J Microbiol Immunol Infect
2003;36:248-253

Mycobacteriosis in patients with fever of unknown origin

Chuen Chin, Susan Shin-Jung Lee, Yao-Shen Chen, Shue-Ren Wann, Hsi-Hsun Lin, Wei-Ru Lin, Chun-Kai Huang, Chih-Hsiang Kao, Muh-Yong Yen, Yung-Ching Liu

Section of Infectious Diseases, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, and National Yang-Ming University, Taipei, Taiwan, ROC

Received: June 26, 2002 Revised: August 20, 2002 Accepted: August 30, 2002

Fever of unknown origin (FUO) is a common syndrome. A total of 94 patients (57 men and 37 women; mean age, 56.3 ± 19 years, range, 18-86 years) who met the criteria of FUO were included in this study. Mycobacteriosis was diagnosed in 22 (23%) of these patients (13 men and 9 women), including 9 with disseminated disease and 13 with pulmonary disease. There was no significant statistical difference in age, sex, short-term survival status (3 months), and other clinical parameters between patients with and without mycobacteriosis. Clinical manifestations may be specific or nonspecific. The most common initial presentations in patients with mycobacteriosis were respiratory tract symptoms, mainly of cough and dyspnea, observed in 11 (50%) patients, and disturbance of consciousness in 6 (27%). The associated conditions included malnutrition (4 patients, 18%), diabetes mellitus (3, 14%), and renal failure (3, 14%). Four (18%) patients had a history of pulmonary tuberculosis or tuberculous spondylitis in their early adulthood. The 2 most common findings on chest radiograph were interstitial (41%) and nonspecific infiltrative (32%) patterns. In conclusion, mycobacteriosis remains the leading cause of FUO in southern Taiwan and it is important to screen for this treatable disease in all cases of FUO.

Key words: Fever of unknown origin, mycobacterial infection, tuberculosis

Fever of unknown origin (FUO) is a challenging problem, which requires an awareness of the myriad etiologies and thoroughness in workup. Petersdorf and Beeson [1] defined FUO in 1961. The criteria selected were: an illness of more than 3 weeks' duration, a fever higher than 38.3°C, and diagnosis uncertain after 1 week of study in hospital. Tuberculosis is a common cause of FUO in the literature [2,3]. Tuberculosis was the most common infectious cause of FUO (49% of all infectious cases) in 2 studies from India [4,5]. Nontuberculous mycobacterial (NTM) infection is also a cause of FUO. The spectrum of diseases causing FUO seems to be influenced by time and geographical factors.

Tuberculosis is endemic in Taiwan. Early screening for tuberculosis in patients with FUO is important because tuberculosis is probably the most readily treatable cause of death in patients with FUO. This 1-year prospective study of patients with FUO in a 1200-bed teaching hospital in southern Taiwan was conducted to determine the proportion and clinical characteristics of mycobacteriosis, a treatable disease.

Corresponding author: Dr. Yung-Ching Liu, Section of Infectious Diseases, Department of Internal Medicine, Kaohsiung Veterans General Hospital, 386, Ta-Chung 1st Road, Kaohsiung, Taiwan, 813, ROC. E-mail: ycliu@isca.vghks.gov.tw

Materials and Methods

This prospective study was undertaken from March 2001 through February 2002. All patients fulfilling the modified criteria for FUO admitted to, referred to, or in consultation with the Section of Infectious Diseases in Kaohsiung Veterans General Hospital (VGHKS) were enrolled. The modified criteria were as follows: repeatedly documented fever with temperature exceeding 38.3°C; a duration of illness of more than or equal to 2 weeks [7], and failure to reach a diagnosis after three outpatient visits or 1 week of "intelligent and invasive" ambulatory investigation or 3 days of inpatient investigation [6] in VGHKS or other hospital without elucidation of a cause. The following examinations were performed in VGHKS before enrollment: a comprehensive history taking; physical examination; complete blood count and differential count; blood biochemistry; urinalysis; stool routine and parasitologic examinations; ≥2 sets of blood culture; ophthalmic funduscopy; chest radiography; abdominal ultrasonography; test for anti-HIV antibody; Weil-Felix test and Widal test.

