HEART & LUNG

Issues in Infectious Disease

Fever of unknown origin (FUO) and a renal mass: Renal cell carcinoma, renal tuberculosis, renal malakoplakia, or xanthogranulomatous pyelonephritis?

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ABSTRACT

Often patients with fevers of unknown origin (FUOs) present with loss of appetite, weight loss, and night sweats, without localizing signs. Some are found to have a renal mass during diagnostic evaluation. In patients with FUOs and a renal mass, the differential diagnosis includes renal tuberculosis, renal cell carcinoma (hypernephroma), renal malakoplakia, and xanthogranulomatous pyelonephritis. A 68-year-old woman presented with an FUO during her diagnostic workup. She manifested an irregularly enlarged kidney on abdominal computed tomography (CT) scan, as well as a highly elevated erythrocyte sedimentation rate of more than 100 mm/hour, an elevated serum ferritin level, and chronic thrombocytosis, which favored a diagnosis of renal cell carcinoma. Renal malakoplakia and renal tuberculosis comprised further differential diagnostic considerations. Microscopic hematuria may be present with any of the disorders in the differential diagnosis, but was absent in this case. An abdominal CT scan was suggestive of xanthogranulomatous pyelonephritis. Because of concerns regarding renal cell carcinoma, the patient received a nephrectomy. The pathologic diagnosis was of xanthogranulomatous pyelonephritis, without renal cell carcinoma.

Fever of unknown origin (FUO) describes conditions associated with prolonged, ie, more than 3 weeks of persistent, undiagnosed fevers higher than 101°F. Petersdorf and Beeson, in their classic work on FUOs in 1961, described clinical categories of FUO that have remained in use over the years.[1] In 1961, FUOs were most commonly attributed to infections followed by malignancy, rheumatic or inflammatory disorders, and other miscellaneous conditions. Since the initial description by Petersdorf and Beeson,[1] the relative frequency of disorders causing FUOs has changed.[2] At present, malignancy rather than infection is regarded as the commonest cause of FUOs. Fevers of unknown origin attributable to rheumatic or inflammatory diseases are less frequent then they were, largely because improved testing has led to fewer patients with prolonged fevers

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undiagnosed. Miscellaneous unusual conditions have been reported over the years to cause FUOs. These entities often constitute the most diagnostically challenging category of disorders causing FUOs, because they are either rare and obscure, or difficult to diagnose.[3-12]

We report on an elderly woman who presented with an FUO suggestive of malignancy.[13-18] Because of concerns regarding malignancy, imaging studies were performed.[12,19,20] Abdominal imaging studies produced negative results, except for an abdominal computed tomography (CT) scan that showed a left-sided renal mass. Renal cell carcinoma, renal malakoplakia, and renal tuberculosis (TB) were included among the diagnostic possibilities.[6,21-23] Abdominal CT findings suggested xanthogranulomatous pyelonephritis.

Case Report

A 68-year-old woman presented with fevers, generalized weakness, and sweats of a month's duration. She also reported decreased appetite and a 20-pound involuntary weight loss during the previous 8 months. During her childhood, she had received BCG, and has been purified protein derivative (PPD)-positive ever since. A physical examination was unremarkable, except for left-flank tenderness. Her leukocyte (WBC) count was 14.1 K/mm^3 (73% neutrophils, 18% lymphocytes, and 7% monocytes), and her platelet count was 728 K/mm^3 (normal range, 168 to 392 K/mm^3). Her level of alkaline phosphatase was elevated at 222 IU/L (normal range, 25 to 100 IU/L). Her erythrocyte sedimentation rate (ESR) was 107 mm/hour, and her C-reactive protein was measured at 183.94 mg/L (normal level, .3 mg/L). Her serum ferritin level was 315 ng/mL (normal range, 10 to 187 ng/mL). A urinalysis indicated 31 WBCs/high power field, but no erythrocytes. Her urine and blood cultures produced negative results. Her T-SPOT was also negative. The patient manifested persistent daily evening fevers throughout hospitalization. She developed chest pain and shortness of breath. Nuclear stress testing produced negative results, and a chest CT scan was positive for pulmonary emboli, and incidentally revealed a left renal mass with multiple staghorn calculi fragments (Figure 1). The patient underwent a total left nephrectomy, with pathology compatible with xanthogranulomatous pyelonephritis with lipid-laden macrophages (foam cells), but no malignancy.

