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CASE REPORT: AGGRESSIVE PROSTATE ADENOCARCINOMA WITH EARLY CARCINOMATOSA LYMPHANGITIS

Relato de caso: adenocarcinoma prostático agressivo com linfangite carcinomatosa precoce

Fernando Ribeiro Amaral[1]
Marcos Túlio Silva Costa[1]
Marcella Oliveira Rabelo[1]
Scárllety Karenn Mendes Oliveira[2]
Sarah Magalhães Medeiros[1]
Priscila Bernardina Miranda Soares[3]

Abstract: Prostate cancer is the second most common neoplasm in man and its incidence increases substantially with age. The indications for screening and the propaedeutic when an altered PSA (prostate-specific antigen) is found still exhibit controversy. The atypical presentation of prostatic adenocarcinoma in this patient, in the form of an extremely aggressive tumor with pulmonary dissemination at diagnosis, influenced the report of this case. He is a 53-year-old male patient with a family history of prostate cancer, complaining of a weak jet and a few years ago. Urologist requested total PSA: 7.02 (6/3/2016). After 4 months, the PSA was 99.77. The patients sought the oncologist, with facies of pain and major lameness. Imaging studies showed neoplastic infiltrate in the medulla and pulmonary nodules with perilymphatic distribution, the latter being an uncommon condition. Chemo-hormone therapy was started according to the CHAARTED protocol, considering a significant volume of systemic disease. After initiation of therapy, the patient presented significant gains in quality of life, partial remission of the lung and lymph node lesions and persistence of bone lesions.

Keywords: Prostatic Neoplasms; Neoplasm Metastasis.

Corresponding author: Fernando Ribeiro Amaral
E-mail: fernando.ribeiro.amaral@gmail.com

1 Universidade Estadual de Montes Claros.
2 Faculdades Integras Pitágoras de Montes Claros.
3 ONCOVIDA Montes Claros.

Resumo: O câncer da próstata é a segunda neoplasia mais comum no homem e sua incidência aumenta substancialmente com a idade. As indicações de rastreamento e a propedêutica diante de um PSA (antígeno prostático específico) alterado ainda exibem controvérsias. A apresentação atípica do adenocarcinoma prostático neste paciente, sob a forma de um tumor extremamente agressivo e com disseminação pulmonar ao diagnóstico, influenciou o relato deste caso. Trata-se de paciente com 53 anos, histórico familiar positivo para câncer de próstata, queixando-se de jato fraco e algúria há 8 meses. Urologista solicitou PSA total: 7,02 (03/06/2016). Após 4 meses, o PSA foi de 99,77. Em seguida, paciente procurou a oncologista, com fácies de dor e claudicação importante. Exames de imagem evidenciaram infiltrado neoplásico na medula e nódulos pulmonares com distribuição perilinfática, sendo este último uma condição incomum. Iniciou-se quimio-hormonioterapia conforme protocolo CHAARTED (ChemoHormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer), considerando volume significativo de doença sistêmica. Após início da terapia, o paciente apresentou ganho expressivo em qualidade de vida, remissão parcial das lesões pulmonares e ganglionares e persistência de lesões ósseas.

Palavras-chave: Neoplasias da Próstata; Metástase Neoplásica.

INTRODUCTION

Prostate cancer is a neoplasia of high prevalence, behind only of tumors of non-melanoma skin cancer in men. It mainly affects the elderly, being considered a tumor that significantly increases the prevalence with age. It can occur indolently in the vast majority of cases, but the rest can have an aggressive growth, spreading to other organs and even causing death.[1]

Typically, patients with prostate cancer present bone metastasis as the most common one, which progresses with important bone pain. In addition, the treatment can be done with various modalities, such as surgery, radiotherapy, chemotherapy and hormone therapy[2].

In this report, it is presented a case of prostate cancer in patient with typical risk factors (age and family history), with common symptoms (but not specific, week urine flow), which a priori had levels of PSA in the range of doubt and a rectal examination without modification. But, with the follow-up, the PSA elevated exaggeratedly, and bone metastases were identified, already with clinical repercussions. What draws attention in this case is the rapid evolution of the tumor, presence of less common metastases in prostate cancer, such as the lung, and the good response to treatment based on strong evidence, the CHAARTED study.