Immunocompromised patients, including patients with neutropenia (white blood cell count <1000 /mm^3 and/or granulocyte <500 /mm^3) for at least 1 week within 3 months before the onset of fever; HIV-positive patients; patients with known hypogammaglobulinemia

(IgG <50%); and patients using more than 10 mg prednisone or its equivalent for at least 2 weeks were excluded. Patients with a subsequent diagnosis of HIV infection who had no history of preexistent immunosuppression were not excluded. In the aforementioned circumstance, the mycobacteriosis was considered an HIV-associated infection. Patients with nosocomial FUO, which was defined by Durack and Street, were also excluded [6].

On admission, potential diagnostic clues (PDCs) and a standardized protocol were suggested to the attending physicians [8] by the authors. The following 3-step diagnostic process was recommended: first, collection of the PDCs to establish the diagnosis in the first inpatient week; second, repeat of history-taking, physical examination and the phase 1 diagnostic protocol in the second inpatient week if the initial PDCs failed to establish a diagnosis; and third, performance of the same procedures and the phase 2 diagnostic protocol as a last resort [8]. In order to lower the hospitalized course, the attending physicians were allowed to perform as few examinations of the protocol as possible.

The causes of FUO were classified as either mycobacterial infections or non-mycobacterial infections (the remaining patients without mycobacterial infections). The main outcome measures were the final diagnosis established at discharge or during a ≥3-month duration of follow-up, and the short-term survival at 3 months after fever onset. Data collected included the duration of fever before initiation of examinations, hospitalized days, time to establish a diagnosis, and delay from fever onset until a diagnosis.

The time to establish a diagnosis was defined as the time between the date of initiating examinations and the date of establishing diagnosis. The time included the outpatient workup. "Delay in diagnosis" was defined as the time between the date of fever onset and the date of diagnosis establishment. Therefore, the estimated delay in diagnosis was the sum of the number of febrile days before initiation of examinations and the time to establish diagnosis.

Diagnosis was determined by analysis of the medical records of patients who were followed up at our institution, or by telephone calls to the treating physicians if clarification was necessary. In some cases, probable diagnoses were established by telephone calls to the patients themselves, their family or friends. A structured data collection form was used to abstract clinical data at the time of discharge from the hospital. The outcome of cases was classified as alive or dead (of any cause) at the time of 3 months after fever onset.

Chest radiography was performed on the day of admission or at the time of referral or consultation. Previous films available for referred patients were also analyzed. Mycobacterial culture and acid-fast stain of specimens including sputum, urine, gastric juice, bone marrow aspirate, cerebrospinal fluid, pleural fluid, and pericardial fluid were performed in patients with suspected mycobacteriosis. We used the MGIT 960 system (Mycobacteria Growth Indicator Tube, Becton Dickinson Co., Sparks, Maryland, US) for mycobacterial cultures, and the BD ProbeTec ET *Mycobacterium tuberculosis*, *Mycobacterium kansasii*, and *Mycobacterium avium* complex kits (Becton Dickinson Co., Sparks, Maryland, US) for rapid identification of *M. tuberculosis*, *M. kansasii*, and *M. avium* complex (MAC), respectively [9]. If NTM other than the aforementioned 3 species was suspected, biochemical tests or polymerase chain reaction with restriction enzyme analysis (polymerase chain reaction [PCR]-restriction enzyme analysis, PRA) was employed to identify the species [10]. The PRA primers were synthesized by GENSET Singapore Biotech, Pte Ltd (Singapore) and the PRA products were analyzed by GeneAmp PCR system 9600 (Perkin-Elmer, Norwalk, Conn., US).

Cases diagnosed by culture, PCR, or typical histopathology with presence of acid-fast bacilli were defined as definite mycobacteriosis. Cases diagnosed by typical histopathology without presence of acid-fast bacilli or by a response to empirical antituberculous therapy were defined as probable mycobacteriosis. Cases diagnosed by the clinical manifestations and the response to empirical antituberculous therapy were defined as possible mycobacteriosis.

The demographic characteristics, clinical features, involved organ systems, positive rate of acid fast stain of sampling specimens, diagnostic procedure, chest radiograph at the time of enrollment and short-term survival at 3 months in patients with mycobacterial infection were analyzed. The results of demographic/clinical variables and the characteristics of chest radiograph were compared using t test or chi-square test.

