Case Report

Paraneoplastic Fever, Leukemoid Reaction and Thrombocytosis in Transitional Cell Carcinoma of Kidney: A Rare Presentation

Rajiv Yadav, Suchet Chaudhary, Poonam Yadav, Abhay Kumar

From, Department of Urology, Renal Transplant and Robotics, Medanta - The Medicity, Gurgaon, India

Correspondence to: Dr Rajiv Yadav, Senior Consultant, Uro-oncology & Robotics, Department Of Urology, Renal Transplant & Robotics, Medanta- The Medicity, Gurgaon, Haryana, India. E mail: drrajivyadav@gmail.com

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ABSTRACT

We report a rare presentation of transitional cell carcinoma of kidney with paraneoplastic fever, leukemoid reaction and thrombocytosis. Description of the case highlights an unusual clinical scenario where fever, leucocytosis, pyuria and raised procalcitonin levels at presentation in a patient with transitional cell carcinoma of kidney may mislead diagnostic work up toward an infective cause (i.e. pyelonephritis). This case will guide clinician to keep a high index of suspicion, in case they encounter such a situation.

Keywords: Paraneoplastic syndrome, Paraneoplastic fever, Leukemoid reaction, Transitional cell carcinoma

Paraneoplastic syndromes are non-metastatic systemic effects accompanying malignant diseases. The reported frequency ranges from 10-15% [1]. These are most commonly seen with cancers of the lung, breast, ovaries or lymphoma [1]. Among the urogenital tumors, renal cell carcinomas are often associated with paraneoplastic syndromes. Paraneoplastic syndromes are extremely uncommon in transitional cell carcinomas (TCC) [2]. Some of the reported paraneoplastic syndromes in TCC are hypercalcemia, [3] acanthosis nigricans, dermatomyositis, [4] polymyositis and rarely leukemoid reaction [5]. Almost all the reports of leukemoid reaction in TCC are described with primary bladder carcinoma [1]. Here we report a rare presentation of the patient with fever and leukemoid reaction in TCC of kidney.

CASE HISTORY

A 54 year old non diabetic, normotensive male presented with high grade fever of three weeks duration. He had no urinary or chest symptoms. There were no complaints of abdominal or flank pain. Investigations at presentation revealed pyuria (20-30 pus cells/hpf) along with raised total leukocyte count (TLC- 14,800/ccmm), platelet count ($530X10^3$/µl) and C reactive protein (CRP- 253mg/L). Liver function tests and alfa feto protein levels were normal. Peripheral blood smear showed- Neutrophilic leucocytosis and thrombocytosis. No parasite or abnormal cells were noted. His urine and blood cultures were sterile. Initial Ultrasonography of abdomen revealed a hypoechoic area in the upper pole of left kidney and also in segment IV of the liver. Subsequent computed tomography (CT) scan showed heterogeneously enhancing area measuring 58 x 50 mm involving the upper pole of left kidney, perinephric stranding, paraaortic hilar lymphadenopathy and a hypodense lesion in liver (**Fig. 1**).

Based upon the initial clinical features, urinary examination and imaging findings, the possibility of infective pathology (pyelonephritis with lobar nephonia and liver abscess) was considered. Therefore, he was started empirically on antibiotic therapy (Cephalosporin +

Aminoglycoside). However, no improvement in fever was noted. Serially done TLC over the next two weeks showed rise upto 53000/mm^3. CRP increased upto 240mg/L and serum procalcitonin (PCT) level was 16.5ng/ml. Interleukin-6 (IL-6) level was 33.92pg/ml (normal range 0.01-5). Further, repeated urine and blood cultures were sterile. Urine cytology showed inflammatory cells only.