CASE REPORT

Patient, 53 years old, male, administrator, non-smoker, drinker, with positive family history of prostate cancer (father died due to this illness), with weight loss of approximately four kilograms and currently in use for Revange®. Main complaint: weak urine flow and painful urination for about 8 months. Urologist requested total PSA : 7.02 (06/03/2016). Rectal Examination without changes (S.I.C.). Since then, the patient was followed up bimonthly with total PSA, until 10/21/2016 resulted in 99.77. Next, the patient presented lumbago and the son doctor requested a computed tomography scan which showed diffuse secondary lesions in lumbar spine and a multiparametric magnetic resonance of prostate that revealed diffuse changes of signal from the left peripheral zone with lymph node enlargement in right external iliac chain. On 11/21/2016, the patient sought the oncologist, with facial pain and important lameness, and with the following result from pathological examination:

Right lobe:

1) Apex: Acinar Prostate Adenocarcinoma , Gleason score 7 (4+3)

2) Third medium: Prostate Adenocarcinoma, Gleason score 9 (4+5)

3) Basis Prostate Adenocarcinoma, Gleason score 9 (4+5)

Left lobe:

1) Apex: Prostate Adenocarcinoma, Gleason score 9 (4+5)

2) Third medium: Prostate Adenocarcinoma, Gleason score 9 (4+5)

Basis: Prostate Adenocarcinoma, Gleason score 9 (4+5)

In possession of anatomopathological results, a bone scintigraphy and computed tomography scan of the chest were requested, whose results showed:

1) Bone scintigraphy: neoplastic infiltrate in

the bone marrow (standard SUPERSCAN).

2) Prostate US: prostate of 40.3 g

3) CT scan of the chest (11/17/2016): small pulmonary nodules with perilymphatic distribution (carcinomatosa lymphangitis?) With multiple osteoblastic lesions diffuse in bone structure, consistent with secondary lesions (FIGURES 1, 2 and 3).

