

CASE REPORT

PSYCHOGENIC FEVER AND THE NAPROXEN TEST: A DIAGNOSTIC CHALLENGE IN A PATIENT WITH POST-OPERATIVE HIGH-GRADE FEVER: A CASE REPORT

Aravind TK, Siddharth Yadav *, Harshdeep Singh

Department of Urology and Renal Transplant, VMMC & Safdarjung Hospital, Delhi, India

* Correspondence to: [✉ drsidiyadav@gmail.com](mailto:drsidiyadav@gmail.com), <https://orcid.org/0000-0002-0231-6645>

ABSTRACT: A multitude of causes exist for the occurrence of high-grade fever in a post operative patient, with psychosomatic origin of fever being extremely rare and hence naturally posing unique diagnostic challenges. After a radical moiety nephrectomy for a malignant renal mass in a horseshoe kidney, a 32-year-old male patient underwent exploratory laparotomy to treat a fecal fistula caused by ischemic colonic injury during the primary surgery. During the postoperative period, the patient developed a high-grade fever with no known cause. Evaluation for all possible organic causes of fever turned negative and a diagnosis of psychogenic fever was considered in light of the patient's concomitant low mental state. Initiation of naproxen with adequate psychoeducation about the disease status and prognosis resulted in fever cessation. We aim to depict the clinical scenario with discussion on psychogenic fever, its pathogenesis and management options.

Doi: 10.48286/aro.2024.91

Impact statement: Psychogenic fever is a less understood entity that is often overlooked during fever evaluation because of its less understood mechanisms. Fever of psychosomatic origin must be considered in patients experiencing long term intensive care, going through cancer management, or in anyone with accompanying psychiatric or psychological issues. There is a lack of understanding regarding the pathogenesis, with attribution to multiple factors for its origin. This article explains the pathophysiology of this unusual clinical situation with a brief account on the role of naproxen in its diagnosis and management.

Key words: renal cell carcinoma; cancer; psychogenic fever; post-operative fever; naproxen test.

Received: July 14, 2024/**Accepted:** August 26, 2024

Published: September 23, 2024

BACKGROUND

A post operative patient after radical nephrectomy for renal cell cancer (RCC) in a horseshoe kidney with resolving wound infection can run fever for a multitude of causes, the common ones being missed include intra-abdominal collection, residual/metastatic disease or concomitant tropical infections such as dengue or

typhoid. Psychogenic fever is a rare stress-related, psychosomatic disease (1). Rarely, a high-grade fever that develops after surgery may have psychosomatic roots, creating special diagnostic difficulties. Herein, we report a case of psychogenic fever in a post operative case of RCC and also briefly discuss the challenges faced during the evaluation and management of the same.

