Letter to Editorial

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Digestive endoscopy in diagnostic medicine

Abstract

Fever of Unknown Origin (FUO) poses a diagnostic dilemma for physicians especially when diagnostic workup is inconclusive. We present a lymphoma case in remission that presented for FUO that did not show up on routine screening tests. This case highlights the role of proper clinical reasoning and endoscopic investigations in patient management and diagnostic medicine.

Keywords: follicular lymphoma, microscopic relapse, fever of unknown origin, digestive endoscopy

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Abbreviations: FUO, fever of unknown origin; PET, positron emission tomography; CT, computed tomography; FDG, fluorodeoxyglucose

Letter to editor

Fever of Unknown origin (FUO) poses a diagnostic dilemma for most physicians especially when a thorough diagnostic workup is inconclusive. It was defined by Beeson and Petersdorf in1961 as a fever that is greater than 38.3 degrees Celsius (°C), persisting for a period longer than three weeks with a failure to reach a diagnosis despite one week of inpatient investigations.[1] The most common etiologies of FUO are infections (21-54%), noninfectious inflammatory causes (13-24%), neoplasms (6-31%) and other causes (4-6.5%).[2] Both non-invasive and invasive diagnostic tools are thought to have pertinent diagnostic value for determining the origin of the fever, but none of these diagnostic tests have sufficient sensitivity or specificity when they are performed in patients with no typical findings or symptoms.[3] We herein report the case of a 73-year-old man whose previous medical history is consistent with the diagnosis of intestinal Non-Hodgkin Lymphoma with high tumor burden in January 2008. At the time, he received systemic therapy consisting of 6 cycles of R-CHOP (Rituximab -Cyclophosphamide - Adriamycin -Vincristine and Prednisone). After complete remission, the patient received maintenance therapy with Rituximab (one dose every eight weeks for two years).

He presented in August 2014 for fever of unknown origin persisting over a month. The patient also complained of vague abdominal discomfort, fatigue, rhinorrhea and non-productive cough. Physical examination was non-contributory, there was no history of recent travel to endemic areas and the workup was significant for normocytic anemia with a hemoglobin level of 8.8 g/dl, thrombocytopenia with platelet count of 80 x 10^9/L, slightly elevated C-reactive protein of 68.1mg/L, Erythrocyte Sedimentation Rate of 86 mm/h and Lactate dehydrogenize of 1306 UI/ml. More thorough investigations revealed no infectious etiology (Hepatitis A/B/C, CMV, EBV, Parvovirus, Wright, Widal, and negative Procalcitonine) or signs of systemic disease. The investigation panel also included both trans-thoracic and transesophageal cardiac ultrasound, Sinus CT-Scan and nasal fibroscopy. A bone marrow biopsy was also performed and the results were negative for lympho-proliferative disease. Whole-body positron emission tomography/Computed Tomography (PET/CT) with [18F] fluorodeoxyglucose (FDG) did not show any hyper-metabolic lesions. Moreover, a gastroscopy and a colonoscopy were performed and blind mucosal biopsies were taken at different sites, as no particular lesions were visible. Since this patient's initial workup was mostly negative for both neoplastic recurrence and infectious etiology, a trial of empiric antibiotic therapy was initiated. Five days later, this approach failed and the patient still suffered from nightly fevers. A trial of corticosteroid was also attempted but the fever reappeared as soon as the drug was halted. Ten days after all investigations were performed, the results of the fundic biopsy were consistent with mucosal and vascular infiltration of diffuse large B-cell lymphoma (CD20+) although both Pet-CT and Bone marrow Biopsy were negative for neoplastic disease. Appropriate systemic chemotherapy was initiated in light of these findings.

Our primary differential diagnosis included infectious etiologies, systemic disease, and a FL relapse. Thorough history and physical exam followed by rigorous blood tests ruled out infectious as well as systemic inflammatory processes. These tests were followed by imaging and endoscopic procedures such as abdominal CT scan (with a diagnostic yield of 17%) and PET-CT Scan.[4] The role of FDG-PET/CT in FUO has been repeatedly studied. This imaging modality has 90% sensitivity in identifying inflammation and malignancy but a relatively low specificity of 40-45% for identifying the origin of the fever. A study of 62 patients newly diagnosed with primary gastric lymphoma demonstrated increased FDG activity in 89% of aggressive NHL and only 71% with MALT.[5] This modality may find a valuable place in the evaluation of FUO, but data demonstrating its efficacy are still lacking. This is most strongly portrayed in the case of our patient that showed no hyper-metabolic lesions although he had an active neoplastic disease responsible for systemic manifestations. A gastroscopy and bone marrow biopsy were high yield in this patient considering the clinical context and previous medical history.[6] Moreover the diagnosis is attributed to the random biopsies performed that allowed the administration of a lifesaving treatment. Our case advocates for a comprehensive workup in patients with FUO and underlines the role of proper clinical reasoning and endoscopic investigations in Diagnostic Medicine.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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