The Persistent Approach to Diagnose Infectious Hepatic Cysts in a Patient With Recurrent Fever: A Case Report

Hirotaka Ikeda 1, Ryuichi Ohta 2, Nozomi Nishikura 1, Yoshinori Ryu 1, Chiaki Sano 3

1. Community Care, Umnan City Hospital, Umnan, JPN
2. Community Care, Umnan City Hospital, Umnan, JPN
3. Community Medicine Management, Shimane University Faculty of Medicine, Izumo, JPN

Abstract

Diagnosing infectious hepatic cysts (IHCs) can be challenging. Moreover, patients with IHCs may present with various symptoms. Diagnosis of IHCs can be even more difficult in patients with multiple liver cysts. For appropriate diagnosis, the detection of infectious sections in the liver is essential. However, diagnosing and determining definite treatments for patients with IHCs can be particularly challenging when they have polycystic liver disease. We present a case of a 70-year-old man who visited a rural community hospital with a primary complaint of recurrent fever and pain in the right upper quadrant. Based on his clinical history, physical examination findings, and imaging findings after three admissions, he was diagnosed with IHCs. This case demonstrates the challenges in diagnosing IHCs in patients with multiple hepatic cysts and highlights the necessity of a careful follow-up of clinical histories and findings of definitive imaging tests in the diagnosis of IHCs in patients with recurrent fever. To diagnose IHCs effectively, a comprehensive approach including history taking, physical examination, and diagnostic testing, is essential. IHCs should be considered by physicians when patients present with recurrent fever. To avoid missing IHCs, physicians in outpatient departments should continuously follow up on patients’ IHC-related symptoms such as fever and right upper quadrant pain.

Introduction

Diagnosing infectious hepatic cysts (IHCs) can be challenging, and patients with IHCs may present with various symptoms. The typical symptoms include fever and abdominal pain; however, there could be other symptoms depending on the location of the infection [1]. Previous studies have shown that infection of liver cysts in the central part of the liver can cause vague symptoms, such as fever and fatigue [1,2]. Superficial infectious liver cysts can cause abdominal pain [3]. Furthermore, when patients have multiple liver cysts and infections, identification of the location of infection among the cysts can be challenging [1-3].

The three treatment options for IHCs are antibiotics, transcutaneous interventions, and surgery [4]. Previous studies have shown various durations of antibiotic treatment, ranging from two to eight weeks. As the rate of completion of antibiotic treatment is approximately 50%, many patients also have to undergo percutaneous interventions or surgery [2,4]. For these latter treatment options, the detection of infectious parts in the liver is essential. However, diagnosing and determining the treatment course of IHCs can be challenging in patients with co-existing polycystic liver disease.

We encountered a case where a patient presented with a fever of unknown origin and was finally diagnosed with an infection of polycystic liver cysts based on imaging and bacterial tests. We present this case to demonstrate the challenges of making a diagnosis in cases of IHC.

Case Presentation

A 70-year-old man visited a rural community hospital with a chief complaint of recurrent fever and pain in the right upper quadrant. One year prior, he had presented with fever and right pleural pain at a university hospital where he was diagnosed with pleuritis without any positive bacterial culture. His past medical history included hypertension, dyslipidemia, lacunar infarction, autosomal dominant polycystic kidney disease (ADPKD) with polycystic liver disease, benign prostatic hyperplasia, and bacterial pleuritis; however, the patient was in good health until two months prior to the current presentation. His medications included cilostazol, fexibuxostat, atorvastatin, telmisartan, amlodipine, nifedipine, and tamsulosin.

