

Case Report

Rare presentation of a prostatic carcinoma as pyrexia of unknown origin: A case report

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Introduction

Pyrexia of unknown origin (PUO) is defined as fever $\geq 38.3^{\circ}\text{C}$ (100.9°F) on multiple occasions for at least three weeks without an identified cause despite intelligent and invasive investigations [1]. While infections and autoimmune disorders are the most common causes, malignancies, particularly hematological and solid organ cancers, must be considered.

Case Presentation

A 74-year-old male with a long history of type 2 diabetes, hypertension and dyslipidemia presented with recurrent episodes of evening pyrexia associated with chills and rigors over several weeks. He also reported reduced appetite and unintentional weight loss for the last six months, along with cough with sputum production. Additionally, he had experienced progressive back pain over the past two months and constipation but denied any obstructive urinary symptoms.

There was a significant family history of malignancy in first degree relatives, including endometrial carcinoma and throat cancer.

On physical examination, the temperature was 100.0°F . He was pale, not icteric and there were no regional or generalized lymphadenopathy or a skin rash. The systemic examination revealed no organomegaly, spinal tenderness or focal neurological deficits. On digital rectal examination an enlarged, hard prostate was noted.

Laboratory investigations revealed normocytic, normochromic anaemia with normal leucocytes with mild thrombocytopenia [WBC: $7.90 \times 10^9/\text{L}$ (neutrophils $5.47 \times 10^9/\text{L}$,

lymphocytes $1.78 \times 10^9/L$, haemoglobin of 8.1 g/dL, platelets: $130 \times 10^9/L$. Blood film showed bicytopenia with leukoerythroblasts and marked rouleaux formation. Inflammatory markers including C-reactive protein (CRP 80mg/L) and erythrocyte sedimentation rate (ESR 140 mm/h) were elevated. Blood and urine cultures were negative. Serum procalcitonin was 0.079 ng/mL (normal range <0.5) making bacterial infection an unlikely aetiology. Biochemically his serum Na: 133 mmol/L, serum K: 4.1 mmol/L, serum creatinine: 64 $\mu\text{mol/L}$, alkaline phosphatase (ALP): 360 U/L (46 - 116U/L), gamma-glutamyl transferase (GGT): 90 U/L and total protein: 55 g/L with serum albumin: 23 g/L (35 - 50 g/L). His PSA (prostate-specific antigen) was 85.5 ng/mL (<6.5 ng/mL) with a normal urine full report.

Ultrasound abdomen revealed mild prostatomegaly (23cc). Chest X-ray showed mild focal widening of the 5th right anterior rib suggestive of a healing fracture or early metastasis. Lumbosacral spine X-ray showed degenerative changes. Contrast enhanced-computed tomography (CECT) of chest, abdomen and pelvis revealed extensive bone metastases and lower para-aortic lymph node metastasis.

Trans rectal ultrasound (TRUS) guided prostate biopsy revealed an adenocarcinoma, small acinar type with a Gleason Score: 4+3 (International Society of Urological Pathology- ISUP Grade 3). There was no perineural invasion or extra prostatic extension.

A diagnosis of metastatic prostate adenocarcinoma (Gleason 4+3, ISUP Grade 3) presenting as pyrexia of unknown origin was made.