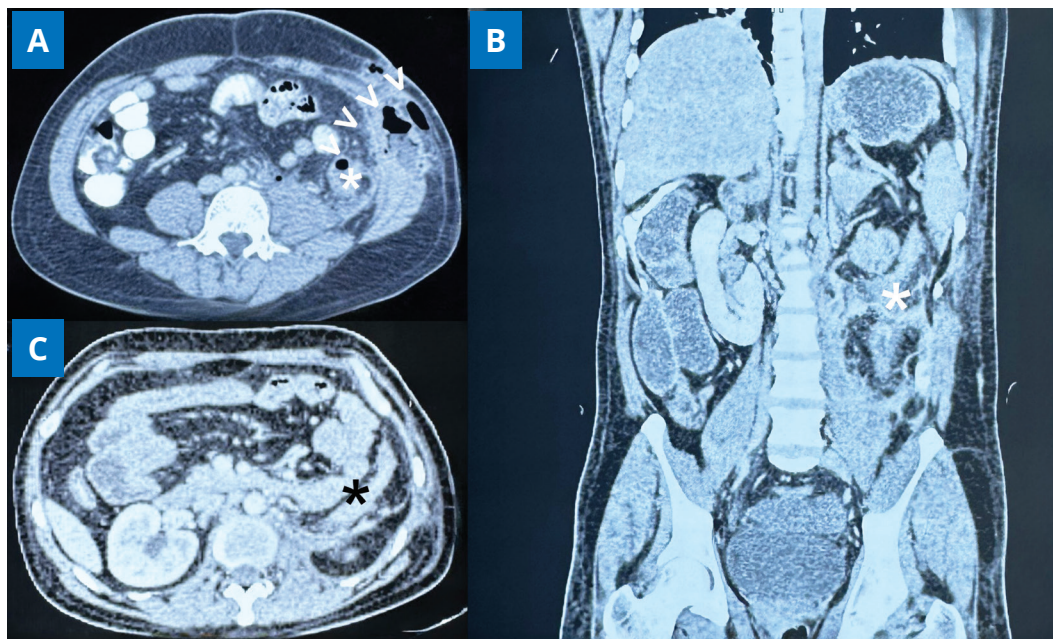


Figure 1. (A, B) Axial and coronal reconstruction sections depict retro colonic collection on the splenic flexure region (marked by *) with tracking into the adjacent subcutaneous space (marked by arrow heads); (C) post operative computed tomography (CECT) whole abdomen and pelvis (axial section) revealing no obvious collection in the renal fossa and retro colonic area (marked by *).

CASE PRESENTATION

A 32-year-old male patient who had undergone radical moiety nephrectomy 15 days prior for a 12 x 11 cm left moiety renal mass in a horseshoe kidney presented with a fecal fistula from the left subcostal incisional site. A computed tomography scan showed a loculated collection in the left retro colic region which was tracking into the adjacent

skin (Figure 1A, B). With a working diagnosis of ischemic insult to the descending colon, the patient was taken for exploratory laparotomy. The procedure revealed an ischemic perforation of the descending colon with surrounding feculent collection, about 5 cm distal to the splenic flexure. An end-to-end anastomosis was performed after a thorough evacuation of the retro colic collection and peritoneal lavage with excision of the devascularized segment, along with a proximal diversion

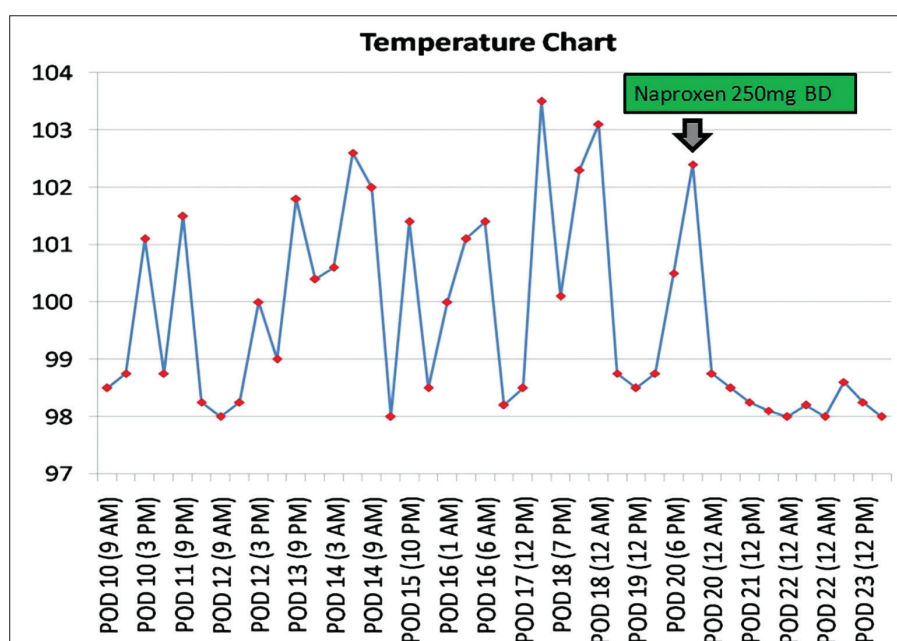


Figure 2. Temperature chart.

ileostomy. Intraoperative cultures sent from the purulent collection turned out to be sterile and the patient was placed on a cephalosporin and metronidazole combination post operatively to account for both aerobic and anaerobic infections.

The patient developed a superficial surgical site infection in the post operative day 2 which was managed conservatively with culture sensitive antibiotics initiated according to wound site cultures with periodic dressings. On post operative day 10, with an actively granulating wound site, the patient started developing high-grade intermittent fever reaching a maximum of 103.5° Fahrenheit in the subsequent days (**Figure 2**) with an initial examination revealing no rashes, vascular access site inflammations, signs of deep venous thrombosis or pneumonia. Relevant investigations to isolate any possible infectious cause of the acute febrile illness (typhoid, dengue, malaria, UTI and COVID-19) all turned out to be negative. On similar grounds, pro-calcitonin levels, chest X-ray and the ultrasound abdomen all turned out unremarkable. Despite antibiotic escalation (meropenem, metronidazole and aminoglycoside), the patient continued to have persistent fever (**Figure 2**).