Figure 1 – Lungs nodules

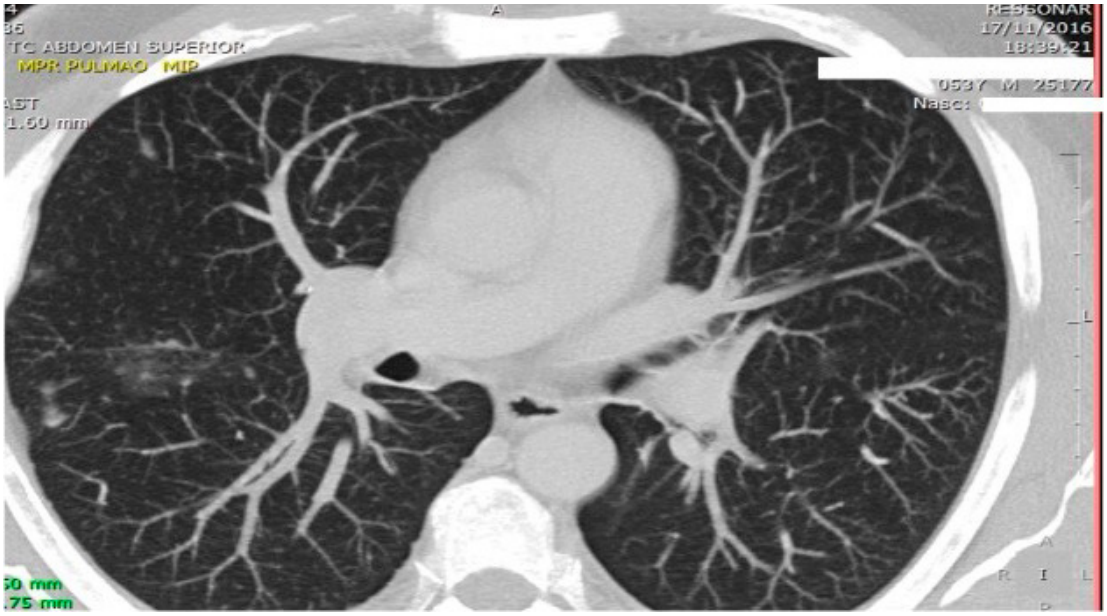


Figure 2 - Osteoblastic lesions

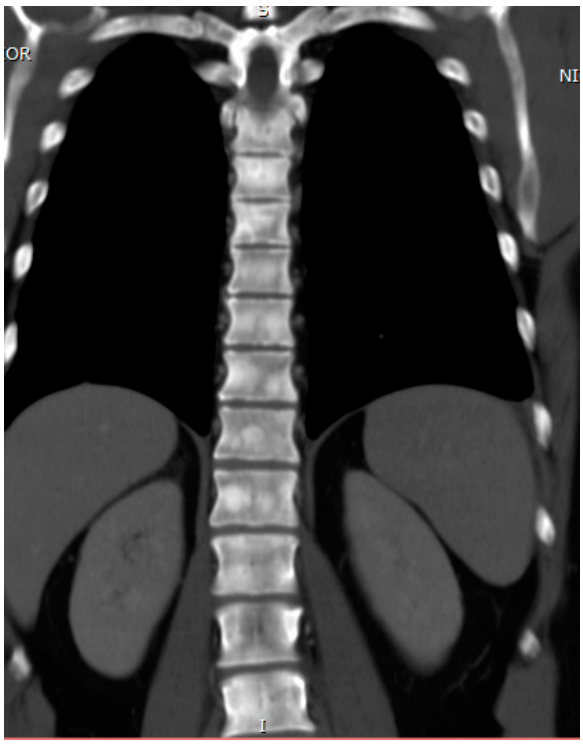
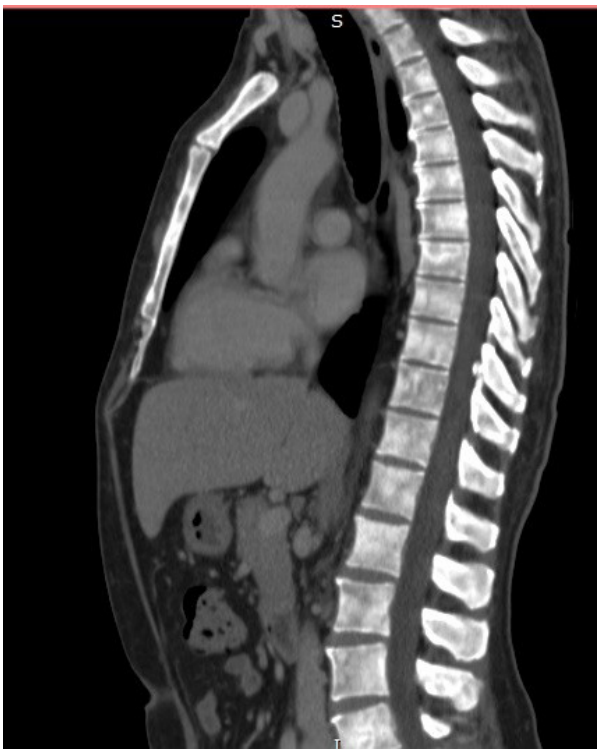


Figure 3 - Osteoblastic lesions



It was started then promptly the chemo-hormone therapy according to CHAARTED protocol, considering significant systemic disease, with Taxotere® 75 mg/m2 EV 21/21 days and Zoladex® 3.6 mg 28/28 days. After the first chemotherapy cycle the patient attends with excellent general condition, without the use of analgesic, without limping.

On 03/29/2017, the chemotherapy is concluded and on 04/17/17 the patient returns with the following exams for evaluation of response:

1. Bone scintigraphy (31/03/2017): SUPERSCAN standard Unchanged comparing to the previous one.

2. Chest TC (03/31/2017): persistence of micro and small pulmonary nodules (carcinomatosa lymphangitis?).

3. MRI Abdomen Total (03/31/2017): study demonstrating stability of dimensions of neoplastic lesion of the peripheral zone of the prostate, highlighting a slight reduction of hypo intense signal related to the reduction of tumor aggressiveness + complete regression of the lymph node in the right external iliac chain + a reduction in the dimensions of the prostate tumor that stretched to the floor of the bladder.

4. TOTAL PSA of 2.91

After beginning the therapy, the patient exhibited an expressive gain in quality of life, partial remission of pulmonary and ganglionary lesions and persistence of bone lesions. Zoladex® was kept and Zometa® 4mg EV was introduced on 05/1/17 both 28/28 days.

DISCUSSION

In Brazil, the prostate cancer is the second most common among men (only behind non-melanoma skin cancer). The increase in the rates of incidence in Brazil can be partially justified by the evolution of diagnostic methods, by the improvement of the quality of information systems in the country and the increase in life expectancy, since this is considered a cancer of the third age.[1.3] Studies show that the possibility of being diagnosed with a prostate cancer of high risk increases significantly after 50 years among white men who have no family history of the disease and after 40 years of age in black men and those who have a relative of first degree with a history of prostate cancer.[4]

Prostate cancer is usually suspected based on rectal examination and/or in the levels of PSA, and the definitive diagnosis depends on histopathological analysis. The rectal examination presents limitations when the prostate lesion is not palpable (initial stages) and, when altered, the differentiation between malignant and benign lesion is difficult. The serum PSA, in clinical use since 1986, is the most often used tumor marker for screening for prostate cancer. It plays an important role in the early diagnosis of this cancer, impacting on the reduction of morbidity and mortality.[5]

