The Diagnostic Approach to Cutaneous Metastases of Adenocarcinoma of the Prostate: A Case Report

Peppy Fourina[1], Riesye Arisanty[2], Sri Adi Sularsito[1], Lili Legiawati[1], Rahadi Rihatmadja[1], Shannaz Nadia Yusharyahya[1]

[1]*Department of Dermatology and Venereology, Faculty of Medicine Universitas Indonesia Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia*

[2]*Department of Pathology, Faculty of Medicine Universitas Indonesia Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia*

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Abstract: The incidence of prostate cancer has increased all over the world, likely due to better detection methods. It becomes one of the most common cancers among elderly men. Almost all cases of prostate cancer are adenocarcinoma. The most common sites for metastases are lymph nodes and bone. We present a case of a 67-year-old man with an ulcer on his lower back for the past 6 months. Three years ago, he was diagnosed with poorly differentiated adenocarcinoma of the prostate with bone metastases. On physical examination, there was a solitary, 2x2x1 cm ulcer with elevated border and yellowish slough. The ulcer was painful and surrounded by erythematous and indurated tissues. There is no inguinal lymphadenopathy. Despite antibiotics, conventional and modern wound dressing, no significant improvement was noted. Considering the history of malignancy, skin biopsy was performed. Histopathological examination revealed scattered atypical cells around the blood vessels that stained positively with prostate-specific antigen (PSA) and alpha-methylacyl-CoA racemase (AMACR), confirming cutaneous metastases of AP. Metastasis of AP to the skin is rare, and indicates a poor prognosis. Early recognition of cutaneous spread manifesting as ulcer that does not respond to proper treatment in the background of malignancy is important.

1 INTRODUCTION

Based on the GLOBOCAN 2012 statistics, prostate cancer is the third most common cancer in Indonesian men after lung and colorectal, with an estimated incidence of 13.663 (WHO, 2012). About all cases of prostate malignancies are adenocarcinoma (Crawford, 2009). Adenocarcinoma of the prostate (AP) favors pelvic lymph nodes and bone for its metastases, while cutaneous metastases are distinctly rare (Patne et al., 2015; Tengue et al., 2017). Cutaneous metastases of AP usually appear as nodule or papule in the abdominal, inguinal region, anterior thigh, and near the umbilicus (Pistone et al., 2013; Alcaraz et al., 2012). Although uncommon, cutaneous metastases usually occur late and indicate grave prognosis (Patne et al., 2015; Wang et al., 2008). Dermatologists have to be aware of the various clinical lesions of cutaneous metastases because early diagnosis and prompt management will result in favorable prognosis. We report a rare case that illustrated the diagnostic approach to cutaneous spread of AP, presented as a chronic ulcer on the lower back.

2 CASE

A 67-year-old male patient was consulted from Internal Medicine Department with a chronic ulcer of 6-month duration located on his lower back. Initially, it began as pruritic papules that later became ulcerated. No previous medications were applied. Past history was noted for diabetes mellitus, hypertension, and prostatic cancer.

Three years before, he complained worsened lower back pain followed with weakness on lower extremities; physical and imaging examination concluded spinal cord compression due to metastasis. Based on a markedly elevated prostate-specific antigen (PSA) and imaging studies, the primary cancer is adenocarcinoma of the prostate. Prostate

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biopsy confirmed a Gleason score of 4+5=9, associated with poorly differentiated prostate adenocarcinoma. Whole abdomen CT scan showed no paraaorta, parailliac, and inguinal lymphadenopathy. After bilateral subcapsular orchiectomy as an androgen deprivation therapy, his PSA dropped from 215 ng/ml to 0.03 ng/ml. He also had 30 radiotherapy session, followed by bone directed therapy using bisphosphonate injections for 24 months.

The patient was moderately ill. A solitary, 2x2x1 cm ulcer was found on his lower back corresponding with lumbar 1-2. It had elevated border and yellowish slough as its base. The ulcer was painful and surrounded by erythematous and indurated tissues (figure 1). No lymphadenopathy was noted. He was treated as bacterial ulcer with normal saline dressing and topical fucidic acid 2% cream.