A decision on obtaining a contrast enhanced computed tomography (CECT) of the abdomen and chest (**Figure 1C**) was made which also failed to reveal any deep space infections or residual or recurrent disease. Considering a persistently low mood of the patient, a psychiatry evaluation was done, which revealed the presence of chronic stress because of the medical illness with associated depressive symptoms, low mood, anxiety symptoms, sleep disturbances and worry about the prognosis and recovery from the disease state.

Considering the presence of psychological factors and absence of any evident organic cause of the fever, a psychosomatic origin of fever was considered. On the tenth day of the fever, the patient was then started on 250 mg of naproxen twice daily, 25 mg of amitriptyline once daily, and 0.25 mg of alprazolam once a night. A prompt defervescence was seen within 24 hours, and there was no recurrence in the following six days (**Figure 2**). Naproxen, a non-steroidal anti-inflammatory drug (NSAID) is typically used to treat inflammatory pain conditions. After consulting with the psychiatry team, the aforementioned regimen was developed to address both the autonomic (amitriptyline and alprazolam) as well as the inflammatory (naproxen) origins of psychogenic fever. Prior to discharge,

the patient was psychoeducated about the medical illness and its prognosis, after which he showed improvements in general mood with amitriptyline discontinued at the time of discharge. Naproxen and alprazolam were stopped 10 days after discharge, with no further recurrence of fever post cessation of the above drugs. Psychiatry follow-up was discontinued after patient recovery as he had no chronic psychiatry illness to necessitate further follow-up. The further post-operative visits were unremarkable, with gradual complete wound healing. The patient underwent ileostomy closure, 3 months post-operatively. The patient is currently on standard follow up protocols for renal cell carcinoma.

DISCUSSION

Pyrexia is a natural thermoregulatory response to any stressful stimulus aimed at restoring homeostasis. The various differentials of a patient with high-grade fever on post-operative day-10 post radical nephrectomy with resolving wound infection would be intra-abdominal collection, chest infection and urinary tract infections, residual or distant metastatic disease. Systemic infections such as dengue, malaria, typhoid also form the differential list with leptospira and scrub typhus being the extremely rare ones. The least thought about cause would be a fever of psychosomatic origin. Psychogenic fever is a stress related psychosomatic response that was first described by Falcon-Lesses (1) in 1930 in an adolescent girl who presented with temperature spikes during stressful situations, such as during visits to the physician or during arguments at home with a characteristic spotless temperature chart in between. Psychogenic fever is commonly observed in patients with psychiatric disorders and in young adolescent females with fever patterns ranging from persistent low-grade fever during the period of chronic stress to unique situations like abrupt fever spikes in patients with psychiatric disease termed as hysterical fever (2). The diagnostic criteria for psychogenic fever (3) includes: axillary temperature above 37 °C; absence of any other disease to account for fever; presentation during a psychosocially stressful situation. Our patient had high-grade fever of psychogenic cause that started on 10th post-operative day with psychiatric evaluation revealing anxiety and stress caused by the ileostomy and uncertainty about the future course of the disease.

The naproxen test was first utilized by Chang and Gross in 1984 in patients with neoplastic fever which showed dramatic defervescence within 2-3 days of administration (4). Neoplastic fever typically results from the release of tumor pyrogens which, either act directly on the hypothalamus or via prostaglandins and naproxen or other anti-inflammatory agents such as diclofenac, when prescribed regularly, result in defervescence (5). On the other hand, patients with infectious causes of fever have higher levels of inflammatory cytokines and the fever typically does not respond to these medications. Psychogenic fever is typically thought to be caused by activation of autonomic system and was traditionally managed by benzodiazepines (5). However, there is growing evidence to suggest a role of inflammatory cytokines in patients with depression and naproxen has been shown to result in resolution of fever in patients with psychogenic fever also (6, 7). The usual antidepressants such as selective serotonin reuptake inhibitors (SSRI) or tricyclic antidepressant (TCA) are typically ineffective in psychogenic fever. A recent report showed resolution of high-grade psychogenic fever resulting from depression with naproxen and authors postulated that the increase in pro-inflammatory cytokines in patients with depression may result in fever which can be effectively managed by naproxen till a final diagnosis of depression is made and its management is started (6). Although all NSAID like ibuprofen, naproxen, diclofenac or indomethacin have demonstrated equal efficacy in neoplastic fever, naproxen showed the earliest response to initiation (8). Hence, we preferred to utilize naproxen over other NSAIDs in our patient with psychogenic fever, a psychological state postulated to have inflammatory cytokine origins similar to those with neoplastic fever. We started our patient on both alprazolam and naproxen along with amitriptyline for its antidepressant effects which resulted in prompt resolution of fever and mood stabilization and all these medications were discontinued 10 days post discharge. Limitations or learning points from the case included the need of psychological assessment and support in patients undergoing cancer surgeries in addition to the knowledge on the possible post operative complications and their course. In our case, we unintentionally missed providing the psychological assessment for the patient considering good motivated mental status and the absence of any previous psychiatric conditions experienced by the pa-