The screening PSA examination has as main objective to detect the largest possible number of cases. Despite of having a high sensitivity, this examination has low specificity for prostate cancer, since other diseases also prostatic may raise its value, such as the benign prostatic hyperplasia. Thus, in order to maintain acceptable rates of diagnosis, many patients undergo unnecessary biopsies. There is an area of doubt, traditionally considered the range of values of PSA between 2.6 and 10.0 ng/ml, in which all patients are considered suspicious for prostate cancer. This zone of doubt, PSA has low specificity, with approximately 75% of prostatic biopsies tested negative for neoplasia. For a better sorting of candidate patients for this procedure,

new parameters have been analyzed. Among them, we have the density of PSA, which is the ratio between the absolute value of the PSA and prostate volume.[5]

It is worth mentioning that, in Brazil, the National Cancer Institute recommends that men from 50 to 70 years, when they are serviced in health services, receive information about the limitations, the risks and the benefits of early detection of this type of cancer, so that they can choose whether or not to perform these exams.[6] This is because some of these tumors can grow quickly, spreading to other organs and can lead to death, but the vast majority grows so slowly (take about 15 years to reach 1 cm3) which is not enough neither to give signs during the life and nor to threaten the man's health Thus, an under diagnosis and under treatment would be negative consequences of screening, since complications such as urinary incontinence (UI) or erectile dysfunction (ED), associated with some forms of treatment of prostate cancer, may reduce the quality of life of man.[2] On the other hand, Screening programs for prostate cancer can diagnose often patients with cancer confined to the organ, reducing mortality.[7]

The need for biopsy of the prostate is based on the level of PSA and/or suspect rectal examination. Age, comorbidities and the therapeutical consequences should be considered before the decision to perform the procedure. It is noteworthy that the isolated elevation of PSA, itself, does not mean immediate biopsy, thus the level of PSA should be dosed again after a few weeks. It should be emphasized that the study by multi-parameter magnetic resonance or functional, has evolved to become the fundamental pillar in the management of patients with prostate cancer. Such a technique is related to the biological properties of the tumor, so that the diffusion relates to the cellularity and Gleason scores, the permeability relates to angiogenesis, and the spectroscopy of protons is related with the metabolism of the cell membrane. The use of these methods in combination increases the diagnosis confidence and allows a better characterization of prostate cancer.[8]

In addition, another relevant factor to be investigated in patients with prostate cancer is the presence of metastasis, which will define its staging and influence considerably the prognosis. It is known that the most common site of hematogenous dissemination of prostate cancer is the bone. The most widely accepted method to detect tumor dissemination in the skeleton is, therefore, the bone scintigraphy. Its routine use in all patients newly diagnosed with prostate cancer is controversial. Recent studies recommend the bone scintigraphy for asymptomatic patients at higher risk of bone metastases, as those with PSA $\geq$ 20 ng/ml or Gleason $\geq$ 8.[9] Whereas for patients with symptoms suggestive of bone metastases its indication is consensual. Most of the morbidities and mortalities in advanced prostate cancer is due directly or indirectly to the metastatic bone impairment, including bone pain, fractures, immobility.

Pulmonary metastases, in turn, are relatively infrequent. [10] When present, the usual pattern of spread is through lymphatic routes, almost always occurring concomitantly with bone metastases and in late stages of the disease. Isolated lung metastasis represent a very rare event.[11] Uncommon fact in the patient under study is the presentation of an adenocarcinoma of the prostate of high degree with bone and lung metastases in an early phase of the disease.

The prostate cancer treatment can vary in multiple modalities of therapy, single or combined. It includes since the active observation, in elderly patients with multiple comorbidities, with frequent evaluation noting if there is growth or changes, to most modern therapies, such as vaccines. Radiation therapy has multiple functions, including control of complications, such as hematuria and urinary obstruction, in addition to the treatment of local tumors, and it is possible to use, for example, brachytherapy with or without the therapy of external radiation as single modality of treatment. Local tumors can be treated with surgery. In addition, the hormonal castration arises as an important modality for patients who are not surgical or who want to avoid surgery as well as chemotherapy is an important treatment for metastatic disease and more aggressive tumors.[12]

