Liver Tuberculosis as an Etiology in Fever of Unknown Origin

Irman Firmansyah, Joko B Jong, Noorwati, Leo Nainggolan

INTRODUCTION

Fever of unknown origin (FUO) is a condition with continuous fever for 3 weeks period and body temperature above 38.3°C, and the etiology has not been found yet; even a one-week intensive study has been conducted, using laboratory and other medical examination. Other terms for this disease i.e.: febris et causa ignota, fever of obscure origin, fever of undetermined origin, fever of unexplained, prolonged fever, pyrexia of unknown origin, fever of unknown origin (FUO). The etiology of FUO, based on disease group is categorized into 6 group i.e., infection (45-55%), neoplasm (12-20%), collagen disease (10-15%), hypersensitivity disorder, metabolic disorder and factious fever.

This case is reported to demonstrate the difficulties in defining the cause of FUO in this patient.

CASE ILLUSTRATION

Mrs. R, 42 years old, was admitted to Cipto Mangunkusumo Hospital, with chief complaint of fever for 2 months before admission. The fever was going up and down; sometimes she had a chill in the morning or evening. There was no cough or influenza. After taking the medicine, the fever subsided but then it came back to high temperature again. She had loss of appetite.

Six weeks before admission, she was admitted to other hospital for 6 week period. For 1 week in ward, the fever subsided once, but then it came back again and never subsided anymore. In other hospital before, she had serial examination, such as thoracic X-ray with normal result, abdominal USG revealed normal liver, gall bladder, and slight enlargement of spleen, and there was no enlargement of para aortic lymph node. In that hospital, the patient also had blood examination for malaria test and widal test, which revealed negative result. The examination of C3, C4 and Ds DNA also revealed normal result. She had normal urination and defecation. Because she felt no improvement, she came to Cipto Mangunkusumo Hospital.

The past Medical History: she never had any liver and heart disease or epigastric pain.

Physical Examination on admission date: her general condition was moderately ill, and her consciousness was fully alert (compositoris). BP 110/70 mmHg, HR 110 x/minute, temp 38°C, RR 28 x/minute. Eyes: pale conjunctiva, no jaundice on sclera. Jugular Vein Pressure (JVP) 5 – 2 cm H2O. Heart examination revealed normal sound I and II, there was no murmur and gallop. The lung field revealed vesicular sound breath, no rales not wheezing. Abdominal examination revealed flat abdomen, no distention, no tenderness, no hepatomegaly or splenomegaly by palpation. Extremites revealed warm extremities, no edema.

The laboratory examination on admission date revealed Hemoglobin 5.5 g %, leukocyte 3800/ml and platelet 150,000/ml, ureum 13 mg/dl, creatinine = 0.9 mg/dl, sodium = 130 meq/l and potassium = 3.6 meq/l, SGOT = 39 U/l, SGPT = 35 U/l.

The examination also revealed negative HIV test result and there was no fungus in the patient’s blood specimen.

On the 7th day of care, BMP was carried out. The interpretation indicated histoplasma and the diagnosis of Histoplasmatosis was established. Amphotericin B was soon suggested consistent with the protocol, i.e.:

- Day 1, a test dose of 5 mg Amphotericin B was administered
- Day 2, 10 mg Amphotericin B was administered
- Day 3, 15 mg Amphotericin B was administered
- Day 4, 20 mg Amphotericin B was administered
- Day 5, 25 mg Amphotericin B was administered
- And so on.
Notes: Amphoterisin B was injected into 500 cc dextrose 5 %, finished in 6 hours period and before administering, we gave 1 ampul of dexamethasone and 1 tablet of paracetamol.

Until the 7th day of Amphoterisin B administration, the patient still had fever about 38-41°C. Amphoterisin B was still given because of unresponsive histoplasmosis.

On the 12th day of Amphoterisin B administration, the patient and his family refused the continuation of Amphoterisin B treatment and with a refusal note, signed by the patient.

Because the patient should have treatment, then Intrakonazol  (Sporanox) 2 x 200 mg was given.