tient. But the learnings obtained from the present case taught us the dire importance of establishing good communication and providing comprehensive care in patients undergoing radical treatment modalities with inclusion of psychological state assessment within the domains of management. Despite being an isolated case encounter, the lessons learnt were much greater and this motivated us to consider inclusion of psychological care in the comprehensive management of patients undergoing cancer surgery as a part of our institutional management protocols.

CONCLUSIONS

Psychogenic fever should be considered in a patient with persistent fever and no obvious source for the same especially when associated with conditions disrupting the normal psychology of the patient. 'Testing' with naproxen or benzodiazepines may help in confirming the diagnosis and resolution of fever till more definitive treatment of psychiatric condition, if required, can be started. A combined effort between doctors and a specialized psychology team is of paramount importance in providing comprehensive care to cancer patients.

COMPLIANCE WITH ETHICAL STANDARDS

Fundings

There were no institutional or private fundings for this article.

Conflict of interests

The Authors have declared no conflict of interests.

Availability of data and materials

The data underlying this article are available in the article.

Authors' contributions

SY was the responsible consultant surgeon in-charge of the overall care of the patient and on whom the final decision on the patient management rested. SY and ATK wrote the first draft of the manuscript. ATK and HS were involved in day to day patient care and follow-up. HS provided insight and valuable inputs to the manuscript, col-

lected references and was responsible for typography of final manuscript draft.

Ethical approval

Human studies and subjects

Informed consent for publishing has been obtained from the patient.

Animal studies

N/A.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data correspond to the real.

REFERENCES

1. Falcon-lesse M, Proger SH. Psychogenic Fever. N Engl J Med. 1930;203:1034-6. doi: 10.1056/NEJM193011202032113.
2. Ziegler LH, Cash PT. A study of the influence of emotions and affects on the surface temperature of the human body. Am J Psychiatr. 1938;95:677-96. doi: 10.1176/ajp.95.3.677.
3. Kaneda Y, Tsuji S, Oka T. Age distribution and gender differences in psychogenic fever patients. Biopsychosoc Med. 2009;3:6. doi: 10.1186/1751-0759-3-6.
4. Chang JC, Gross HM. Utility of naproxen in the differential diagnosis of fever of undetermined origin in patients with cancer. Am J Med. 1984;76(4):597-603. doi: 10.1016/0002-9343(84)90283-3.
5. Vinkers CH, Groenink L, van Bogaert MJ, Westphal KG, Kalkman CJ, van Oorschot R, et al. Stress-induced hyperthermia and infection-induced fever: two of a kind? Physiol Behav. 2009;98(1-2):37-43. doi: 10.1016/j.physbeh.2009.04.004.
6. Moideen S, Anver PC, Uvais NA, Sreeraj VS, Ul Haq Katshu MZ. Positive naproxen test in psychogenic fever. Prim Care Companion CNS Disord. 2021;23(3):20I02630. doi: 10.4088/PCC.20I02630.
7. Felger JC, Lotrich FE. Inflammatory cytokines in depression: neurobiological mechanisms and therapeutic implications. Neuroscience. 2013;246:199-229. doi: 10.1016/j.neuroscience.2013.04.060.
8. Zhang H, Wu Y, Lin Z, Zhong X, Liu T, Huang Z, et al. Naproxen for the treatment of neoplastic fever: A PRISMA-compliant systematic review and meta-analysis. Medicine. 2019;98(22):e15840. doi: 10.1097/MD.00000000000015840.