At this point, detailed hematology work up was initiated along with a repeat imaging studies. Bone marrow examination was normal. Biopsy of liver lesion was done, which showed an infiltrating tumor with malignant cells in acinar pattern. Immunohistochemistry (IHC) stains were positive for Cytokeratine (CK), P63, CK7 and Uroplakin. Stains were negative for Vimentin, Synapophysin, CK20 and TTF1. A diagnosis of metastatic TCC was made. Subsequent PET-CT showed extensive skeletal metastasis, lytic lesion in the lumbar vertebra and liver metastasis (**Fig. 2**).

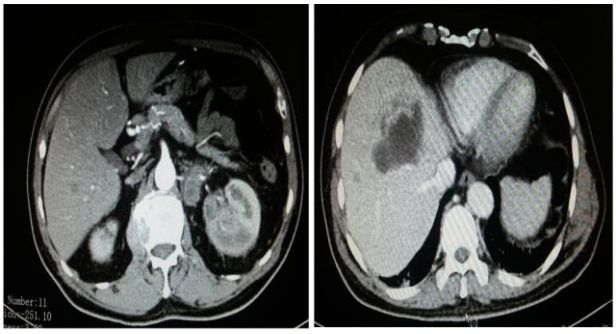

Figure 1 - (a) Axial Computed tomography scan showing heterogeneously enhancing infiltrative lesion in upper pole of left kidney, with perinephric standing and hilar lymphadenopathy (b) Axial CT showing hypodense lesion in liver

After extensive workup to rule out infectious cause for fever, he was started on oral Naproxen to treat the paraneoplastic fever. It resulted in complete lysis of fever, control of constitutional symptoms and improvement in performance status. Patient was started on chemotherapy (Gemcitabine + Carboplatin). However, he died of advanced disease within two months.

DISCUSSION

Paraneoplastic syndromes have varied presentations with fever being the most common symptom. Various presentations of paraneoplastic syndromes can occasionally mislead the diagnosis especially in instances where the symptoms manifest before the diagnosis of the underlying carcinoma. Our patient had a TCC of kidney with metastases to liver. He presented with fever, leucocytosis and thrombocytosis, without any supporting laboratory evidence of infection or myeloproliferative disorders. The presence of pyuria and CT picture of hypodense poorly enhanced portion of kidney and hypodense lesion in liver, further misled us to the initial working diagnosis of acute pyelonephritis with liver abscess.

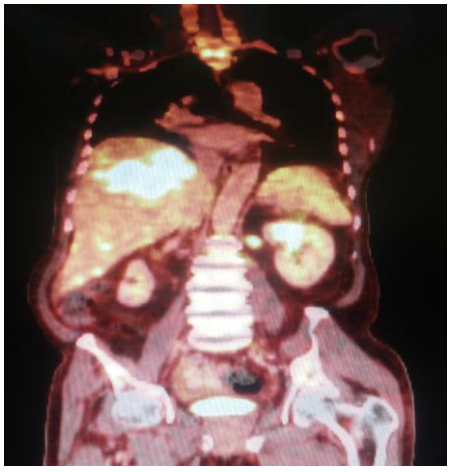

Figure 2 - Coronal section of FDG 18 PET showing metabolically active lesion in left kidney and liver

In literature, there have been only a few case reports of paraneoplastic leukemoid reaction in TCC and that too mostly in TCC of bladder. Presence of leucocytosis or thrombocytosis is also considered a prognostic indicator with poor clinical outcomes in advanced tumors [6]. Leukocytosis has been attributed to the auto-production of granulocyte colony-stimulating factor (G-CSF). Wetzler et al have reported a case of TCC of Kidney with high levels of GM-CSF and increased leukocytosis correlating with the tumour burden [7].

As observed in our patient, initial presentation with paraneoplastic fever before the diagnosis of cancer can be misleading. It is sometimes difficult to determine the cause of high fever because the blood counts and CRP are not discriminatory. Elevated TLC and CRP levels can be observed in both infective and neoplastic causes of fever [8]. In some of these situations, PCT is considered to be a valuable marker for evaluation of bacterial infections. However in oncology practice, there are conflicting reports

regarding the utility of serum PCT in differentiating the fever caused by bacterial infection or neoplastic fever.