On the 37th day care, she had repeated abdominal USG before biopsy. Physical examination revealed hepatosplenomegaly. USG result indicated hepatosplenomegaly and enlargement of Para aortic lymph node and around the liver hillus. The patient had immediate liver biopsy.

We also considered TB as the cause of prolonged fever in this patient. Then, Mantoux test was carried out for screening test as well as repeated thoracic X-ray. There was negative result for Mantoux test and normal thoracic X-ray.

On the 42nd day, the pathology anatomy examination result indicated liver tuberculosis along with cheesy-melt appearance.

On the 43rd day, the patient had anti tuberculosis drugs i.e. rifampin 1 x 450 mg, INH 1 x 300 mg, Pyrazinamide 3 x 500 mg, Ethambutol 2 x 250 mg and pyridoxine 3 x 10 mg. On the 43rd day, the fever subsided; the temperature was 37.5°C.

On the 45th day, 3 days after anti tuberculosis treatment, the patient’s sclera was jaundice. SGOT and SGPT were carried out and revealed 182 U/l and 157 U/l respectively.

The Anti tuberculosis drug was still given with the following regimen:
• Ethambutol 2 x 250 mg
• Streptomycin 1 x 750 mg
• Ofloxacin 1 x 400 mg

Rifampin-test was considered but because of cost problem, it wasn’t carried out. Repeated USG result indicated no obstruction signs.

The patient went home with improved condition and the fever subsided. The patient was given INH 1 x 100 mg gradually for 3 days and then the dose was increased to 2 x 100 mg; while other therapies were continued. Rifampin was not given in this patient.

DISCUSSION

When admitted to the hospital, the patient had diagnosis of prolonged fever because she had 2 months fever and various examinations before admission, but the etiology was not known yet. This is consistent with the definition of various literatures.1, 2, 3

Various etiologies of fever in this patient had been explored by laboratory and other medical examination such as negative widal test, negative malaria test, negative HIV test, normal Thorax X-ray and normal abdominal USG.

Because there were no optimal results, bone marrow puncture (BMP) was carried out.

First BMP interpretation revealed CGL impression. Then repeated interpretation was conducted because there was no leukocytosis in peripheral blood, and there was histoplasma, so histoplasmosis was suspected. The patient was given histoplasmosis treatment i.e. using Amphoterisin B.

This is consistent with various literature that the drug of choice for histoplasmosis is Amphoterisin B.6,7 After
given Amphoterisin B appropriate to the protocol for 12 days, the patient still had fever.

Because there was no improvement, repeated thoracic X-ray and Mantoux test were carried out in order to find the possibility of cryptic TB. The result revealed normal X-ray and negative Mantoux test.

The patient had repeated abdominal USG and revealed hepatosplenomegaly and enlargement of Para aortic lymph node. Biopsy was carried out immediately, the histopathology result revealed liver tuberculosis.

The patient was immediately treated with anti tuberculosis drug, i.e.:
- Rifampin 1 x 450 mg,
- INH 1 x 300 mg,
- Pyrazinamide 3 x 500 mg,
- Ethambutol 2 x 250 mg and
- Pyridoxine 3 x 10 mg.

On the 3rd day after anti tuberculosis treatment, the patient had jaundice eyes and she had SGOT/SGPT examination, there was SGOT elevation of 182 U/l and SGPT 157 U/l, it was assumed that the patient had hepatitis drug induced.

Anti tuberculosis was still given with tailored-dose and substitute rifampin with streptomycin. The given regiment’s were streptomycin 1 x 750 mg, Ethambutol 2 x 250 mg, Ofloxacin 1 x 400 mg. INH was temporarily stopped. These have been consistent with the literature, that the drug of choice for tuberculosis hepatitis is anti tuberculosis drugs. Literature also states that Rifampicin may damage the liver.

With the adjusted anti tuberculosis drugs, the patient was getting better, the fever subsided, and the jaundice eyes came back to normal.

CONCLUSION

The adjusted anti tuberculosis drugs improved the patient’s condition, fever subsided, and no jaundice eyes anymore. Of course, this is consistent with liver tuberculosis along with cheesy-melt process.

REFERENCES