CASE REPORT

Pleomorphic giant cell carcinoma of prostate: A rare case report

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Abstract

Adenocarcinoma of prostate with pleomorphic giant cells is very rarely encountered entity. It is necessary to identify this variant due to its highly aggressive clinical course and bad prognosis. Though this variant has been described in other sites, very few cases has been reported in the prostate till date. We report one such case with typical features with discussion on the differential diagnosis that must be considered when such case is encountered.

Keywords: Prostate, Pleomorphic, Giant cell, Carcinoma

Introduction

Adenocarcinoma of the prostate with pleomorphic giant-cells is an extremely rare unusual subtype with aggressive clinical course and poor prognosis. Many patients survive for less than a year after diagnosis. Thorough literature search revealed only 30 cases of prostate adenocarcinoma with pleomorphic giant cells till date [1].

Case Report

A 70 year old male presented with urinary obstruction for the past 2 months, complete obstruction in the last 7 days and hematuria for 15 days. Digital rectal examination revealed an enlarged indurated and fixed prostate. He was a known hypertensive and was on medication for the same. There was no history of any surgery, radiotherapy or chemotherapy in the past. His blood examination revealed anaemia and eosinophilia. Serum Prostate Specific Antigen (PSA) which was 11 ng/ml two months prior had increased to 52.98 ng/ml at admission. Computerised Tomography (CT) scan and Magnetic Resonance Imaging (MRI) scan revealed enlarged prostate with heterogeneously enhancing nodular lesions, with extracapsular extension and metastases to bilateral external iliaclymph nodes, liver, left lung and bilateral iliac bones, pubic bone and sacrum. Urinary bladder was spared. On Technetium 99m-Methyl Diphosphonate (99mTc MDP) whole body bone scan, osteoblastic metastases to sternum, cervical, thoracic, lumbar vertebrae and 1st and 6th ribs was noted. A 12-core needle biopsy from the prostate was submitted to the surgical pathology department. The tissues were formalin fixed, processed and embedded in paraffin. Haematoxylin and eosin stain was used to study the morphology. Microscopy of 6 cores taken from right side revealed a high-grade adenocarcinoma with neoplastic cells in diffuse sheets, fused glands and cribriform pattern with Gleason's score 5+4=9; grade group 5. The other 6 cores from the left side revealed large pleomorphic cells, with bizarre enlarged nuclei, nucleoli were prominent, some showing atypical mitotic figures. Cytoplasm was abundant and showed small hyaline globules.

Mononuclear as well as multinucleated giant cells were present. Necrosis was also seen. Spindle cell morphology or heterologous elements were not seen. Hence a diagnosis of pleomorphic giant cell carcinoma of prostate was made. The patient was advised chemotherapy. Six months of follow up revealed good response to treatment.

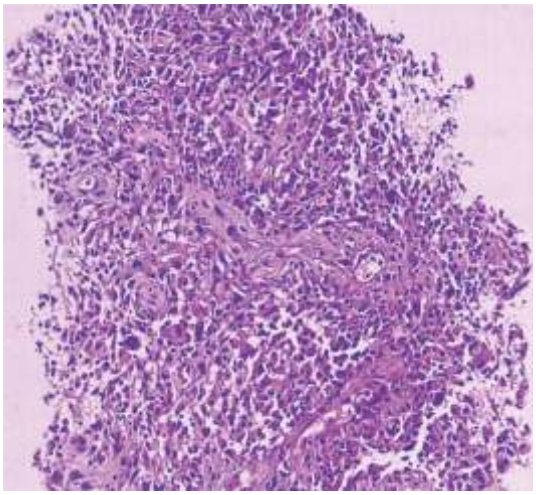

Figure 1: Mononuclear and multinucleated giant cells with nuclear atypia, atypicalmitotic figures. (×100; H & E Stain)

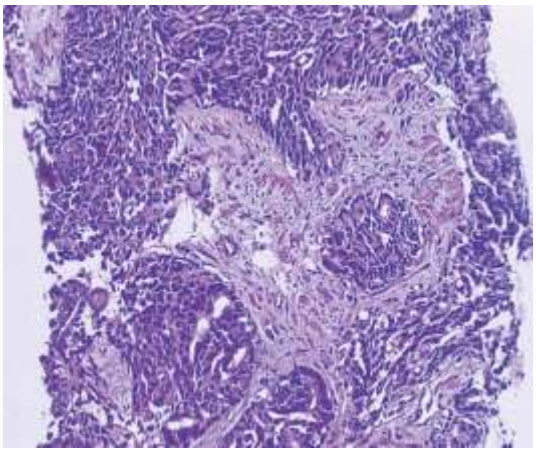

Figure 2: High grade prostate adenocarcinoma with Gleason's pattern 4 & 5; Score 9. (× 100; H & E Stain)

