63 - Primary myeloid sarcoma of the prostate: a diagnostic challenge

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INTRODUCTION

Myeloid sarcoma (MS) is defined as the growth of myeloid blasts inside an extra-medullary site leading to the formation of one or more tumor masses that destroy the normal architecture pattern of the tissue. The most common sites are the skin, bone or lymph node, but it can affect every site of the human body. Generally, MS is divided in primary MS, when it is diagnosed in patient without a history of myeloid leukemia, MDS or myeloproliferative disorders but these develop with an involvement of blood or bone marrow after a period that ranges from five to twelve months and in secondary MS if it occurs with or following the onset of systemic bone marrow leukemia or represents a relapse of hematological disorder. It was included in acute myeloid leukemia (AML) and related neoplasms in the WHO Classification of Tumors of Hematopoietic and Lymphoid Tissue and it is maintained in this category also in the new 2016 revision of this classification. In literature, twenty-five cases of Myeloid Sarcoma of the Prostate (MSP) have been described, among these, eleven are primary MS, twelve are secondary MS (two cases are not available to investigate). We describe another case of primary MSP with the development of an AML at high risk after three weeks.

CASE REPORT

A 66-year-old white male, with a history of cardiac surgery (mitral valve replacement and double aorta-coronary bypass) presented at Urology Department with lower urinary tract symptoms (LUTS) as nocturia and weak stream. The serological values of PSA revealed: 4.63 ng/ml total PSA, 1.03 ng/ml free PSA and 22% PSA ratio. At trans-rectal ultrasound (TRUS) the prostate appears with normal and symmetric shape, with volume of 44 cm3. Urologist's diagnosis was benign prostatic hyperplasia (BPH) and he was treated by doxazosine and a prostate supplement. At that time the patient presented the following blood count: WBC 4.08 (103/µl), Hb 14.7 (g/dl), PLT 139 (103/µl). At follow-up after two months patient's serological total PSA values resulted increased to 7.31 ng/ml, with 1.04 ng/ml free PSA and 14% PSA ratio. Suspecting it was acute prostatitis, it was prescribed an antibiotic therapy but the PSA exams performed after a week reveals gain to both total PSA (12.38 ng/ml) and free PSA (1.54 ng/ml). During this period, patient shows general symptoms such as weakness and nocturnal low-grade fever and for this reason begins a cardiologic check-up that results normal. After these investigations, a prostate biopsy was performed. At time the prostate volume was 58 cm^3 with normal echo-structure with small mixed area on the right side. In the same day, the patient turns to emergency room for uncontrolled gross hematuria that was managed with a three-way catheter bladder irrigation. In this setting, a blood complete count was performed, which showed: WBC 74.720 (10^3/µl), Hb 14.7 (g/dl), PLT 52 (103/µl). Hematologic consultation and a blood smear reveal an AML, more characterized in the following days when the patient is settled in Hematology Department. The immunophenotype profile resulted to be composed of two cell populations: 45% positive to CD34+ and 55% CD34-, both positive to CD13, CD33, CD117, CD123, CD38 and MPO. The karyotype resulted complex and molecular investigation showed the presence of 9098 copies of WT-1/104 copies of ABL, the presence of NPM1 gene mutation (808 copies/104 copies of ABL, subtype A) and presence of FLT3 gene mutation in heterozygosity. These reports defined the hematological disorder as high-risk AML. The patient received chemotherapy based on FLAIE protocol (Fludarabine, Cytarabine, Idarubicin and Etoposide). During this period in Hematology Department, the bladder catheter was set in situ because the patient presented a urine stasis when he tried to remove the catheter. During hospitalization, the pathological report of previous prostate biopsy declared the absence of any epithelial neoplastic lesions, but it also underlined the presence of a diffuse infiltrate of cellular elements with blastic aspect (CD45+, CD68+/-, CD20-, CD3-, CD15-, MPO-) (Figure 1). After first chemotherapeutic cycle, the patient was discharged from the department in a full hematologic recovery state and after a week he was invited to clinic office to assess the therapeutic response. The bone marrow aspirate revealed a minimal residual disease. During the second chemotherapeutic cycle, the patient showed a total PSA of 5.66 ng/ml. The catheter was removed and a suprapubic ultrasound was performed (the TRUS was contraindicated because of his hematologic state) that showed a reduced volume of prostate compared to the volume before chemotherapy. The MSP was confirmed not only by pathologic report, but by ultrasound (volume), serological (PSA) and hematology (blood count) data too (Figure 2).

