DIAGNOSTIC DILEMMAS AND PRIMARY TREATMENT BY RADIOTHERAPY IN PRIMARY SQUAMOUS CELL CARCINOMA OF PROSTATE

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ABSTRACT: Primary squamous cell carcinoma of the prostate (PSCC) is a rare disorder affecting the prostate forming 0.5% of prostate malignancies. Due to rarity of presentation there are many dilemmas regarding the clinical features, investigation and the best option in the management of PSCC. Here we studied 2 cases of PSCC retrospectively regarding the common clinical presentation, the investigations to prove the diagnosis and treatment of the patient by radiotherapy as the primary treatment. We reviewed the previous published literature about PSCC to ascertain the best treatment option based on the stage of the disease.

KEY WORDS: Prostate, Squamous Cell Carcinoma, diagnosis, Treatment modalities.

INTRODUCTION: PSCC is an extremely rare pathological and clinical entity comprising 0.5-1% of the prostate malignancies¹. 95% of the prostatic carcinomas are adenocarcinomas. Only 50 cases of PSCC are reported in English literature². There are very few studies in the literature with large sample size. PSCC is a more aggressive tumour than adenocarcinomas with a poor prognosis. A dismal prognosis has been usually associated with PSCC of the prostate. The average survival time has been estimated to be 14 months². As reported by Thompson et al, 5 out of 7 patients of their series survived less than 1 year³. In this context, scant information is available hitherto concerning the most valid treatment option for prostate PSCC. It usually presents with urinary symptoms of bladder outlet obstruction⁴. It is characterized by a high degree of malignancy, commonly metastasizing to the bone (mainly with osteolytic lesions), liver and lungs with a median survival time of 14 months². The histological diagnosis depends on the criteria as described by Mott¹. The treatment is usually a multimodality approach with radiotherapy (RT) and chemotherapy (CT) forming the main stay and surgery in localized malignancy. Here we have tried to investigate the dilemmas in clinical presentation, the diagnosis of PSCC and treat 2 cases by radiotherapy as the primary mode of treatment.

MATERIALS AND METHODS: The study was done retrospectively on two patients after reviewing all the medical records of the patients who were admitted with symptoms of urinary disturbance and treated over the period of past 3 years January 2010 to December 2012 in our hospital. Both the patients were proved by histology to be cases of PSCC. Both the patients were studied in detail regarding clinical history and examination, radiological assessment with ultrasonography of the abdomen and pelvis, computerized tomography of the abdomen, transrectal biopsy of prostate, histopathological examination of the biopsy specimen, tumor marker assays. The treatment modalities were explained to patients. Both the patients underwent radiotherapy (RT). Patients were followed up for one year regarding recurrence of symptoms and recurrence of the disease radiologically.

Case 1: An 82 year old male patient presented with complaints of increased frequency of urination since 3 months. The patients also had hesitancy, frequency and nocturia. Examination of the patient revealed that the urinary bladder was not distended. Prostate was enlarged with a hard nodule. Rectal wall over the prostate was not involved. Cystoscopy was normal. A provisional diagnosis of carcinoma of the prostate was made. Serum PSA was 13.4 ng/ml. Ultrasonography showed a nodule within the peripheral zone of the prostate. Transrectal biopsy of the prostate was done under local anaesthesia. Histopathology demonstrated nests and sheets of moderately differentiated squamous carcinomatous cells characterized by intercellular bridges. Focal areas presented with evidence of keratin pearl formation (FIGURE-1). No squamous metaplasia or transitional cell or adenocarcinomatous components could be observed. Primary or metastatic lesions in the respiratory organs and the alimentary tract were excluded by thorough investigation. A bone scintigram showed features of age related degenerative changes in the bone. There was no scintigraphic evidence of metastasis in the skeleton. The patient underwent radiotherapy. He received external beam radiotherapy using IMRT technique to a dose of 45 GY/25# GTV for 5 weeks. Patient tolerated the treatment well. The patient is disease free at the end of year of follow up.

Case 2: A seventy five year old male patient presented with history of difficulty in urination. The patient had symptoms of prostatism since 6 months. Digital per rectal examination revealed an uneven surface of the prostate with a hard nodule. Provisional diagnosis of carcinoma of the prostate was done. His PSA was 7 ng/ml. Ultrasonography of abdomen showed a nodule within the peripheral zone of the prostate without involving the capsule. A transrectal biopsy of the prostate was done under local anaesthesia. The histopathology showed features favouring squamous cell carcinoma of the prostate (FIGURE-2). Cystoscopy was normal. Investigations were done to look for primary in the respiratory and the alimentary tract. Colonoscopy of the patient was normal. Bone scintigraphy showed no evidence of metastasis. A diagnosis of PSCC was done as it satisfied Motts criteria. All the treatment options were explained to the patient. He opted for radiotherapy (RT). The patient received external beam radiotherapy using IMRT technique to a dose of 46/25# GTV for 5 weeks. Patient tolerated the treatment well. He is disease free at the end of 1 year of follow up.

RESULTS: In the present study both the patients were elderly above 75 years of age. Both the patients had increase in frequency of urination as main symptom (TABLE-1). In both the patients digital per rectal examination revealed nodular prostate with the overlying rectal wall free (TABLE-2). Both the patients had localized disease radiologically. Serum PSA was marginally raised in both the patients. The histopathological examination of the biopsy specimen satisfied Motts criteria in both the cases. Immunohistochemistry was also suggestive of squamous cell carcinoma (TABLE-3). Cystoscopy in the both the patients were normal. Investigations to look for primary in other organs was negative in both the cases. Bone scintigraphy in both the cases did not show any evidence of metastasis. Both the patients were treated by radiotherapy for 5 weeks (TABLE-4). Both the patients are disease at the end of one year of follow up (TABLE-5).