In a retrospective study, Yaegashi et al found PCT as a valuable investigation in determining the cause of fever in patients with advanced urological cancer [8]. They noted that there were no differences in TLC, CRP or body temperature between bacterial infections and non-bacterial cause of fever; however, the PCT levels were significantly higher in the former than the latter. On the contrary, Penel et al in their study found no difference in serum CRP and PCT levels between the infection and paraneoplastic fever group [9]. They reported that the PCT and CRP levels had poor prognostic value in infection.

Similar to PCT, IL6 is a marker of tissue inflammation and injury. In our patient, in addition to PCT and CRP, serum IL6 was also raised. Matzaraki et al have reported about the correlation of PCT and IL-6 in patients of solid tumor with or without liver metastasis [10]. In their study, serum PCT level were found to be significantly increased in patients with generalized metastatic disease while markedly raised IL-6 levels were noted in patients with liver metastases. They concluded that PCT is related to disease stage in cancer patients, whereas IL-6 concentration seems to be a more specific marker of liver metastasis.

CONCLUSION

This case demonstrates a rare presentation of TCC of kidney with paraneoplastic fever, thrombocytosis and leukemoid reaction. It is important to keep this possibility while investigating for fever in presence of an infiltrative renal lesion.

REFERENCES

1. Mongha R, Narayan S, Das R, Kundu A. Fever and leukemoid reaction: a rare paraneoplastic manifestation of bladder carcinoma. Indian J Cancer. 2008; 45: 131-2.
2. Sacco E, Pinto F, Sasso F, Racioppi M, Gulino G, Volpe A, et al. Paraneoplastic syndromes in patients with urological malignancies. Urol Int. 2009; 83: 1-11.
3. Block NL and Whitmore WF. Leukemoid reaction, thrombocytosis and hypercalcemia associated with bladder cancer. J Urol. 1973; 110: 660-3.
4. Fitzpatrick J, Wallace WA, Lang S, Aboumarzouk OM, Windsor P, Nabi G. Recurrent dermatomyositis manifesting as a sign of recurrent transitional cell carcinoma of urinary bladder: Long-term survival. Urol Ann. 2014; 6: 264-6.
5. Miller JI, Sarver RG, Drach GW. Leukemoid reaction: a rare paraneoplastic syndrome associated with advanced bladder carcinoma. Urology. 1994; 44: 444-6.
6. Pascual Samaniego M, Torrecilla Garcia-Ripoll JR, Calleja Escudero J, Egea Camacho J, Rivera Ferro J, Fernandez del Busto E. Hypercalcemia, leukemoid reaction, and thrombocytosis as paraneoplastic presentation of transitional cell carcinoma of the kidney. Actas Urol Esp. 2001; 25: 400-3.
7. Wetzler M, Estrov Z, Talpaz M, Markowitz A, Gutterman JU, Kurzrock R. Granulocyte-macrophage colony-stimulating factor as a cause of paraneoplastic leukaemoid reaction in advanced transitional cell carcinoma. J Intern Med. 1993; 234: 417-20.
8. Yaegashi H, Izumi K, Kitagawa Y, Kadono Y, Konaka H, Mizokami A, et al. Differential diagnosis between bacterial infection and neoplastic fever in patients with advanced urological cancer: the role of procalcitonin. Int J Urol. 2014; 21: 104-6.
9. Penel N, Fournier C, Clisant S, N'Guyen M. Causes of fever and value of C-reactive protein and procalcitonin in differentiating infections from paraneoplastic fever. Support Care Cancer. 2004; 12: 593-8.
10. Matzaraki V, Alexandraki KI, Venetsanou K, Piperi C, Myrianthefs P, Malamos N, et al. Evaluation of serum procalcitonin and interleukin-6 levels as markers of liver metastasis. Clin Biochem. 2007; 40: 336-42.

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