For decades, it consisted, as first-line treatment for metastasis prostate cancer sensitive to hormone, castration, or surgical or by deprivation of androgens, using agonist or antagonist to LHRH (Receiver of Luteinizing hormone).[13] Knowing the importance of androgenic path in the progression of prostate cancer, the initial treatment of cancer sensitive to castration involves lower levels of androgens through the use mainly of similar GnRH (Receiver hormonal chorionic gonadotropin). There is a concordance in setting castration such as testosterone levels below 50 ng/dL, emphasizing, however, that the literature indicates clinical benefits in maintaining lower levels, as 20 ng/dLL.[12]

Several institutions began to follow the new studies. As to chemotherapy in patients with prostate cancer sensitive to castration, the majority of the panel composed for the First Brazilian Consensus on Advanced Prostate Cancer, of the Brazilian Society of Clinical Oncology and Brazilian Society of Urology, agrees with the association of Docetaxel® with the hormonal suppression for patients with high volume disease. It was considered as more adequate definition for high volume that exposed by CHAARTED trial, which defines as the presence of visceral disease and/or four or more bone metastases, being at least one extra pelvic waist and vertebral column.[12] It should be noted that, despite of the CHAARTED trial have shown that there is an increase in survival in patients with low volume, there was no suitability in the statistical analysis of this group due to the low number of deaths observed and the small number of patients.[14]

The European Association of Urology (UAE), European Society for Radiotherapy and Oncology (ESTRO) and the International Society of Geriatric Oncology (SIOG) also recommend the use of Docetaxel® associated with hormone therapy in patients with CA of metastasis prostate at the time of diagnosis, if they have condition to receive this treatment. To deliver this recommendation, consider the three studies: GETUG 15 trial, CHAARTED and Stampede[13]

In a meta-analysis, an association of results of three major randomized clinical trials (CHAARTED, GETUG-15, STAMPEDE), with expressive results due to comprising 93% of all men who were randomized to treatment and 1271 deaths, shows a Hazard Ratio of 0.77, which represents an absolute improvement in 4 years of 9%. Moreover, the addition of Docetaxel® to standard treatment showed improvement in failure-free survival rate, with HR of 0.64, which represents an absolute reduction in failure rate of 16%.. Thus, the meta-analysis confirms that there is reliable and sufficient evidence to indicate Docetaxel® in addition to standard treatment, which for such a long time has remained as first-line treatment. Even in these trials, it is noted increase in side effects with the addition of Docetaxel®, being the most neutro-

penia. 16 deaths have been attributed to the drug. Even though, the benefits outcome the risk for the indication of this addition, and this is the standard treatment for men in conditions to receive chemotherapy.

The patient in this study had risk factors classically described for prostatic carcinoma, with emphasis on age and positive family history. The symptoms are common in prostate cancer, but not specific to this disease, combining high levels of PSA in the range of doubt and a rectal examination without modification. The monitoring, however, evidencing very high PSA values, associated with the development of probable bone pain in backbone (bone metastases are usually symptomatic) awakens more suspicion to prostate cancer. In the literature, there are other cases of disease identified from the metastasis, as a case of a 60-year-old patient, in whom the initial manifestation was cervical lymphadenopathy and dyspnea, possessing also bone metastases. In this patient, the PSA levels (approximately 100 mg/ml) were similar to our patient. [15]

In subsequent evaluations, prostate cancer is diagnosed, with probable quick evolution, possessing high risk for dissemination, which was associated, in our patient, to common metastasis, such as the bone, and even less common in prostate cancer, such as pulmonary. Some reports found in the literature show pulmonary metastasis in the recurrence of disease, different from the patient of this case, who exhibited them at the initial diagnosis.[16,17]

Another point to be highlighted is a good response to treatment of this patient based on strong evidences in the case, the CHAARTED assay. Quality of life improvement was reported such as symptomatic relief, especially of pain, and improvement of general condition and gear. The primary tumor and regional lymph nodes associated, besides not exhibiting progression, obtained a reduction, adding even regression of metastatic pulmonary lesions and stability of bone lesions. PSA also showed significant decrease in their levels, being that in one measure was approximately 99 ng/ml falling down to 2.97 ng/ml.

FINAL CONSIDERATIONS

Knowing the importance of prostate cancer in the country, due to its high prevalence and incidence, and the importance of disseminating knowledge about a successful treatment in a patient with advanced stage of disease (even with less typical metastases, as the pulmonary), this report aims to disseminate the work performed in a patient in whom it was possible to promote a better quality of life and survival, which may be valid for patients with similar condition.

Finally, it is worth noting that the report is in accordance with the ethical question, having been assessed by the ethics committee - Unimontes (number 1.074.475).

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