The patient’s vital signs were as follows: blood temperature, 38.2 °C; blood pressure, 149/77 mmHg; heart rate, 97 beats per minute; respiratory rate, 18 breaths per minute; and SpO2, 93%. Physical examination did not reveal any enlarged cervical lymph nodes. Inspiratory late crackles were heard in the right lower lung.
The abdomen was soft with flat tenderness in the right upper quadrant and indirect fist percussion of the liver without Murphy’s sign. There was no evidence of arthritis in the knees or hands. Laboratory data showed no abnormality in liver function with elevated C-reactive protein levels (Table 1).

| Markers                        | Two months prior | Day of admission | Ranges          |
|--------------------------------|------------------|------------------|-----------------|
| White blood cells              | 14.1 × 10³/μL    | 8.3 × 10³/μL     | 3.5–9.1 × 10³/μL|
| Red blood cells                | 4.11 × 10⁶/μL    | 3.34 × 10⁶/μL    | 3.76–5.50 × 10⁶/μL|
| Platelets                      | 10.0 × 10⁹/μL    | 17.3 × 10⁹/μL    | 13.0–36.9 × 10⁹/μL|
| Total protein                  | 7.7 g/dL         | 6.4 g/dL         | 6.5–8.3 g/dL    |
| Albumin                        | 4.1 g/dL         | 2.7 g/dL         | 3.8–5.3 g/dL    |
| Total bilirubin                | 1.5 mg/dL        | 0.6 mg/dL        | 0.2–1.2 mg/dL   |
| Direct bilirubin               | 0.5 mg/dL        | 0.3 mg/dL        | 0–0.4 mg/dL     |
| Aspartate aminotransferase     | 23 IU/L          | 25 IU/L          | 8–38 IU/L       |
| Alanine aminotransferase       | 21 IU/L          | 26 IU/L          | 4–43 IU/L       |
| Alkaline phosphatase           | 122 U/L          | 256 U/L          | 106–322 U/L     |
| γ-Glutamyl transpeptidase      | 66 IU/L          | 106 IU/L         | <48 IU/L        |
| Blood urea nitrogen            | 17.6 mg/dL       | 34.1 mg/dL       | 8–20 mg/dL      |
| Creatinine                     | 1.26 mg/dL       | 1.61 mg/dL       | 0.40–1.10 mg/dL |
| Serum Na                       | 133 mEq/L        | 132 mEq/L        | 135–150 mEq/L   |
| Serum K                        | 4.1 mEq/L        | 4.1 mEq/L        | 3.5–5.3 mEq/L   |
| Serum Cl                       | 96 mEq/L         | 102 mEq/L        | 98–110 mEq/L    |
| C-reactive protein             | 14.5 mg/dL       | 13.9 mg/dL       | <0.30 mg/dL     |
| IgG4                           | -                | 81 mg/dL         | <135 mg/dL      |
| Urine test                     |                  |                  |                 |
| Leucocyte                      | (-)              | (-)              | (-)             |
| Protein                        | (-)              | (-)              | (-)             |
| Glucose                        | (-)              | (-)              | (-)             |
| Bilirubin                      | (-)              | (-)              | (-)             |
| Ketone                         | (-)              | (-)              | (-)             |
| Blood                          | (-)              | (-)              | (-)             |
| Antinuclear antibody           | -                | <40              | -               |
| Interferon-Gamma Release Assays| -                | (-)              | (-)             |

**TABLE 1: Laboratory data two months prior and on the day of admission**

Na: Sodium; K: Potassium; Cl: Chlorine; IgG4: Immunoglobulin G4

Contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis revealed no evidence of IHCs, any intra-abdominal abscess, or a solid renal or hepatic mass (Figure 1).
He was tentatively diagnosed with an IHC. Blood cultures were obtained, and the patient was treated with cefmetazole. After the treatment was initiated, his fever resolved. Since there was no evidence of bacteremia, a urinary tract infection, or IHCs, his treatment was discontinued on the 10th day and he was discharged. After discharge, the patient was followed up at the outpatient department for recurrent symptoms.

One day before his scheduled follow-up visit, he developed pain in the right upper quadrant and fever, for which he visited our hospital and was admitted. His vital signs were normal except for a fever of 38.6 °C. Physical examination revealed right pleural pain, late crackles on the right chest, and no abdominal tenderness. Laboratory data revealed no abnormalities in liver function (Table 1). Two days after admission, one set of blood cultures grew Klebsiella pneumoniae. We performed enhanced computed tomography (CT) of the liver to ascertain an infectious liver cyst. CT revealed an enhanced area on several cysts in the liver (Figure 2).
The patient was then diagnosed with bacteremia and IHCs; he was treated with cefotiam based on the culture results. The 14-day treatment was effective for this patient. He was then referred to the university hospital for further interventions for infectious liver cysts and the prevention of recurrent infections. The patient was diagnosed with an infection of multiple hepatic cysts at the university hospital. Considering the risk of operation of the cysts and recurrence of infections, he was treated with minocycline.