Discussion

In patients with an FUO and a renal mass, the most common disorder, far and away, is revealed to be renal cell carcinoma.[1-12] Patients with renal TB usually have radiologic abnormalities involving both the upper and lower genitourinary (GU) tracts, and these provide a clue to the diagnosis. Patients with renal TB often present

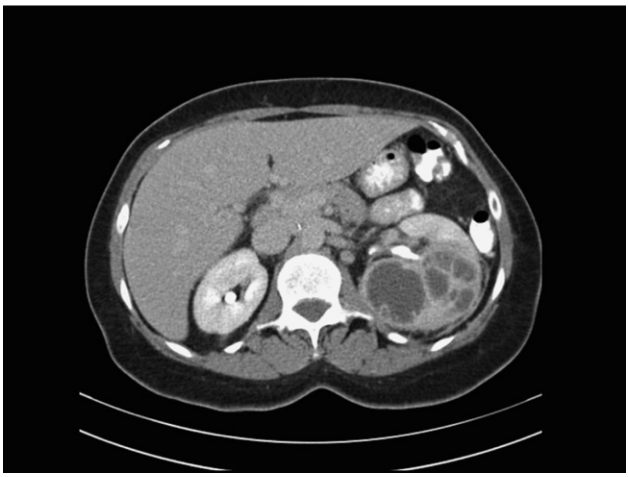

Figure 1 – Computed tomography scan of left kidney shows xanthogranulomatous pyelonephritis with renal enlargement, loss of cortical sharpness with infiltration of Gerota's fascia, staghorn calculus fragment, areas of hypodensity, and cystic regions.

with sterile pyuria with or without microscopic hematuria, with a urine pH of less than 5.5. Renal calcifications are usually present in renal TB.[21-23] The appearance of the upper tracts on abdominal CT scans shows changes suggesting cortical abnormalities that resemble chronic pyelonephritis. With renal TB, the ureters are also abnormal, ie, scalloped, corkscrew, or kinked.[22,23] Few other GU disorders present with both upper and lower tract involvement (eg, malakoplakia).[21] Malakoplakia is a rare disorder of unknown etiology pathologically characterized by the periodic acid-Schiff-positive staining of Michaelis-Gutmann bodies. Both the kidneys and the bladder may be involved. The renal involvement may be unilateral or bilateral. Malakoplakia may rarely present with an FUO.[21,23-33] Fevers of unknown origin attributable to renal cell carcinoma may not present with a flank mass or hematuria.[4-6]

In our patient with an FUO, the nephrectomy specimen demonstrated pathology compatible with xanthogranulomatous pyelonephritis with typical lipid-laden macrophages. As in other cases of xanthogranulomatous pyelonephritis, our patient exhibited renal calculi, ie, broken fragments of staghorn calculi. Unlike most cases of xanthogranulomatous pyelonephritis, however, fever, weight loss, and loss of appetite were prominent in our patient. Xanthogranulomatous pyelonephritis may be considered a rare form of chronic pyelonephritis, and involves a chronic granulomatous process characterized by chronic suppurative renal inflammation, often associated with recurrent urinary tract infections (UTIs). Most patients with xanthogranulomatous pyelonephritis have a history of recurrent urinary tract infections attributable to a variety of Gram-negative aerobic bacilli. In patients with xanthogranulomatous pyelonephritis, renal calculi comprise the foci of recurrent UTIs.[7,9] Common symptoms include abdominal or flank pain,