal pain. On physical examination, he was pale and tachycardic, without lymph node enlargement, with asymmetrical breasts (right nodule) and splenomegaly. Laboratory data showed sever anemia with reticulocytosis, consistent with a leukoerythroblastic picture and a possible bone marrow invasion.

Imaging exams demonstrated alterations in the breast, prostate, seminal vesicles, testis, liver, lungs, spine and lymph nodes. The MRI of the pelvis stands out, with extensive prostate damage, with lymph node enlargement, in addition to multiple bone lesions suggestive of metastasis (Figure 1).

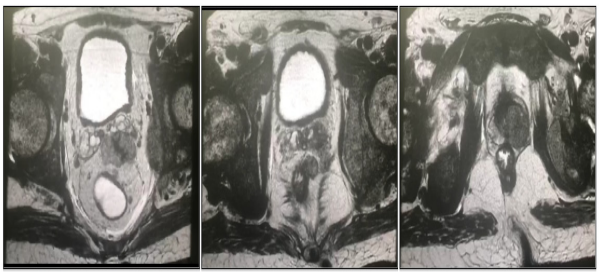

Figure 1: Pelvic MRI demonstrating a lesion centered on the left side of the prostate, showing signs of posterior extension to the ipsilateral seminal vesicle, with a malignant appearance. Lymph node enlargement and bone lesions suspicious for metastasis.

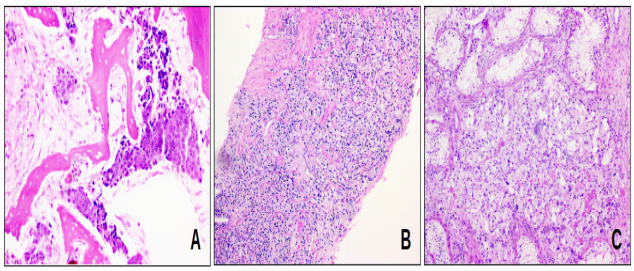

Figure 2: (A)Bone marrow metastatic poorly differentiated carcinoma. (B) Prostatic adenocarcinoma. (C) Testicle with metastatic implant of prostatic origin.

The bone marrow biopsy impression (Figure 2A) was of a poorly differentiated metastatic epithelial neoplasm. The immunohistochemical study indicated primary prostate site by positivity for AE1/AE3, CK20, Racemase and PSA, with a high proliferative index (Ki67> 70%), being negative for other markers related to pulmonary, gastrointestinal, renal, hepatic origin and germinal histogenesis. After this diagnosis, androgen blockade with Leuprolide and Bicalutamide, palliative radiotherapy for spinal pain, associated with chemotherapy with Docetaxel was instituted.

Subsequent prostate biopsy (Figure 2B) backed the diagnosis of an usual pattern acinar adenocarcinoma, Gleason 9 (4 + 5), ISUP 5. In the proceeding, bilateral orchiectomy was also performed, and the left testicle presented prostate cancer metastasis (Figure 2C).

A pathogenic alteration with a BRCA2 gene mutation was confirmed on the genetic test. Afterwards, Carboplatin was associated to the treatment, later being replaced by Cisplatin, folowed by clinical improvement.

Discussion

Currently, many treatment strategies are effective for patients with prostate cancer who have germline/somatic modifications in the DNA restoration pathway mechanism for BRCA1 and BRCA2. Chemotherapy drugs are a beneficial treatment, and platinum-based cycles are highly sensitive for these patients [8]. Treatment with Docetaxel associated with Cisplatin is important due to the exposure that the mutation generates to the activity of these drugs, improving the prognosis [9]. Because of this, the patient in this case received the addition of Cisplastin after the BRCA2 mutation was diagnosed.

Targeted therapies, such as PARP inhibitors (poly-ADP ribose polymerase), are used in BRCA-linked breast and ovarian tumors and are also recommended for BRCA patients with metastatic prostate cancer [8]. These inhibitors were not used for our patient, mainly because he was receiving care in the Unified Health System (SUS), universal, public and free in Brazil, but without availability of such medications.

Hormone therapy is treatment to stop your body from producing the male hormone testosterone or to block the effects of testosterone on the cancer. Prostate cancer cells rely on testosterone to help them grow. In this case, bilateral orchiectomy was chosen for this purpose [3]. Some medications also work in order to control testosterone in the body may be options. Radiotherapy can be used in men with very large prostate tumors or cancer that has spread to nearby lymph nodes (locally advanced prostate cancer) combined with hormone therapy. But in cases with distant metastasis, radiation therapy is used to relieve pain or other symptoms, as in the patient report. Surgery is not often used to treat metastatic prostate cancer in bone [10].

Furthermore, radioisotopes such as samarium-153 and strontium-89 have been a therapeutic choice, either as monotherapy or in combination with chemotherapy, in management of advanced prostate cancer to offer symptomatic palliation, especially in men with high-volume metastatic bone disease. However, have potential to cause marrow toxicity and should be used with caution [10].

Among other possible therapeutic options, an autologous cellular immunotherapy approved for treatment of asymptomatic or minimally symptomatic (Sipuleucel-T) [10]. Medications used to treat thinning bones (osteoporosis) may be helpful in preventing broken bones in men with prostate cancer that has spread to the bones, as bisphosphonates5. For the patient in this case, they seem to be good alternatives for therapeutic follow-up.

Conclusion

Continuous advances have provided a new understanding of the diagnosis, staging, and treatment of metastatic and ad-

vanced prostate cancer. Genetic research is advised on patients with agressive disease and those with a strong family history of prostate cancer. The diagnosis of a BRCA2 mutation may be helpful in terms of genetic counseling, risk assessement and early screening. Lastly, molecular studies allow treatment optimization and prognostic improvement.

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