When no significant improvement was achieved after 2 weeks, the ulcer was treated with cutimed sorbact gel and cutimed siltech. Still, it has not healed by two weeks. Cutaneous metastases from PA was considered along with the differential diagnoses of bacterial ulcer and squamous cell carcinoma. We performed bacterial culture and incisional biopsy. Bacterial culture was positive for Pseudomonas aeruginosa, sensitive to Levofloxacine.

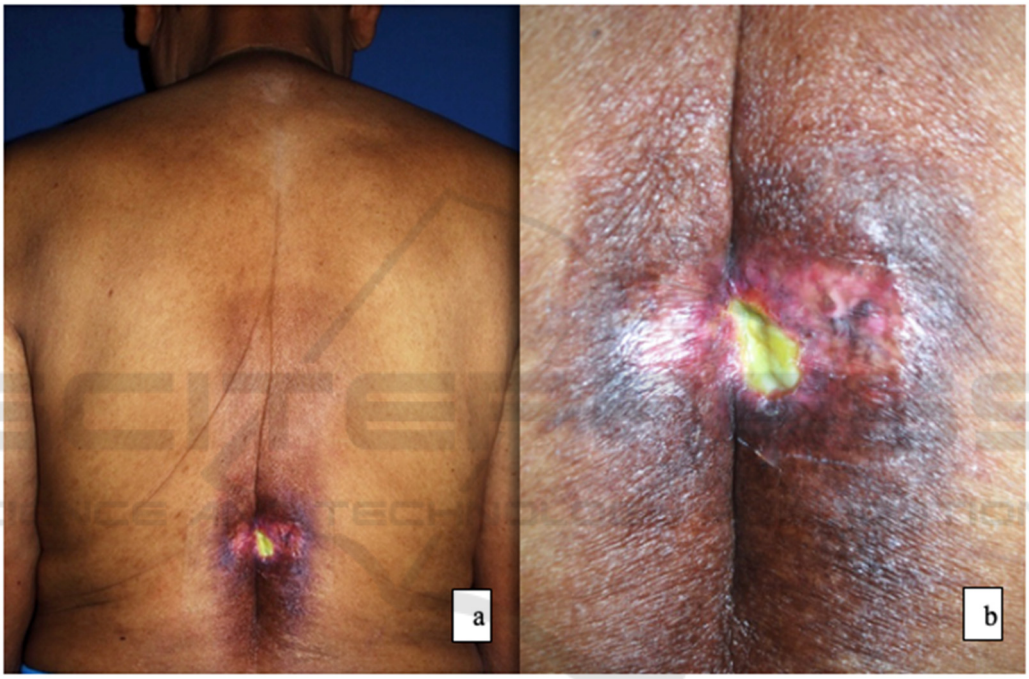

Figure 1. (a)(b). Solitary ulcer at the lower back

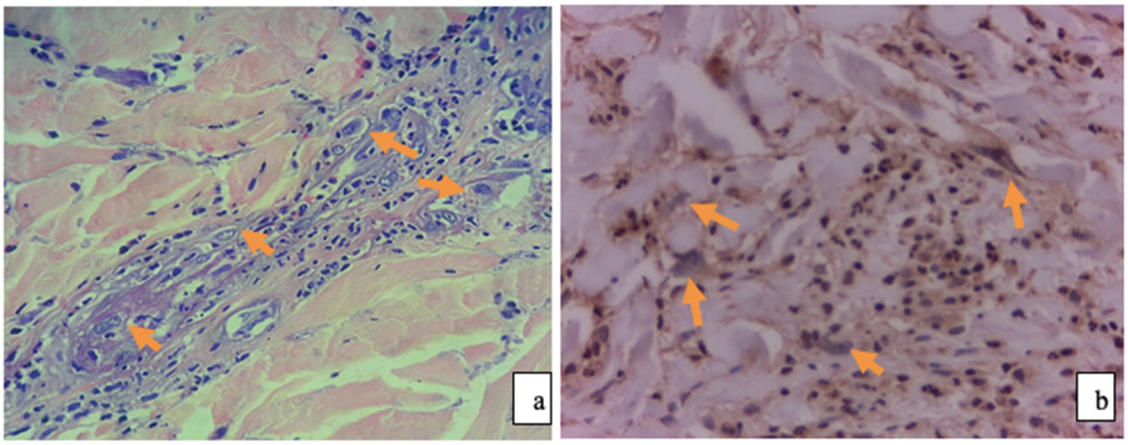

Figure 2. Histopathological and immunohistochemistry examination: (a). scattered atypical cells (H&E 400x), (b). the cells were positive for AMACR stain

Table 1. Sensitivity, specificity, positive predictive value, and negative predictive value for PSA and AMACR highly specific for AP[15]

Prostatic markers	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)
PSA	100%	90,6%	89,5%	100%
AMACR	66,7%	77,3%	86,1%	77,3%

Histopathological examination revealed scattered atypical cells around the blood vessels, suggesting metastasis (figure 2a). Immunohistochemistry was positive for PSA and AMACR (figure 2b). These finding strongly supported the diagnosis of cutaneous spread of AP.

3 DISCUSSION

Cutaneous metastasis is defined as a spread of malignant cells from a primary cancer to the skin. The exact mechanism of metastasis remains unclear. Malignant cells may spread beyond the prostate through some hypotheses, such as direct infiltration, lymphatic, hematogenous, or combination of these routes (Rattanasirivilai et al., 2011; Rodriguez-Lojo et al., 2016). A meta-analysis study by Krathen et al. (2003) found the overall incidence of cutaneous metastasis in 2003 was 5.3% from 20,380 cases. The most common tumor which spread to the skin was breast cancer, with an incidence of 24%. Skin metastates from AP are rare, with an incidence of 0.7% (Crawford, 2009; Stanko et al., 2007).