Results

During the 1-year period of study, 94 patients (57 men, 37 women) fulfilled the modified criteria for FUO. Seventy-eight (83%) of these patients were transferred from local clinics or hospitals. The final diagnosis responsible for FUO consisted of infectious diseases in 54 (57.4%) patients, hematologic/neoplastic diseases in 8 (8.5%), noninfectious inflammatory diseases in 7

Table 1. Demographic and clinical characteristics of FUO patients with and without mycobacteriosis

	Mycobacteriosis[a] (n = 22)	Non-mycobacteriosis[b] (n = 72)
Age (years, range)	61.6 ± 14.9 (35-85)	54.8 ± 20.0 (18-86)
Sex (M/F)	13/9	44/28
Febrile days before admission/referral (range)	37.4 ± 49.7 (7-240)	36.7 ± 36.4 (1-180)
Hospitalized days (range)	24.6 ± 18.5 (6-91)	23.9 ± 18.4 (3-92)
Time to establish diagnosis (days, range)	28.5 ± 19.2 (10-82)	21.7 ± 41.9 (1-333)
Diagnostic delay (days, range)	65.9 ± 49.8 (27-256)	57.8 ± 53.5 (15-355)
Survival status[c] (alive/dead)	19/3	59/13

Abbreviation: FUO = fever of unknown origin

[a]Non-tuberculous mycobacteriosis (*Mycobacterium avium* complex and *M. abscessus* infection) included.

[b]FUO patients due to underlying diseases other than mycobacteriosis.

[c]Short-term survival (3 months after discharge from hospital, died of any cause). Six patients survived no more than 6 months.

(7.4%), miscellaneous conditions in 8 (8.5%), and undiagnosed cases in 17 (18.1%) patients. There were 45 bacterial infections, 2 viral, 1 fungal, and 6 other infections. Mycobacteriosis was the cause of FUO in 22 (23 %, 13 men and 9 women) patients, including 19 tuberculous patients (12 men and 7 women) and 3 nontuberculous patients (1 man and 2 women). The 22 mycobacterial infections included 18 definite, 1 probable, and 3 possible cases.

Comparisons of demographic and clinical characteristics of patients with mycobacterial and without mycobacterial infection are listed in Table 1.

Table 2. Initial symptoms/signs of patients with mycobacteriosis-associated FUO (n = 22)

Symptom/sign	No. of cases (%)
Productive cough	11 (50)
Confusion	6 (27)
Abdominal pain	6 (27)
Dyspnea	5 (23)
Weight loss	4 (18)
Headache	3 (14)
Dry cough	3 (14)
Sore throat	3 (14)
Chest pain	3 (14)
Dysuria	2 (9)
Weakness of lower limbs	2 (9)
Legs edema	2 (9)
Urinary frequency	1 (5)
Watery diarrhea	1 (5)
Ataxia	1 (5)
Neck lymphadenopathy	1 (5)
Slurred speech	1 (5)
Dizziness	1 (5)
Cold sweating	1 (5)
Skin rash/erythema of lower limbs with tenderness	1 (5)
Skin rash/erythema of lower limbs without tenderness	2 (9)
Dry eyes	1 (5)
Arthralgia	1 (5)

Abbreviation: FUO = fever of unknown origin.

No significant statistical differences in these parameters were found between the 2 groups.

Some initial symptoms of the patients with mycobacteriosis-associated FUO were nonspecific, such as general malaise, poor appetite, nausea, and vomiting (Table 2). The most common specific initial symptoms were productive cough (11 cases, 50%), confusion (6, 27%), abdominal pain (6, 27%), and dyspnea (5, 23%).

Malnutrition was the most frequently associated condition, present in 4 patients (Table 3). Three patients had a history of pulmonary tuberculosis or tuberculous spondylitis. Two patients had other coincident infections, one with *Staphylococcus aureus* spondylitis and the other with HIV infection. One patient had multidrug allergy.

