Neoplastic Fever: All who Shiver are not Infected

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Abstract
We report the case of previously healthy 14 years old male who presented high grade fever and headache. There was a history of convulsion at age of 7 years, so MRI Brain was done. It was suggestive of a central nervous system neoplasm. Our patient had only two days of fever which is an unusual presentation of a neoplasm. The paper should be of interest to the clinicians as neoplastic fever as cause of acute febrile illness is considered as a remote possibility.

Introduction
Neoplastic fever is a challenging yet essential clinical diagnosis. Neoplastic fever is a well recognized phenomenon occurring in certain patients with cancer. It has been seen in Hodgkin’s disease, non-Hodgkin’s lymphomas, acute and chronic leukemia, multiple myeloma, and other solid tumors. Neoplastic fever has been the major cause of fever of undetermined origin in patients with cancer.

Case Report
14 years old male was admitted with complaints of fever with chills and headache since two days. He did not have any other complaints. On admission, patient was febrile, (temp =101⁰ Fahrenheit), pulse -120/min, BP: 120/80 mm Hg, RR: 16/min, with Hepatosplenomegaly. Other systemic examination was normal. There was no neck stiffness. Patient gave history of left eye ptosis since childhood. Patients was started on injections--Artesunate and Ceftriaxone. Complete Blood Count – report showed Hb – 12 g/dl, WBC count 14000 per microliter, platelet count 480000 per microliter, peripheral smear for ‘Malarial parasite was negative, Urine routine and microscopy normal, X-ray chest normal. Sonography of abdomen showed hepatosplenomegaly. Patient still continued to have fever with chills two days after admission so higher antibiotic Ceftazidime and quinine was started. Blood culture was sterile. 2D echocardiography was normal. Fundoscopy showed no evidence of papilledema. Patients ESR was 54, Mantoux test was negative. Inspite of being on antibiotics and antimalarials, patient was still having fever spikes and showing no focus of infection. In view of raised ESR, we decided to start on empirical antituberculosis treatment. Patient’s father revealed that patient had one episode of generalized convulsions at age of 7 years, which was treated as febrile convulsions. So we performed an do MRI brain which showed heterogeneously enhancing extraossial lesions along the left anterior temporal lobe with involvement of left orbit, left cavernous sinus and left temporal fossa. This finding were suggestive of a neoplastic etiology.

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The differential diagnosis were lymphoma, sarcoidosis or metastasis. Patient was referred to neurosurgery department for surgical intervention. Subsequently to Tata hospital where he was diagnosed as suffering from ALK positive Anaplastic Large cell Lymphoma. Patient was started on chemotherapy and radiotherapy. Patient is now currently in palliative care.

**Discussion**

Fever is a common presenting complaint in clinical practice. Fever of unknown etiology still remains a perplexing problem to both clinicians and investigators. Acute fever or acute febrile illness (a rapid onset of fever and symptoms such as headache, chills or muscle and joint pains) is common can be caused by very diverse pathogens. Differential diagnosis include dengue, malaria, typhoid/paratyphoid, leptospirosis, and pneumonia (FIND, 2012). Our patient had presented with only two days of high grade fever with headache which is a rare presentation of neoplastic fever. All investigation were normal ruling out common causes of acute febrile illness.

Classic adult pyrexia of unknown origin is fever of 38.3°C or greater for at least 3 weeks with no identified cause after three days of hospital evaluation or three outpatient visits. Common causes are infections, neoplasms, and connective tissue disorders. A thorough history and physical examination, along with basic investigations usually provides clue to a possible diagnosis that can guide the choice of further investigations. If the initial evaluation provides no diagnostic clues, further investigations including imaging studies and serological tests may be indicated.1,4

In appropriate clinical settings, therapeutic trials of antitubercular drugs may be accepted. It is particularly helpful in cases where there is a history of prolonged low-grade fever with evening rise along with raised ESR, a positive tuberculin test.

Neoplastic fever, i.e. fever arising solely as a manifestation of malignancy, is a troublesome symptom and is difficult to manage.5 The mechanism of neoplastic fever production involves cytokines such as tumor necrosis factor (TNF), interleukins 1 and 6 (IL-1, IL-6) and interferon (IFN), produced either by host macrophages in response to tumor, or sometimes by the tumor itself. The cytokines stimulate production of prostaglandins which act on the hypothalamus causing a change in the thermostatic set point.6-8

Naproxen was very effective in suppressing tumor fever and this property may be useful in elucidating the clinician’s suspicion of cancer in patients with prolonged, undiagnosed fever. Naproxen has unique ability to suppress tumoral cytokines in preference over infectious cytokines. While the “naproxen challenge” may be useful in evaluating prolonged fever suspected to be of neoplastic origin, it must be performed when there is high degree of clinical suspicion. In our case the patient had only 2 days history of high grade fever.

This case report is unique in a way: A healthy 14 years old male who presented with only two days history of high grade fever with chills and headache was diagnosed as a case of central nervous system neoplasm. In our case, patient was diagnosed early on day 7 of fever and referred to Cancer care unit for further workup and management.

**Conclusion**

Any case presenting with acute fever not responding to standard line of treatment and having all primary routine investigations normal, workup for neoplasm as a cause of fever should be kept in mind.

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**References**