DISCUSSION: PSCC is a very rare clinical entity affecting the prostate ¹. The histogenesis of this cancer has not been clarified. Two chief origins are presumed: the basal cells of prostatic acini⁵ and the transitional epithelia lining major ducts³. There are other theories proposed to explain PSCC histogenesis. They are:- 1) a metaplastic transformation of adenocarcinoma cells, 2) a collision-type

tumor, with the squamous component developing from metaplastic foci after radiation or hormonal therapy⁶.

Squamous metaplasia is known for occurring in the prostate in chronic prostatitis, around prostatic infarcts and after estrogen therapy or radiation therapy. In some cases, this has been misdiagnosed as squamous cell carcinoma (SCC)⁵.

Mott suggested the strict criteria for the diagnosis of PSCC: (i) a clearly malignant neoplasm's judged by invasion, disordered growth and cellular anaplasia; (ii) definite squamous features of keratinization, squamous pearls and/or numerous distinct intercellular bridges; (iii) a lack of any glandular or acinar pattern; (iv) no prior estrogen therapy; and (v) an absence of primary squamous cancer elsewhere, particularly in the bladder¹.

Even though prostate PSCC has been described in association with the use of a luteinising hormone-releasing hormone agonist and flutamide or after seed implantation for adenocarcinoma, all of these explanations could not reach satisfactory evidence^{7,8}.

Usual presentation is bladder outlet obstruction⁴. Consistency of the prostate is variable and not always hard. Different from primary adenocarcinoma, serum PSA and acid phosphatase levels are within normal limits, even with metastasis. Therefore, some cases have been preoperatively misdiagnosed as benign prostatic hyperplasia (BPH). Instead, SCC antigen in the blood is elevated and corresponds to the treatment effect or progression of squamous cancer of the Prostate⁹. The serum PSA levels in most of the cases are normal⁴.

PSCC is very rare tumor and the prognosis is very poor. This cancer is independent of androgen and early metastatic spread is not uncommon. The average post-diagnosis survival is estimated to be 14 months². The information regarding the best treatment for PSCC is unavailable. Multimodality approach is tried. There are studies where combined radiotherapy (RT)-chemotherapy (CT) has been tried¹⁰. In some studies radical surgeries have been tried¹¹.

It does appear feasible that at least some localised tumors can be resected with similar modalities to comparably staged adenocarcinoma of the prostate and long-term survivors in this setting have been reported¹².

Though some patients were treated with radical surgeries like cysto-prostatectomy with bilateral pelvic lymphadenectomy with total urethrectomy the survival of the patient were between 15 to 40 months¹¹. PSCC is generally refractory to hormonal therapy. Some of them respond to combined CT- RT.

Many drugs have been tried. CDDP-based regimens are the most established ones, possibly combined with bleomycin (BLM), peplomycin (PEP) and methotrexate (MTX)⁹.

Even after so many studies definite conclusion has not been possible regarding the best treatment for PSCC.

In an organ confined disease surgical extirpation can be done. RT in an early stage disease needs to be investigated. RT is useful in locally advanced disease. RT might be useful, especially if combined with chemotherapy, in order to achieve local control with organ functional preservation.

The most effective drugs to be used have yet to be established.

In both the cases we studied the patients presented with symptoms of prostatism. Diagnosis was with thorough clinical examination, ultrasonography of the abdomen and the pelvis, transrectal biopsy of the prostate. In both the cases the histopathological findings satisfied the Mott's criteria. Both the patients opted for RT. Both the patients were disease free during the follow up.

CONCLUSION: The usual presenting feature in PSCC is symptoms of prostatism in the seventh decade. Digital rectal examination helps in the diagnosing carcinoma of the prostate. Transrectal biopsy and histological features help in making a diagnosis of PSCC. Serum PSA can be raised in few cases. Radiological features help in staging the disease and planning the modality of treatment. In early localized disease surgery can be tried. RT can also be helpful in very elderly patients who are not fit for surgery. Radical surgeries have not shown to increase the survival in advanced cases. RT is useful in locally advanced disease. Combined CT-RT may help to achieve local control with organ preservation. The most effective drug to be used is yet to be established.

As the sample size in our study is small there is a need for long term studies with bigger sample size.

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Figure 1:

Case-1- Histopathology showing nests and sheets of moderately differentiated squamous carcinomatous cells characterized by intercellular bridges. Focal areas presented with evidence of keratin pearl formation.

Figure 2:

Case-2- Histopathology demonstrated nests and sheets of moderately differentiated squamous carcinomatous cells characterized by intercellular bridges. No squamous metaplasia or transitional cell or adenocarcinomatous components could be observed.

Table -1: Symptoms of the patients

SYMPTOMS	CASE-1	CASE-2
Increased frequency of urination	present	Present
Hesitancy	present	Present
Frequency	Present	Present
Nocturia	Present	Present

Table-2: Examination findings

EXAMINATION	CASE-1	CASE-2
Digital per rectal examination	Solitary hard nodule	Uneven surface with hard nodule
Rectal wall over prostate	free	Free
cystoscopy	normal	Normal

Table-3: Investigation

INVESTIGATION	CASE-1	CASE-2
Ultrasonography and CT of abdomen	localised disease	Localized disease
Histopathological examination	Satisfied Motts criteria	Satisfied Motts criteria
Bone scintigram	No metastasis	No metastasis
Serum PSA	raised	Raised

Table-4: Treatment

TREATMENT	CASE-1	CASE-2
EXTERNAL BEAM RADIOTHERAPY	yes	Yes

Table-5: Follow up

FOLLOW UP	CASE-1	CASE-2
I year	Disease free	Disease free

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