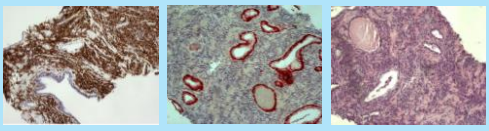

Figure 1 - The first image shows the expression of CD45 (CD45, 10X). In the second image immunohistochemical antibody cocktail staining (p63/HMWCK/AMACR) was used, while the last one was stained with HE staining (10X)."

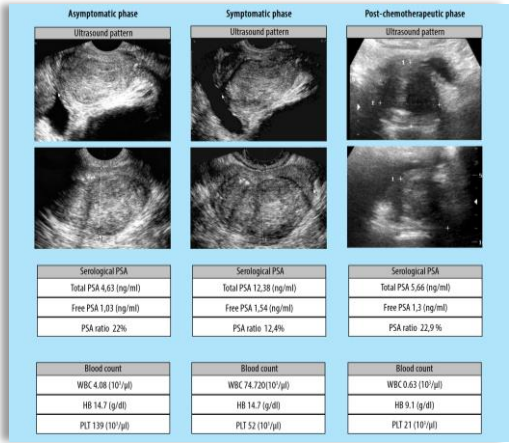

Figure 2 – The image represents in chronological order three groups of data of the case reported: ultrasound prostate pattern, serological level of PSA and main values of blood count all collected in the asymptomatic phase related to leukemia but with only LUTS symptoms, in the symptomatic phase weakness and nocturnal low-grade fever) of leukemia and after the first cycle of chemotherapy.

DISCUSSION

An MSP is a diagnostic challenge with a high probability of initial misdiagnosis. There are many reasons: it is rare and incidence has been limited to case reports, the median age of presentation at diagnosis of MSP is 66.5 years (1) in which both BPH and prostate cancer (PC) are common, the clinical manifestations are unspecific such as progressive LUTS, acute urinary retention, hematuria and enlarged prostate at rectal examination. PSA has not shown a high specificity and sensibility: in our and other cases reported in literature PSA presented a rise in symptomatic phase and a reduction post-chemotherapy but in other cases it was at normal levels (2). Clinically, even unspecific, there are red flags who alert physicians on possible MSP, especially for secondary MSP: weakness, nocturnal low-grade fever, weight loss, hemorrhagic manifestation, increased susceptibility to infections or no response to BPH-therapy. A routine complete blood count is not recommended in every patient with LUTS or in patients who will undergo prostate biopsy but it will be useful in patient who manifest the red flag symptoms. For primary MS complete blood count is useless, because in this case it is normal and the only possibility is a pathological diagnosis. Among primary MSP reported in literature the tissue diagnosis was obtained via TURP in 56.2%, prostate biopsy in 31.2% and prostatectomy in 12.5% (1). Immunohistochemical markers useful in MS are MPO and CD68. In our case, the blast population in prostate was MPO negative. This is explained by pathologist as waste antigen preservation due to fixation and coarctation of the tissue. Currently, imaging studies have demonstrated to observe a prostate lesion but without specific sign of MS. In the first line, ultrasound techniques (suprapubic and TRUS) can show an enlarged prostate while PET-CT and MRI of the pelvis can underline a suspected prostatic mass. Unfortunately, sensibility and specificity of imaging techniques have not been evaluated. Treatment for MS with or without systemic disease is typical therapy for AML (3).

CONCLUSION

A clinical pattern of LUTS and enlarged prostate at rectal examination is a challenge for Urologists who have called to consider common and uncommon (or rare) diagnosis such as MSP. An accurate medical history and the use of blood complete count in high risk patients help physicians to suspect secondary MSP, while for primary MSP the only tools are imaging study and tissue diagnosis. A multidisciplinary work-up among Urologists, Hematologists and Pathologists is necessary to avoid misdiagnosis.

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