Synchronous Occurrence of Prostate Carcinoma and Multiple Myeloma: A Case Report

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Abstract We describe a rare case of metastatic prostate cancer to bone marrow and synchronous multiple myeloma as the second malignant disease. Various diagnostic procedures, including cytomorphology and immunohistochemistry analyses together contributed to the detection of metastasis of prostate cancer and synchronous plasma cell proliferation in the bone marrow. The association between these two disorders is poorly understood however, some studies show that bone marrow microenvironment may play a crucial role. The need for further research in this regard is required to unfold this fascinating association.

Keywords Synchronous · Prostate cancer · Multiple myeloma · Cytomorphology · BMME

Introduction

Synchronous occurrence of prostate cancer and multiple myeloma is a rare event with very few cases reported in literature [1–5]. The association between these two disorders is poorly understood however it has been suggested that bone marrow microenvironment (BMME) may play a

crucial role [6]. BMME is a niche composed of a cellular compartment (stromal cells, osteoblasts, osteoclasts, endothelial cells, and immune cells) and a non-cellular compartment including the extracellular matrix (ECM), cytokines, growth factors, and chemokines [7]. Microenvironment for myeloma and prostate cancer show many important similarities. Interleukin-6 (IL-6) and Insulin-like growth factor 1 (IGF-1) which are essential growth factors for myeloma cells also play a key role in prostate cancer. Both increase proliferation by activating the RAS–MAPK signal transduction pathway and suppressing apoptosis. Stromal-derived factor 1 (SDF1) which is a chemo-attractant causing selective adhesion of myeloma cells to bone has recently been implicated in the pathogenesis of metastatic prostate cancer cells to bone. Possibility of the impact of immunosuppression from multiple myeloma and chemokines released by circulating myeloma cells including IGF-1, IL6, SDF1 and VEGF on the progression of prostate cancer to detectable stages is suggested [6]. The need for further research in this regard is required to unfold this fascinating association.

Here, we describe a case of a carcinoma prostate with metastasis to bone marrow and synchronous multiple myeloma. To the best of our knowledge this is the first case reported from India. A possible association based on the literature data between the two diseases is also described.

Case Report

A 62 year male patient presented with complaints of low backpain and radiation of pain to both legs since 1 year. The patient had no history of trauma. Physical examination revealed lower back tenderness. The patient was advised a spinal magnetic resonance imaging (MRI). MRI spine

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Fig. 1 Adenocarcinoma of the prostate: Gleason pattern 3 + 3 = 6 with small glands, glands fusion and cribriform type (H&E $\times 200$)

Fig. 2 Bone marrow aspirate shows tumor cells arranged in a glandular fashion. MGG $\times 1,000$

showed diffuse marrow infiltration. A skeletal survey conducted showed multiple lytic lesions in the skull. CT guided fine needle aspiration cytology for confirmation of diagnosis, from L5 vertebra was suggestive of a metastatic adenocarcinoma deposits.

A complete hemogram showed a hemoglobin of 9.6 g %, platelet count $289 \times 10^9/l$ and a WBC count of $4.1 \times 10^9/l$. Differential leucocyte count showed 73 % polymorphs, 17 % lymphocytes, 6 % monocytes, 3 % eosinophils, 1 % basophil and an occasional myelocyte. Peripheral smear examination showed mild anisocytosis with microcytes and few macrocytes. Mild hypochromasia was also noted. Blood chemistry showed serum albumin = 3.9 g/dl (3.5–5.5 g/dl), total protein = 7.4 g/dl (6–8.3 g/dl), alkaline phosphatase = 417 IU/l (20–140 IU/l), LDH = 595.9 IU/l (140–280 U/l) and uric acid = 5.12 mg/dl (2–8.5 mg/dl). Serum creatinine was 1.2 mg % (0.6–1.2 mg %), blood urea was 39 mg % (26–40 mg %). Serum calcium was 8.1 mg/dl (9–10.5 mg/dl).

Clinical suspicion of a prostatic lesion in an elderly male with metastatic deposits in the spine was considered. However, a detailed history did not reveal any urinary complaints. A per rectal examination done revealed a hard nodular growth in the prostate gland. The ultrasound of prostate showed an ill defined growth. Prostate specific antigen (PSA) levels were 122 ng/l (0.04–4 ng/l). A prostate biopsy performed under transrectal ultrasonographic guidance confirmed features of prostatic adenocarcinoma (Gleason score 3 + 3 = 6) (Fig. 1). Multiple osteolytic lesions in skull and vertebra warranted us to perform a serum protein electrophoresis which showed M-band concentration of 0.50 g/dl, which was later shown by immunofixation electrophoresis to be IgA and lambda paraproteins.