Nine (41%) of the 22 patients had disseminated mycobacteriosis, including one with disseminated MAC infection. The lung was the sole organ involved in the remaining 13 patients (59%, 13/22) including one with MAC infection and one with *M. abscessus* infection of

Table 3. Associated illness or conditions in patients with mycobacteriosis-associated FUO (n = 22)

Underlying condition	No. of cases (%)
Malnutrition	4 (18)
Diabetes	3 (14)
Renal insufficiency or uremia	3 (14)
Previous tuberculosis history	3 (14)
Old stroke with bed ridden state	1 (5)
Hypertension	1 (5)
Cirrhosis	1 (5)
Parkinsonism	1 (5)
Subtotal gastrectomy	1 (5)
Staphylococcus aureus spondylitis	1 (5)
Coincident HIV infection	1 (5)
Multidrug allergy	1 (5)

Abbreviations: FUO = fever of unknown origin; HIV = human immunodeficiency virus

the lung. The sites of mycobacteriosis included the central nervous system in 3 (14%) cases, peritoneum in 1 (5%), pericardium in 1, bone marrow in 1, liver in 2 (9%), vertebrae in 1, psoas muscle in 1, tonsils in 1, lymph nodes in 3 (14%), skin in 2 (9%), and lung in 18 (82%). In one patient with a clinical diagnosis of possible tuberculosis, adrenal gland involvement was also suspected.

The most frequently used diagnostic tools were culture of clinical specimens, histopathology, and PCR. Cultures for mycobacteriosis yielded positive results in 16 (73%) of 22 patients. Pathological examination of biopsy specimen was performed in 5 patients and PCR analysis of specimens along with specimen culture was employed in 3 patients. Tuberculosis was diagnosed in 3 (14%) patients based on information including clinical presentations, radiological findings, and the response to empirical antituberculous therapy.

Acid-fast stain of the specimens, including sputum and body fluids (pleural fluid, pericardial fluid, or cerebrospinal fluid), were performed in patients of high possibility of tuberculosis. Acid-fast bacilli were found in only 3 of 132 (range, 3-12 culture sets per patient; mean, 6 sets) smears. All the 3 specimens were sputum. The yield rate of acid-fast staining was 2.2%.

The characteristics and comparison of chest radiographs between mycobacteriosis and non-mycobacteriosis patients are shown in Table 4. The presence of an interstitial pattern and nonspecific infiltration (ill-defined shadows) on chest radiographs was significantly more common in patients with mycobacteriosis than in those patients with diseases other than mycobacteriosis. Two patients in the mycobacteriosis group had miscellaneous features on chest radiograph. One of the two patients had an old destroyed lung pattern on chest radiograph, which aided in the diagnosis. He had a history of pulmonary tuberculosis and developed MAC pneumonia later. The MAC infection presented with FUO.

Eighteen (82%) patients in the mycobacteriosis group survived for at least 3 months (16 patients survived ≥6 months) after fever onset, and 62 (86%) patients in the non-mycobacteriosis group survived. However, 6 patients in the mycobacteriosis group died within 6 months of fever onset. Causes of death were nosocomial pneumonia with respiratory failure in 2 patients, acute intracranial hemorrhage in 1 patient, a progressive course of weakness with sudden death in 1 patient, and sudden death of unknown cause in 2 patients. Sudden death and progressive weakness may be due to the involvement of the central nervous system. Acute hydrocephalus and tuberculous meningitis was possible. No autopsy was performed to establish the cause of death in these 6 patients.

Discussion

This study included 94 patients who fulfilled the criteria for FUO. Seventy-eight (83%) of these patients were transferred from local clinics or hospitals. The minimum diagnostic evaluation for FUO is not standardized among local clinics, hospitals, or medical centers in Taiwan, which may have led to overestimation and skewing of the distribution of some diseases. However, this study sketches the geographic distribution of FUO patients with mycobacteriosis in southern Taiwan.

Tuberculosis (19 cases, 20%) was the most common etiology of FUO in this study. The relative proportion of tuberculosis in this study was higher than in previous

Table 4. Patterns of chest radiograph in patients with FUO

Pattern[a]	Mycobacteriosis (n = 22)	Non-mycobacteriosis[b] (n = 72)	*p*
Interstitial (21)	9	12	0.017
Consolidation (9)	3	6	0.459
Pleural effusion (13)	4	9	0.499
Pleural thickening (6)	1	5	0.687
Honeycomb (1)	1	0	0.069
Nodular (10)	3	7	0.602
Fibrotic or fibrocalcified change (10)	4	6	0.190
Atelectasis (3)	2	1	0.072
Cardiomegaly (24)	5	19	0.730
Nonspecific infiltrates[c] (13)	7	6	0.005
Other findings	2	12	

Abbreviation: FUO = fever of unknown origin

[a]Chest radiograph may demonstrate several patterns.