Discussion

This case demonstrated the need for the persistent approach in diagnosing IHC in patients with multiple hepatic cysts and revealed that careful follow-up of patients’ clinical histories and findings of definitive imaging tests can aid in the diagnosis of IHCs in patients with recurrent fever.

Diagnosing IHCs is challenging due to the difficulty in detecting the location of infections. IHCs are more often found in women than in men, with an estimated female-to-male ratio of 1-1.5:1 [1]. Symptoms include fever, chills (50%), and abdominal pain (41.7%) [4]. ADPKD is prevalent in patients with IHC [2]. In our case, the patient had ADPKD and multiple cysts with abdominal pain; therefore, CT could not detect the location of the infection as several lesions were enhanced in the liver [5,6]. In addition, there are various pathways for the infection of liver cysts. Therefore, a diagnosis of IHCs should be made based on a range of clinical information and considering the pathophysiology of the patient’s condition.

Blood cultures may be effective in the diagnosis of IHCs; however, they lead to successful pathogen isolation in only about half of IHC cases [7]. Furthermore, bacteria are isolated from aspirate cultures in only 52% of IHC cases. Klebsiella pneumoniae was revealed to be the most commonly isolated pathogen in a Japanese study [8]. An infection could be caused by the surrounding organs, hematogenous seeding from the systemic circulation, biliary infection, protein vein pyemia, or trauma [8]. In our case, there were no preceding events of trauma or liver function abnormalities that could lead to vein pyemia or transient infection from the biliary tract without biliary infections. Therefore, a comprehensive approach is required for the diagnosis of IHCs, including continuous history taking, physical examination, blood tests, and additional imaging tests.

Previous studies have shown that enhanced CT and magnetic resonance imaging (MRI) do not have high sensitivity and specificity; therefore, imaging tests alone cannot reliably diagnose IHCs [2,9,10]. In our case, the patient was not diagnosed during the first three admissions. For the diagnosis of causes of fever of unknown origin and recurrent fever, imaging tests can be used; however, their diagnostic accuracy may not be high. In addition, the combined use of CT and MRI may not improve the validity of IHC diagnosis [9,10]. The diagnosis of IHCs should thus be performed clinically, including history taking and physical examination.
A practical approach for the diagnosis of IHC should include follow-up of symptoms, consideration of the vagueness of symptoms in older patients, and imaging tests at appropriate intervals. Older patients tend not to have specific symptoms and do not seek help from others until the symptoms get severe [11,12]. Continuous follow-up without early closure as a diagnostic bias is essential to diagnose IHCs. Besides, older people, especially those living in rural areas, may prefer primary care physicians [13-15]. Therefore, primary care physicians living in rural areas should follow up on the patients’ symptoms (such as fever of unknown origin) persistently not to miss the diagnosis of IHCs.

In this case, we followed up with the patient post-discharge to identify definitive diagnostic clues such as changes in MRI and CT or blood cultures. For the diagnosis of IHCs, follow-up of symptoms is critical because HCs can recur in more than 20% of patients [8]. Without a clinical follow-up, patients may visit other medical institutions because of their changing help-seeking behaviors from rural to urban institutions, thus bypassing primary care [16,17]. Patients with a previous IHC should be followed up to detect symptoms related to the HIC to determine the optimal timing for interventional treatments.

Conclusions

The diagnosis of an IHC can be often missed, and therefore needs persistence to be diagnosed. To diagnose IHC effectively, a comprehensive approach, including history taking, physical examination, and diagnostic tests, is essential. IHCs should be considered by physicians when patients present with recurrent fever. To avoid missing an IHC, primary care physicians should carefully follow up various symptoms in patients presenting in outpatient departments, while respecting their help-seeking behaviors.