Discussion

Pleomorphic giant cell variant of prostate adenocarcinoma is a new variant mentioned in the WHO classification 2016. It is associated with higher mortality than the conventional acinar adenocarcinomas [2]. Clinical course is aggressive. Pleomorphic giant cell carcinoma has been reported in various organs like bladder, pancreas, ovary, oesophagus, breast and lung as well [3-9]. However, in prostate very few cases have been reported. Thirty cases have been reported between 2005-2018 [1]. Further, no cases have been reported till date. Characteristic histologic findings of this subtype include large cells which are dyscohesive, with abundant cytoplasm, enlarged mononuclear and multinuclear, atypical or bizarre nuclei, having prominent nucleoli. Cells may show small hyaline globules within the cytoplasm and atypical mitotic figures. Presence of necrosis is another important finding. It lacks significant spindle cell component. Marked atypia and presence of pleomorphic component ranges from 5% to up to 70% [10]. The pleomorphic giant cell component can coexist or be a component of the prostatic adenocarcinoma of high grade or other types of prostatic epithelial carcinomas [11].

According to WHO, Gleason's score or grading is not recommended for the rare variants [12]. Only the coexisting adenocarcinoma if present can be graded which almost always is of high grade with Gleason's score of 9-10 and Grade group 5. Histogenesis of this entity is not known. But it is suggested that chemotherapy and radiotherapy could be the etiological factors which can lead to development of this variant [13]. However, this has not been proved. Differential diagnoses that may be considered in these cases include sarcomatoid carcinoma, Radiation atypia, pleomorphic variant

of bladder carcinoma and metastatic carcinoma with pleomorphic giant cells. Sarcomatoid carcinoma have significant spindle cell component, with very few or no bizarre giant cells. However, differentiating these two will be of no clinical significance. Radiation atypia can show hyperchromasia, bizarre cells and necrosis. However, these changes are not atypical but are of degenerative nature with smudgy nuclear chromatin. In pleomorphic carcinoma of bladder with extension into prostate, primary tumour has to be demonstrated in the urinary bladder, which may also show in-situ urothelial component and PSA will be negative. In addition, the conventional prostatic adenocarcinoma of prostate component which usually coexist, will be absent. For metastatic pleomorphic carcinoma history is critical, with a panel of immunostains in addition to PSA.

But again, the presence of coexisting typical primary prostatic adenocarcinoma can rule out a metastatic carcinoma to prostate. In our case, there was presence of coexisting typical high-grade prostatic adenocarcinoma on right side and pleomorphic giant cells component on the left side, constituting almost up to 50%. PSA levels were high, there was absence of urinary bladder involvement, osteoblastic metastasis to bones was present, all of which point towards the diagnosis of primaryhigh-grade prostatic adenocarcinoma with a rare pleomorphic giant cell carcinoma variant. Hence, this eliminated the need for immunohistochemistry (IHC). However, Immunohistochemical staining is not diagnostic since the giant cells may be negative for PSA, or may show varying degree of positivity. Strong positivity for Cam 5.2 and Cytokeratin AE1/AE3 is noted in the giant cells [12].

Parwani and his associates in 2006 [14] reported 6 cases, their observations being, marked pleomorphism and bizarre cells constituted 5-70% in different cases. The coexisting histologic components were conventional acinar adenocarcinoma, squamous carcinoma, ductal adenocarcinoma and small cell carcinoma. Staining of giant cells for PSA varied from 0-50%, 2 cases had received chemotherapy and radiotherapy few years back. All the cases had aggressive clinical course, three of them with wide spread disease, two alive for 3 months and 1 year respectively at the time of follow up, and one succumbed. Alharbi *et al.* [1] in the year 2018 identified and reported 30 cases of prostatic adenocarcinoma with focal pleomorphic giant cell features during the period 2005-2018. Literature search revealed that no more cases have been reported later till date. Diagnostic specimens included needle biopsies, TUR, bladder biopsies, radical prostatectomy and orchidectomy. According to their observations, most of them showed extensive disease, with high grade prostatic adenocarcinoma (Grade group 5). They observed that areas with pleomorphic giant cell features were focal and constituted less than 5%. Many of those diagnosed as prostate adenocarcinoma with such giant cells did not survive for more than a year after diagnosis. In contrast to the 30 cases reported by Alharbi [1], where they found that pleomorphic giant cell component constituted less than 5% in their series, our case showed entirely pleomorphic giant cell morphologyin 6 out of 12 cores taken from right half of prostate while the other half showed conventional high grade adenocarcinoma. Lotan *et al.* [15] performed next-generation sequencing on cases of this rare variant and found that such rare variant of prostate carcinoma frequently show DNA damage

repair mutations, and also found that homologous DNA repair genes and mismatch repair genes showed bi-allelic pathogenic mutations.

Conclusion

We report this case since occurrence of this variant is extremely rare and it showed all the typical morphological features and the aggressive nature as described in the WHO classification. One should be aware that poor prognosis is associated with this subtype.

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