[b]FUO patients due to underlying diseases other than mycobacteriosis.

[c]Nonspecific infiltrates was defined as ill-defined shadows other than the aforementioned radiographic characteristics.

studies from North and South America and Europe [1, 2,8,11-15]. In the 2 studies from Japan [14,15], 2% to 11% of patients with FUO had tuberculosis. The proportion of tuberculosis in the present study was similar to 2 studies from India [4,5], which showed 21% to 30% of patients with FUO had tuberculosis. This phenomenon may be attributable to the higher prevalence of tuberculosis (650 per 100 000 in 1993 survey) and incidence (62.7 per 100 000 in 2000) in Taiwan [16] and the lack of thorough investigations made in the early presentations of tuberculosis in local clinics or hospitals.

The median age of patients in this study was 61.6 years in the mycobacteriosis group and 54.8 years in the non-mycobacteriosis group. Although this difference did not reach significance, the mycobacteriosis group was somewhat older. This result was similar to the findings of Norman that tuberculosis occurred much more commonly in elderly rather than in young patients with FUO [11].

Clinical manifestations were of considerable diversity (Table 2). Productive cough, dyspnea, and confusion were the most common presenting symptoms among the patients with mycobacteriosis-associated FUO. These symptoms may reflect the involvement of the respiratory tract and central nervous system.

In this study, malnutrition was the most frequently associated condition, but we could not determine if it was a predisposing factor or the result of mycobacteriosis. Apart from nutritional status, diabetes mellitus and renal insufficiency or uremia were the most common underlying conditions. Hemodialysis patients are at risk for the development of this infection due to a depressed cellular immunity, as suggested by several studies during the past 2 decades [3,17,18]. Three patients had a history of pulmonary tuberculosis or tuberculous spondylitis in their early adulthood. Reactivated tuberculosis presented as FUO in these patients. These cases suggest the importance of comprehensive history taking.

Biopsy and PCR of sterile specimens are rapid methods to obtain a diagnosis in selected patients. The yield rate of acid fast staining was 2.2% in this study. Although this rate was low, it provided a diagnosis within 15 minutes. Acid-fast staining is convenient to perform in a local clinic or hospital and this staining could obtain an early diagnosis.

Chest radiograph showed various manifestations, but patients with FUO and whose chest films showing interstitial pattern and nonspecific infiltration had a higher probability of mycobacteriosis. When there are pulmonary complaints or abnormalities on physical examination, chest radiograph is a very useful diagnostic modality, but even in patients without pulmonary disorders, this simple technique is of use in some cases [19].

Arnow and Flaherty [20] reported that the forms of tuberculosis that most often caused FUO were disseminated disease without the characteristic miliary pattern on chest radiograph or extrapulmonary disease without clear localizing features. Serial chest radiographs may demonstrate subtle but increasing infiltrates and sputum smears may be positive for acid-fast bacilli in only one-fourth to one-half of cases. Differences between this study and that of Arnow and Flaherty include: (1) pulmonary mycobacteriosis (including tuberculosis) occurred somewhat more often than disseminated disease; (2) radiographic characteristics were more diverse than simply an increased infiltrative pattern; (3) a lower rate of acid-fast smears of the sputum was found (14% vs 25%) in patients in this study.

Patients with prolonged FUO may seek medical attention from several physicians. The physician may not realize the whole disease course, not to mention the subtle changes on the serial chest radiographs. In this study, the mean febrile period before enrollment was 37. 4 days in the mycobacteriosis group (Table 1), and the chest film in these patients often showed a chronic interstitial pattern in addition to an increasing infiltrative pattern. Thus, patients with pulmonary mycobacteriosis-associated FUO lacking of a typical chest film of mycobacteriosis were left to diagnose. These findings may also reflect that the physicians in local hospitals or clinics did not recognize the clinical and radiographic spectrum of mycobacteriosis comprehensively. In this study, most patients with FUO had uncommon manifestations of common diseases rather than common presentations of uncommon diseases. The mycobacteriosis presented by masquerading as a prolonged fever of obscure origin. The low positive rate of acid fast staining of sputum may have been due to the poor quality in specimen collection, inexperience of the microbiologic examiner, or scant amount of acid fast bacilli, leading to delay in diagnosis.