AP favors bones and lymph nodes for its metastases (Tengue et al., 2017; Brown et al., 2014). The result of whole spine MRI and bone scan revealed osteoblastic lesions as metastases to spine, cranium, costae, sacroiliac, and ischium. For this bone metastases, the patient had 30 radiotherapy session and followed by bone directed therapy with bisphosphonate injections once in a month for 24 months. Whole abdomen CT scan showed no para aorta, para iliac, and inguinal lymphadenopathy.

Cutaneous metastases of PA have more than one of clinical morphology, they most frequently appear as nodules or papules in the abdominal wall, inguinal region, anterior thigh, and near the umbilicus as Sister Mary Joseph nodules (Mak et al., 2014; Wang et al., 2008). They usually asymptomatic and rarely ulcerated (AbAziz et al., 2013).

Immunohistochemistry might aid to confirm the origin tumor of cutaneous metastases (Rodriquez et al., 2016). In our patient, the specimen was positive for PSA and AMACR, strongly supported the diagnosis of skin metastases from the patient's AP. PSA and AMACR staining is widely used to identify metastasis of AP. PSA is a serine protease member of the human glandular kallikrein family which is highly specific for AP, because it is synthesized in the prostate ductal and acinar epithelium. AMACR is a peroxisomal and mitochondrial enzyme that plays a key role in beta oxidation of fatty acid. It is identified as being overexpressed in AP cells (Oh et al., 2016).

4 CONCLUSION

Cutaneous spread of AP is rare, but it happens in 0.7% of all skin metastases cases. Patient's complain and physical appearance can vary from one patient to another. Malignancy should always be kept in mind when working up on diagnosis of unhealed skin lesion after adequate local and systemic treatment done. The combination of clinical history, physical examination, laboratory tests, routine pathology, and immunohistochemistry assay can provide enough information for a diagnosis of metastatic adenocarcinoma of the prostate.

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