Fig. 3 **a** Trephine imprint smear shows many plasma cells with few binucleated forms MGG $\times 400$. **b** High power view shows cluster of plasma cells MGG $\times 1,000$

Fig. 4 **a, b** Trephine biopsy shows hypercellular marrow spaces with extensive infiltration by prostatic adenocarcinoma along with interstitial excess of plasma cells H&E $\times 1,000$

Therefore, a bone marrow examination was done which showed infiltration by malignant epithelial cells which were arranged in a glandular fashion (Fig. 2) It also showed 12 % plasma cells on aspirate smears (Fig. 3) and interstitial increase in biopsy sections as well (Fig. 4). IHC performed for demonstrating clonality of plasma cells by kappa and lambda showed the plasma cells to be monoclonal for lambda.

A final diagnosis of prostatic adenocarcinoma with bone marrow metastasis with synchronous multiple myeloma was made. The patient was subsequently started on COP-MP regimen in August 2013 for multiple myeloma. It consisted of weekly doses of vincristine, endoxan and prednisolone and monthly doses of melphalan and prednisone. The cycle was repeated every 7 weeks depending on the hematological parameters. He is also receiving injection leuprolide 22.5 mg every 3 monthly for medical orchiectomy. He has received two cycles and is due for the third one in December. Later on he will be put on oral hormonal therapy. Patient is responding favourably to the

treatment. There is a decrease in the M-band concentration and also lytic bone lesions.

Discussion

The incidence of the simultaneous occurrence of prostate cancer and hematolymphoid malignancies has been reported to be 1.2 % [8]. However, synchronous diagnosis of a prostatic carcinoma and multiple myeloma in the same patient is very rare [6]. Even more rare is prostate cancer metastatic to bone marrow and synchronous multiple myeloma.

For the diagnosis of multiple myeloma 10 % or more clonal plasma cells on bone marrow examination or biopsy-proven plasmacytoma, presence of serum and/or urinary monoclonal protein (except in patients with true non-secretory multiple myeloma), and evidence of end-organ damage (hypercalcemia, renal insufficiency, anemia, or bone lesions) related to the underlying plasma cell disorder are required [9]. In our case findings in favour of multiple myeloma were anemia, multiple osteolytic bony lesions in skull and vertebra and presence of 12 % clonal plasma cells which showed monoclonality for lambda light chain. Immunofixation (IFE) confirmed the presence of M-band for IgA and lambda. However there was no evidence of hypercalcemia or renal insufficiency. Multiple myeloma was suspected in this case because of the presence of multiple osteolytic lesions in skull and vertebra and the presence of M-band which showed IgA and lambda on IFE.

The mechanism by which these disorder multiple myeloma and prostate cancer influence each other development has been studied. Kao et al. [6] suggested the possible impact of immunosuppression from multiple myeloma and chemokines including IGF-1, IL-6, SDF-1 and VEGF released by circulating myeloma cells on the progression of prostate cancer.

Data suggests that myeloma cells may stimulate the production of IL-6 from stromal and bone cells. IL-6 is an essential activating growth factor and antiapoptotic agent for myeloma cells, it also plays a key role in signaling through the MAPK pathway in prostate cancer cells [6]. IGF-1 has also been described as a paracrine growth and survival factor in multiple myeloma [6]. Chan et al. reported that there was a 4.3 relative risk for prostate cancer in the group with the highest quartile of plasma IGF-1 compared to the lowest quartile [6]. Both IL-6 and IGF-1 increase proliferation by activating the RAS–MAPK signal transduction pathway and suppressing apoptosis. VEGF which is secreted by some myeloma cells lines, is an important mediator of angiogenesis. VEGF overexpression is present in the majority of prostate cancer patients and

correlates with poorer survival. SDF1 and IGF1 are potential chemoattractants causing selective adhesion of myeloma cells to bone. SDF has recently been shown as a chemoattractant of metastatic prostate cancer cells to bone potent growth factor which is thought to regulate the progression of prostate cancer. Impaired immune response has been hypothesized as a mechanism for the progression of prostate cancer.

Studies show that 45–90 % of advanced myeloma cells have c-myc dysregulation. C-myc mutations correlate with a higher grade of malignancy. C-myc amplification also correlates with a worse prognosis in patients with prostate cancer [6].

Kahr et al. [10] reported a patient with testicular plasmacytoma after chemical castration for prostate cancer. They suggested that surgical stress may have exacerbated the clinical course of the myeloma, partly because of elevated IL-6 levels after surgery, which would stimulate the growth of myelomas.

Another explanation is that immune dysfunction caused by multiple myeloma leads to more rapid progression of latent cancers or prostatic intraepithelial neoplasia which would have otherwise been asymptomatic and/or clinically insignificant. These tumors now exhibit a more aggressive phenotype which now presents with either a rising PSA or palpable mass [6].

Although, some association has been suggested, still further genetic studies are necessary, as there is some evidence pointing towards a common pathway between these two neoplasms.

Conflict of interest The author(s) declare that they have no competing interests.

Ethical standard This has been approved by the ethics committee of the institute.

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Informed consent Written informed consent was obtained from the patient for publication of this case and accompanying images.

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