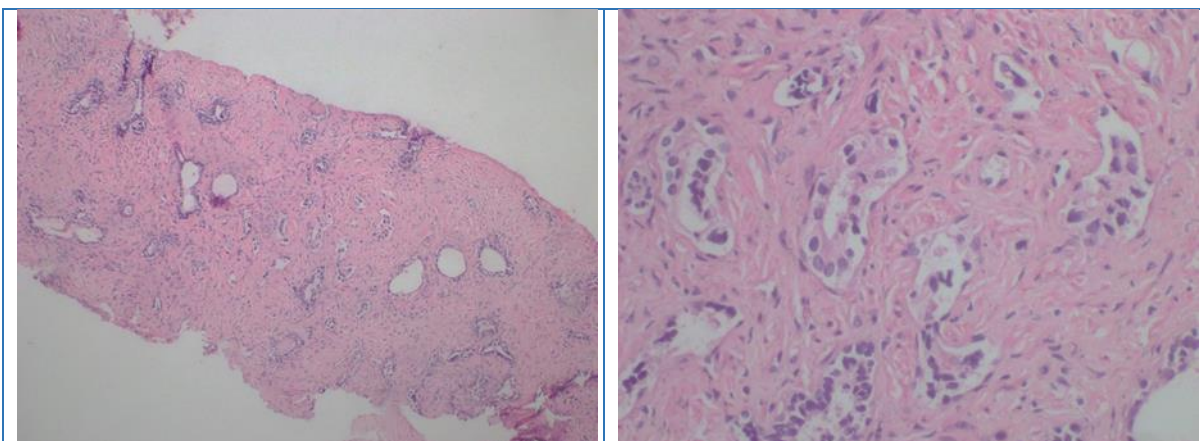


Figure 1: Histology of prostate biopsy- adenocarcinoma, small acinar type

The patient underwent bilateral sub capsular orchidectomy for androgen deprivation therapy. He also received blood transfusions for anemia. Further oncological management was planned, including palliative care and targeted therapy based on disease progression. Fever settled after starting the definitive therapy for prostate carcinoma.

Discussion

Prostatic carcinoma is typically insidious, presenting with lower urinary tract symptoms, backache and hypercalcemic symptoms or remaining asymptomatic until the advanced stages. Rarely, it can manifest as PUO, as in this case. The underlying postulated mechanisms for fever include tumor-induced inflammation leading to cytokine release bone marrow infiltration causing anemia, bicytopenia and an inflammatory response and extensive bone metastases contributing to systemic inflammation (high ALP, ESR, and CRP) [1].

The absence of symptoms of bladder outflow obstruction made the diagnostic process difficult, highlighting the need for a high index of suspicion in an elderly male with unexplained fever and weight loss.

When a patient presents with a febrile illness, differentiating an infectious etiology from malignancy is important, as long-term antibiotic therapy is required for prostatitis or prostate abscess which may delay the histological diagnosis of prostate carcinoma. A definitive diagnosis of prostate carcinoma will require a biopsy. It is mandatory to safely exclude infection prior to a prostate biopsy. Procalcitonin plays a pivotal role in excluding an infective etiology. A negative procalcitonin in our case helped in excluding a possible prostatic abscess which paved the way for an early histological diagnosis. [3].

A previously published case report described fever as the initial presentation of castration-resistant prostatic carcinoma which later responded to systemic chemotherapy. That patient had been initially diagnosed with prostate cancer and had received androgen deprivation therapy. After 8 months of treatment initiation, he presented with fever and was found to have an elevated prostate specific antigen (1639 ng/mL). He was diagnosed as castration-resistant prostate cancer and started on systemic chemotherapy. With that the fever resolved completely [4]. Fever can be a presentation of hormone- refractory prostate carcinoma as well. An 81-year-old man was reported to have presented with prolonged fever and constitutional symptoms and was subsequently diagnosed with prostate carcinoma with extensive bone metastases. Notably, his fever also resolved following initiation of chemotherapy [55].

Although lymphoma, leukemia, and colorectal cancer are the most common malignancies that cause PUO, urological malignancies have also been rarely reported. Among the urological malignancies associated with paraneoplastic syndromes, prostate cancer is considered the second most common. Fever and other related symptoms resolved with hormonal therapy or chemotherapy in all the cases reported [6].

Conclusion

This case report emphasizes the fact that prostate carcinoma should be considered as a differential diagnosis in elderly males presenting with PUO, particularly in the presence of anemia, elevated inflammatory markers, and bone metastases. A normal plain radiograph of spine may not detect skeletal metastasis. Early recognition and appropriate management are crucial to improve patient outcomes.

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