Fever of Unknown Origin (FUO)

Background

Fever of unknown origin (FUO) was defined in 1961 by Petersdorf and Beeson as the following: (1) a temperature greater than 38.3°C (101°F) on several occasions, (2) more than 3 weeks' duration of illness, and (3) failure to reach a diagnosis despite one week of inpatient investigation.[1]

History

Diagnostic approach to fever of unknown origin (FUO) in adults

Inquire about symptoms involving all major organ systems, including a detailed history of general symptoms (e.g., fever, weight loss, night sweats, headaches, rashes).

Record all symptoms, even if they disappeared before the examination. Previous illnesses are important, including surgeries and psychiatric illnesses.

Provide a detailed evaluation including the following:

Family history

Immunization status

Occupational history

Travel history

Nutrition (including consumption of dairy products)

Drug history (over-the-counter medications, prescription medications, illicit substances)

Sexual history

Recreational habits

Animal contacts (including possible exposure to ticks and other vectors)

Physical

Definitive documentation of fever and exclusion of factitious fever are essential early steps in the physical examination.

Measure the fever more than once and in the presence of a nurse to exclude manipulation of thermometers.

Electronic thermometers facilitate the rapid and unequivocal documentation of fever.

The pattern of fever (continuous, remittent, intermittent) is usually of little help in the evaluation.

In general, specific fever patterns do not correlate strongly with specific diseases. Notable exceptions include tertian and quartan malaria. However, most people who are naive about malaria are not diagnosed with FUO because they are usually diagnosed with malaria before 3 weeks have elapsed.

Other diseases (e.g. brucellosis, borreliosis, Hodgkin disease tend to cause recurrent episodes of fever.

Repeat a regular physical examination daily while the patient is hospitalized. Pay special attention to rashes, new or changing cardiac murmurs, signs of arthritis, abdominal tenderness or rigidity, lymph node enlargement, funduscopic changes, and neurologic deficits.

Causes

Bacterial diseases

Tuberculosis (TB)

Urinary tract infections (UTIs

Endocarditis

Hepatobiliary infections

Osteomyelitis

Rickettsia

Chlamydia

 Systemic bacterial illnesses

Spirochetal diseases

Viral diseases
HIV
AIDS
Herpes viruses
Fungal infections
Parasitic infections
Neoplasms
Lymphomas
Leukemias
Other solid tumors
Malignant histiocytosis
Collagen vascular and autoimmune diseases
Collagen vascular and autoimmune
SLE
Systemic-onset JRA is a cause of FUO and is often difficult to diagnose. High-spiking fevers, nonpruritic rashes, arthralgias and myalgias, pharyngitis, and lymphadenopathy, common. Laboratory abnormalities include pronounced leukocytosis, an elevated erythrocyte sedimentation rate (ESR), anemia, and abnormal liver function tests. These findings usually trigger a search for an infectious cause; thus, they delay the correct diagnosis.
Consider polyateritis nodosa (PAN)
Granulomatous diseases
Sarcoidosis
Regional enteritis: Crohn disease is the most common gastrointestinal cause of FUO. Diarrhea and other abdominal symptoms are occasionally absent, particularly in young adults. The diagnosis is established with endoscopy and biopsy.
Granulomatous hepatitis
Drug fever.
Inherited diseases: In patients of Mediterranean descent with FUO, familiar Mediterranian fever is most often the cause. Recurrent febrile episodes at varying intervals are associated with pleural, abdominal, or joint pain due to polyserositis. This is a diagnosis of exclusion.
Endocrine disorders
Hyperthyroidism and subacute thyroiditis are the 2 most common endocrinologic causes of FUO. In fact, fever is often the major clinical sign, in addition to weight loss.
Peripheral pulmonary emboli and occult Thrombophlebitis
Kikuchi disease
Factitious fever
Other vasculitides
Giant cell arteritis
Polymyalgia rheumatica
PAN

Pathophysiology
FUOs are caused by infections (30-40%), neoplasms (20-30%), collagen vascular diseases (10-20%), and numerous miscellaneous diseases (15-20%). The literature also reveals that between 5 and 15% of FUO cases defy diagnosis, despite exhaustive studies.

Case Study A.
28- year old female complained that she could not recover from high fever, cough and pneumonia despite the inpatient therapy for over 13 days. She requested to investigate her health and consult her.
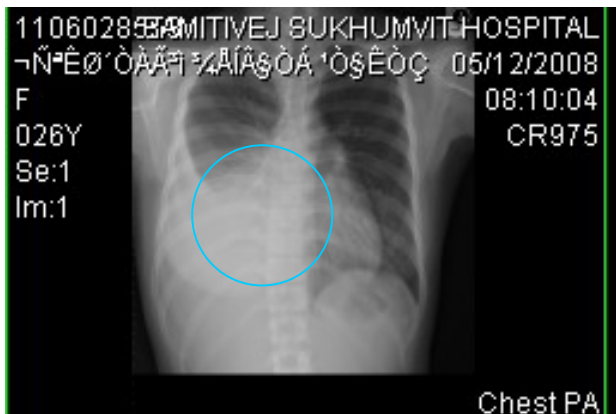
Pic.6. CT image:The film reveals large right
pleural infusion as below

Prescribed medication for the inpatient:
1. Cifloxin,
2. Miracid,
3. Tusilan,
4. Flemex,
5. Roxin
6. Benosyl,
7. Motilium,
8. Dextromethophan,
9. Chlorpheniramine,
10. Tylenol,
11. Paracetamol,
12. Clarinese
13. Tylenol

History:
- Temperature greater than 39.3°C - 40°C for more than 13 days (raising three times a day) and failure to reach a recovery despite pneumonia diagnosis and 2 weeks of inpatient therapy.
CT scan: The film reveals large right pleural infusion as in Pic.1.

- Worsening headache, cough, chest pain

- Pain in the stomach, vomiting

- Vertigo

Discussions

Ψ-TI diagnostics revealed:
    A) Infection with two types of Staphylococcus: in lungs and blood system.
    B) Stomach – Acute Gastritis with tendency to mutation (cancer).
    C) Herpes infection.
 Thus we estimated that Fever of Unknown Origin (FUO) was caused by:
    (1) seasonal flu developped into pneumonia (Staphylococcus of 2 types) and
    (2) complicated by acute gastritis.
The first condition (1) might be justified by 2 factors:
    a) Due to known case of genetic tendency to lung cancer,
    b) Due to healthcare associated pneumonia (HCAN))
The second condition (2) of acute gastritis was caused by a reaction to the prescription medications and could have developed into acute case with high fever temperature and compromised immune response (the patient could not eat for about 2 weeks).
Thus we proposed regular Ψ-TC correction (under daily supervision), followed by with specific care and diets to elevate the acute digestive system condition. The patient underwent 10 sessions of Ψ-TC correction.

Conclusion:

Correct evaluation of body functions and bacterial infection types allowed to focus on acute inflammation in the stomach area as an emergency cause and to propose the correct management program. As a result the patient started to recover quickly. Temperature lowered to 37.2°C on the second day and normalized on the 4th day without any recession. In 2 weeks the patient was practically healthy.

Pic.7. CT: The film has shown significant decreased right pleural infusion

Results

The patient recovered well in two weeks:
- Good appetite,
- Sleeps well.

Additionally the patient remarked: Sharpening of senses of perception - taste, smell, speech and thinking enhanced.
The changes about speech and communication skills were observed and commented by the outsiders.

Verifications:

Ψ-TC correction results after 10 sessions, were verified by CT scan: The film has shown significant decreased right pleural infusion