The short-term (3 months) associated mortality rate between the 2 groups was similar. Mycobacteriosis resulted in prolonged stay in the hospital. In this series, the stay caused 2 patients to nosocomial pneumonia and respiratory failure. Both mycobacteriosis and nosocomial pneumonia contributed to the mortality. A longer period of follow-up as well as autopsy study is needed to establish the cause of death.

Fever of unknown origin caused by mycobacteriosis is a diagnostic challenge. Survival of patients with mycobacteriosis was comparable to patients without mycobacteriosis in this series. Clinicians should consider tuberculosis in all patients with prolonged fever, because a high index of suspicion is essential for establishing the diagnosis [2,3]. The results of this study suggest that tuberculosis should be considered in all FUO patients in southern Taiwan, especially elderly patients with pulmonary infiltrates on chest film and respiratory or neurologic symptoms. Given the relentless sequelae, a trial with antituberculous agents should be considered in patients with consistent clinical manifestations, even in the absence of a definite culture result.

References

1. Petersdorf RG, Beeson PB. Fever of unexplained origin: report on 100 cases. Medicine 1961;40:1-30.
2. Sepkowitz. Tuberculosis as the cause of fever of unknown origin. Intern J Infect Dis 1997;2:47-51.
3. Collazos J, Guerra E, Mayo J, Martinez E. Tuberculosis as a cause of recurrent fever of unknown origin. J Infect 2000;41: 269-72.
4. Handa R, Singh S, Singh N, Wali JP. Fever of unknown origin: a prospective study. Trop Doct 1996;26:169-70.
5. Sharma BK, Kumari S, Varma SC, Sagar S, Singh S. Prolonged undiagnosed fever in northern India. Trop Geogr Med 1992; 44:32-6.
6. Durack DT, Street AC. Fever of unknown origin: reexamined and redefined. Curr Clin Top Infect Dis 1991;11:35-51.
7. Gelfand JA, Dinarello CA. Fever of unknown origin. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL, eds. Harrison's Principles of Internal Medicine. 14th ed. New York: McGraw-Hill; 1998:781.
8. de Kleijn EM, Vandenbroucke JP, van der Meer JW. Fever of unknown origin (FUO): I. a prospective multicenter study of 167 patients with FUO, using fixed epidemiologic entry criteria. Medicine 1997;76:392-400.
9. Huang TS, Chen CS, Lee SJ, Huang WK, Liu YC. Comparison of the BACTEC MGIT 960 and BACTEC 460 TB systems for detection of mycobacteria in clinical specimens. Ann Clin Lab Sci 2001;31:279-83.
10. Huang TS, Liu YC, Huang WK, Chen CS, Tu HZ, Cheng DL. Evaluation of polymerase chain reaction-restriction enzyme analysis of mycobacteria cultured in BACTEC 12B bottles. J Formos Med Assoc 1996;95:530-5.
11. Norman DC. Fever in the elderly. Clin Infect Dis 2000;31:148-51.
12. Esposito AL, Gleckman RA. Fever of unknown origin in the elderly. J Am Geriatr Soc 1978;26:498-505.
13. Knockaert DC, Vanneste LJ, Bobbaers HJ. Fever of unknown origin in elderly patients. J Am Geriatr Soc 1993;41:1187-92.
14. Iikuni Y, Okada J, Kondo H, Kashiwazaki S. Current fever of unknown origin 1982-1992. Intern Med 1994;33:67-73.
15. Shoh S, Imamura A, Imai Y, Igarashi A, Yazawa M, Hirahara K, Kagoshima M, Ono M, Nakauma K, Iguchi K. Fever of unknown origin: a review of 80 patients from the Shin'etsu area of Japan from 1986-1992. Intern Med 1994;33:74-6.
16. Center for Disease Control. Tuberculosis Annual Report 2000. Taiwan, ROC: Center for Disease Control; 2002:13-7.
17. Cengiz K. Increased incidence of tuberculosis in patients undergoing hemodialysis. Nephron 1996;73:421-4.
18. Mitwalli A. Tuberculosis in patients on maintenance dialysis. Am J Kidney Dis 1991;18:579-82.
19. de Kleijn EM, van Lier HJ, van der Meer JW. Fever of unknown origin (FUO): II. diagnostic procedures in a prospective multicenter study of 167 patients. Medicine 1997;76:401-14.
20. Arnow PM, Flaherty JP. Fever of unknown origin. Lancet 1997; 350:575-80.