Additional Information

Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**

1. Morii K, Yamamoto T, Nakamura S, Okushin H: Infectious hepatic cyst: an understimated complication. Intern Med. 2018, 57:2123-9. 10.2169/internalmedicine.6511-17
2. Lantinga MA, Dreinh JP, Gevers TJ: Diagnostic criteria in renal and hepatic cyst infection. Nephrol Dial Transplant. 2015, 30:744-51. 10.1093/ndt/gfu227
3. Mori E, Akai Y, Matsumoto T, et al.: Hepatic cyst infection in a healthy older male. BMJ Case Rep, 2012, 2012:10.1136/bcr.04.2011.4156
4. Lantinga MA, Geuwend A, Gevers TJ, Dreinh JP: Systematic review: the management of hepatic cyst infection. Aliment Pharmacol Ther. 2015, 41:255-61. 10.1111/apt.13047
5. Sallee M, Rafat C, Zahar JR, Paulnier B, Grünfeld JP, Knebelmann B, Falbhour F: Cyst infections in patients with autosomal dominant polycystic kidney disease. Clin J Am Soc Nephrol. 2009, 4:1185-9. 10.2215/CJN.01870509
6. Alam A, Perrone RD: Managing cyst infections in ADPKD: an old problem looking for new answers . Clin J Am Soc Nephrol. 2009, 4:1154-5. 10.2215/CJN.03270509
7. Jouret F, Lhomefl R, Devuyt O, Annet L, Pirson Y, Hassoun Z, Kanaan N: Diagnosis of cyst infection in patients with autosomal dominant polycystic kidney disease: attributes and limitations of the current modalities. Nephrol Dial Transplant. 2012, 27:3746-51. 10.1093/ndt/gjf6552
8. Miyazato M, Tomiyama M, Natomi H, et al.: A study of 23 cases of infected liver cysts treated at our hospital (Article in Japanese). Kanzo. 2019, 60:117-26.
9. Lantinga MA, Gevers TJ, Dreinh JP: Evaluation of hepatic cystic lesions. World J Gastroenterol. 2013, 19:3545-54. 10.3748/wg.v19.125.3545
10. Mortelé KJ, Segatto E, Ros PR: The infected liver: radiologic-pathologic correlation. Radiographics. 2004, 24:957-55. 10.1148/rv.24045717
11. Ohta R, Ryu Y, Kitayuguchi J, Gomi T, Katsume T: Challenges and solutions in the continuity of home care for rural older people: a thematic analysis. Home Health Care Serv Q. 2020, 39:126-39. 10.1080/01621424.2020.1739185
12. Ohta R, Ryu Y, Kitayuguchi J, Sano C, Könings KD: Educational intervention to improve citizen’s healthcare participation perception in rural Japanese communities: a pilot study. Int J Environ Res Public Health. 2021, 18:10.3390/ijerph181041762
13. Ohta R, Sato M, Kitayuguchi J, Maeno T, Sano C: Potential help-seeking behaviors associated with better self-rated health among rural older patients: a cross-sectional study. Int J Environ Res Public Health. 2021, 18:10.3390/ijerph18179116
14. Ohta R, Sato M, Ryu Y, Kitayuguchi J, Maeno T, Sano C: What resources do elderly people choose for managing their symptoms? Clarification of rural older people’s choices of help-seeking behaviors in Japan. BMC Health Serv Res. 2021, 21:640. 10.1186/s12913-021-06684-x
15. Ohta R, Sato M, Kitayuguchi J, Maeno T, Sano C: The association between the self-management of mild
symptoms and quality of life of elderly populations in rural communities: a cross-sectional study. Int J Environ Res Public Health. 2021, 18:10.3390/ijerph18168857

16. Ohta R, Ueno A, Kitayuguchi J, Moriwaki Y, Otani J, Sano C: Comprehensive care through family medicine: improving the sustainability of aging societies. Geriatrics (Basel). 2021, 6:10.3390/geriatrics6020059

17. Hopman P, de Bruin SR, Forjaz MJ, et al.: Effectiveness of comprehensive care programs for patients with multiple chronic conditions or frailty: a systematic literature review. Health Policy. 2016, 120:818-32. 10.1016/j.healthpol.2016.04.002